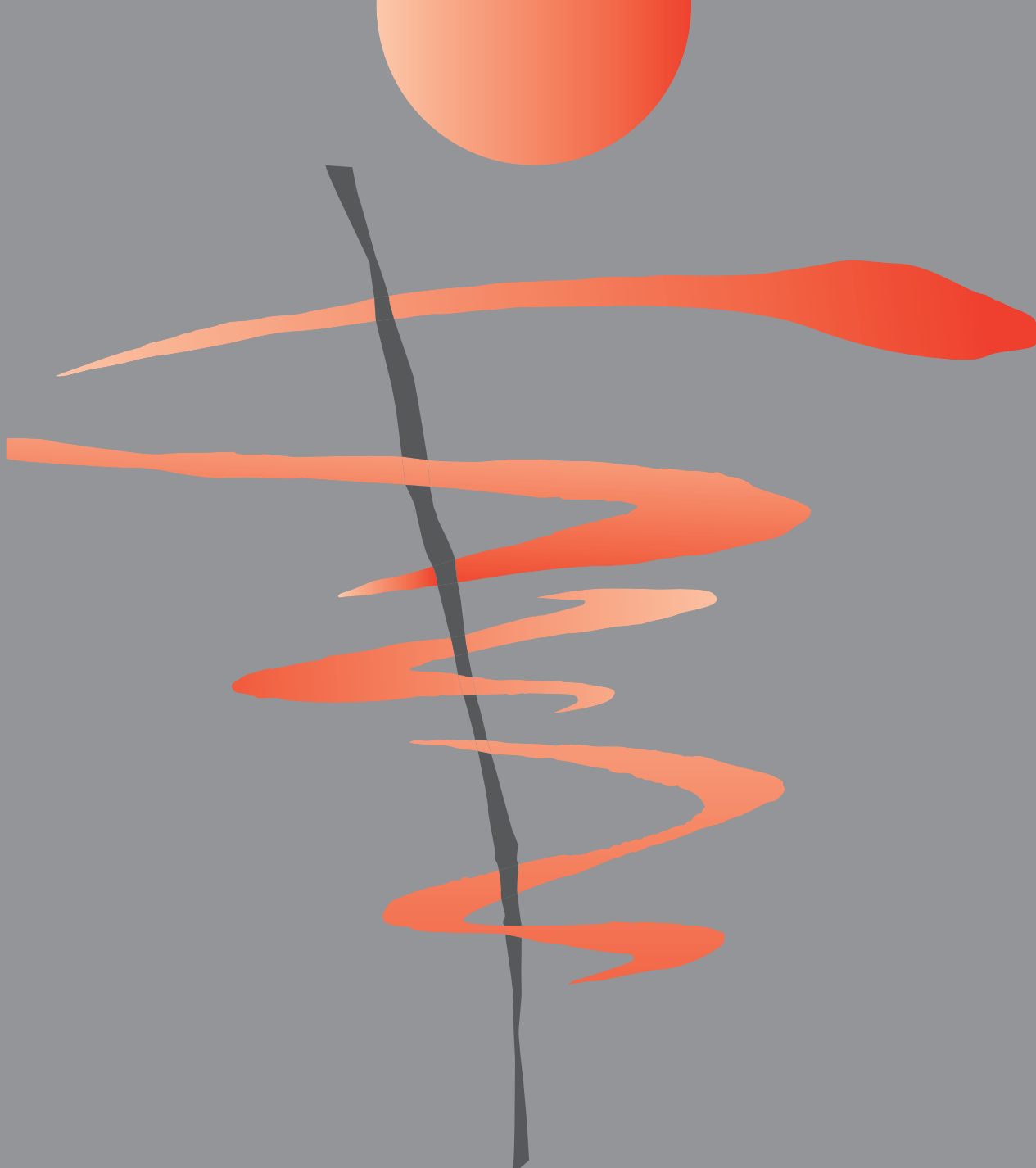




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- Letter to editors
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EDITORIAL

Pioneering Open Science in Bangladesh: A call to action for Data Article adoption

M Mostafa Zaman¹   | Tanvir C Turin²   | Md Shahinul Alam³  



¹Department of Public Health and Informatics, Bangabandhu Sheikh Mujib Medical University (currently, Bangladesh Medical University), Dhaka, Bangladesh

²Department of Family Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

³Department of Hepatology, Bangabandhu Sheikh Mujib Medical University (currently, Bangladesh Medical University), Dhaka, Bangladesh

Correspondence

M Mostafa Zaman
zamanmm@bsmmu.edu.bd

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Open Science principles demand that research data be accessible and reusable [1]. This commitment is acutely very relevant for Bangladesh, where vast health datasets remain siloed despite their potential to accelerate scientific progress. As one of the world's most densely populated nations (~170 million) [2], Bangladesh's healthcare infrastructure includes large hospitals managing thousands of inpatient admissions and vast outpatient volumes on a daily basis. These facilities generate a wealth of patient data both in the form of health administrative data (e.g., diagnoses, vital statistics, billing records) and health care records (e.g., clinical notes, lab results). Though primarily generated for operational purposes or clinical care—not research—these datasets exhibit significant potential for secondary use in health research [3]. Recognised globally as secondary data, they enable research in epidemiology, surveillance, healthcare utilisation patterns, health economics, health system performance or policy research [3]. Data Articles [4] offer a powerful mechanism to align these secondary data with Open Science goals [1] and accelerate the growth of scientific research in Bangladesh. Data Article, also known as a Data Note, Data Paper, or Database Article, is a type of scientific publication focused on the detailed description of a dataset, rather than presenting new research findings, theories, or interpretations [4]. The primary aim is to make datasets more visible, accessible, and reusable for the wider research community. For

Bangladesh's rapidly evolving health research landscape, this represents a strategic opportunity. Systematically publishing existing data as Data Articles will democratise access to local evidence, incentivise data quality, and position Bangladeshi institutions as contributors to global science.

Publishing Data Articles is still relatively underutilised, despite the presence of more than 200 dedicated journals [5]. A few journals began this journey long ago. These articles are peer-reviewed publications that exclusively describe datasets, detailing their structure, collection methodologies, and reuse potential without hypothesis testing (such as using statistical tests typically employed in conventional analytical studies) or novel interpretation. Crucially, they transform raw data into FAIR-aligned [6] scholarly assets by providing comprehensive contextual metadata that exceeds standalone repository documentation. This is especially important for the secondary data due to the concern exist regarding their quality, completeness, preservation, sensitivity/specificity, and reusability.

Datasets published through Data Articles are increasingly being recognised as scholarly products [7]. These are citable publications conferring academic credits to authors. While distinct from analytical research papers, these peer-reviewed papers provide essential contextual metadata that

Key messages

Big hospital datasets in Bangladesh remain siloed despite their potential to accelerate scientific progress. Though primarily generated for clinical care—not research—these datasets exhibit significant potential for secondary use. Data Articles offer a powerful mechanism to align these data to accelerate the growth of scientific evidence. A Data Article focuses on describing a dataset and key findings rather than testing hypothesis or interpretations. It makes datasets more visible, accessible and reusable. Pioneering this movement in Bangladesh, the Bangabandhu Sheikh Mujib Medical University Journal launches a dedicated Data Article category, creating a pathway for sharing routine hospital data of scientific importance.

exceeds standalone repository records, enhancing reproducibility and reuse potential. To ensure ethical compliance and FAIR alignment, datasets must be rigorously anonymised, deposited in certified repositories, and shared under open licenses.

Pioneering this movement in Bangladesh, the Bangabandhu Sheikh Mujib Medical University Journal (BSMMUJ) will launch a dedicated Data Article category in July 2025. This initiative creates a formal pathway for sharing routine healthcare data of scientific importance, following the FAIR (Findable, Accessible, Interoperable, and Reusable) principles [6].

The format of Data Articles differs from that of other conventional research articles. As Bangladesh's inaugural initiative, we outline the key features of Data Article for implementation by BSMMUJ:

- A. The anonymised dataset and metadata must be deposited in a certified repository and made available for reuse under a standard open licence (*e.g.*, CC BY 4.0) and DOI [4]. Manuscripts must include a permanent repository link. Trusted data repositories (such as Figshare, Mendeley Data, Zenodo, Harvard Dataverse) need to be used. In the long run, BSMMUJ shall create its own repository.
- B. A Data Article should include the following components:
 1. The Introduction should provide the background and introduce the dataset. It should justify the publication of such a dataset with a confocal objective.
 2. The Methods should describe the acquisition of data, processing/cleaning procedures, its completeness, accuracy, limitations, and accessibility. Any transformation of data (*e.g.*, the creation of new or dummy variables) should be described. Any related articles already published from the dataset should be mentioned.
 3. The Findings should be limited to descriptive summary only (*e.g.*, frequencies, distributions) using ≤ 5 tables/figures. Inferential statistics should be avoided.
 4. The Discussion should focus on the value of the data, comparing and contrasting similar datasets. However, interpretation and conclusion should be avoided. Data limitations and potential areas for improvement should be identified. Finally, comments may be made regarding the utility of the dataset without drawing any conclusions.

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Conflict of interest

We do not have any conflict of interest

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We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

References

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RESEARCH ARTICLE

Short-term outcome of physiotherapy and surgical treatment of obstetrical brachial plexus palsy



Krishna Priya Das¹ | Rumpa Mani Chowdhury² | Sk. Murad Ahmed¹ | Md. Moniruzaman¹ |
Mohammad Shahidullah²

¹Department of Orthopaedics, Bangabandhu Sheikh Mujib Medical University (currently Bangladesh Medical University), Dhaka, Bangladesh

²Department of Neonatology, Bangabandhu Sheikh Mujib Medical University (currently Bangladesh Medical University), Dhaka, Bangladesh

Abstract

Background: Birth injury to the brachial plexus is referred to as obstetric brachial plexus palsy (OBPP). This study aimed to evaluate the clinical presentation and treatment outcomes of OBPP.

Methods: This study was conducted in the Orthopaedic and Neonatology Department at Bangabandhu Sheikh Mujib Medical University. Infants with OBPP who presented within six months were included and initially treated with physiotherapy for up to six months. There were incomplete (neuropraxia and axonotmesis) and complete (neurotmesis) injuries. If biceps power was recovered of birth ($\geq M3$), therapy was continued for up to 18 months. If there was no significant improvement ($\leq M2$), surgery was performed. The final outcome was assessed after 18 months using the Mallet score, the Raimondi score, and the Medical Research Council muscle grading scale.

Results: Out of 200 OBPP cases, 90% were enrolled through the outpatient department. One-fourth were identified during the neonatal period. The majority (96%) were born via vaginal delivery, with shoulder dystocia occurring in 68% of cases. Instrumental deliveries resulted in more severe injuries. Females and right-sided involvement were predominant. The overall satisfactory result with physiotherapy was observed in 65%, cases, whereas after surgery, it improved to 80%. However, when considering the upper trunk only, it approached 85% with physiotherapy and 98% after surgery (Mallet score > 15 , Medical Research Council grade ≥ 4 , Raimondi score ≥ 2). For lower trunk and panplexus cases, satisfactory outcomes following physiotherapy and surgery were 41%.

Conclusion: Treatment initiated within six months have ensured nearly full recovery of most upper trunk and incomplete OBPP cases, but outcomes of severely affected lower trunk and panpalsy cases was poor.

Key messages

Obstetric brachial plexus injury in babies leads to brachial palsy, known as obstetric brachial plexus palsy. Early detection and intervention are crucial for preventing deformity and disability. The interventions include physiotherapy, nerve repair or reconstruction, and muscle or tendon transfer as appropriate. We achieved satisfactory outcomes in 80% of cases with combined physiotherapy and surgery. Upper trunk and incomplete palsies showed better results than lower trunk and panpalsies.

Correspondence

Krishna Priya Das
kpdas74@bsmmu.edu.bd

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M Mostafa Zaman
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Taufiq Morshed
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Introduction

The network of nerves that transmits signals from the spinal cord (C5-T1) to the shoulder, arm, elbow, forearm, wrist, and hand is known as the brachial plexus. Obstetrical brachial plexus palsy (OBPP) is due to an injury to the brachial plexus in newborns, believed to result from mechanical forces during labour and delivery [1, 2, 3, 4]. Globally, the incidence rate ranges from 0.5 to 4 cases per 1,000 newborns [5, 6]. Multiple risk factors, notably fetal macrosomia, breech presentation, maternal diabetes, prolapsed hand, cephalic presentation with shoulder dystocia, cephalopelvic disproportion, primipara, and prolonged labour, have been identified [2, 3, 6].

The upper trunk palsies (C5,6), represent the most common anatomical pattern of OBPP, followed by extended upper trunk (C5,6,7) palsies. Isolated lower trunk palsies are often reported, while pan palsies (C5-T1) are less so common [2, 3, 4]. Postganglionic injuries (rupture) are more prevalent than preganglionic root avulsion and are classified as neurapraxia, axonotmesis, or neurotmesis, according to Seddon's classification [2, 3, 7].

In Bangladesh, 62% of births still occur at home, and over 56% are assisted by traditional birth attendants. The incidence and prevalence of birth brachial plexus injuries in Bangladesh is not available [8]. Studies reported spontaneous recovery from neuropraxia within the first two months of life, but the percentage varies from as high as 92% to as low as 30% [9]. It is now widely recognised that the rate of recovery is lower than previously believed and that more children with neurotmesis and root avulsion injuries need early intervention and monitoring to improve their prognosis [2, 9, 10, 11]. Only 66% of affected children made a full recovery, and 10% to 15% suffered significant long-term impairment [12, 13].

There is limited research on OBPP in Bangladesh. Our primary objective was to ascertain the clinical presentation and the likelihood of spontaneous recovery through physiotherapy. Our secondary objectives were to examine the results of intra-plexus (primary) surgery, those who were not improved within six months of age with physiotherapy and also found out the improvement of deformity correction by secondary surgery.

Methods

This operational research was conducted in the Department of Orthopaedics at Bangabandhu Sheikh Mujib Medical University (BSMMU) from January 2022 to June 2024. Patients presenting with upper limb weakness due to OBPP irrespective of stage and clinical form, whether isolated or associated with other conditions such as fractures or glenohumeral dislocation, were included. We excluded lethal congenital anomalies and any other neurological or neuromuscular pathologies. A total of 200 cases of OBPP enrolled within six months of birth. The patients were collected from the neonatology (inpatients) and the hand clinic (referrals from other centres or hospitals) at the orthopaedic outpatient department in BSMMU.

Following patient enrolment, intervention (rehabilitation and surgery) and follow-ups were provided in the orthopaedic department, under the hand and reconstructive surgery division. Diagnosis was primarily clinical. The rehabilitation protocol commenced two weeks after birth and continued until six months of age. Any suspected fractures were confirmed by X-ray, after which immobilisation was done for up to three weeks. Electrodiagnosis and magnetic resonance imaging of the brachial plexus were performed exclusively in severe cases of panpalsy or when significant improvement had not been observed within three months of assessment age [1, 3, 4].

Physiotherapy

The physician first demonstrated physiotherapy to the parents, who were advised to perform the exercises regularly for a minimum of six months. The first group consists of passive, gentle, repeated, and systematic shoulder, elbow, wrist, and fingers mobilisation, irrespective of age and type of OBPP. Sessions lasting 10 to 15 minutes, conducted at least eight times per day, were encouraged. The second group of exercises, aimed at infants aged at least three months, includes engaging interactive activities with colourful toys that produced sounds and light balloons, designed to stimulate recovery through bimanual gripping. Furthermore, shoulder external rotation (airplane) splinting played an important role for those with developed shoulder adduction and internal rotation deformities. A wrist splint was recommended for those who exhibited wrist drop along with thumb adduction deformity. Those who showed satisfactory improvement in biceps function, as measured by the Medical Research Council (MRC) scale $\geq$ M3 within six months following physiotherapy, continued with the exercise programme for up to 18 months. If satisfactory improvement in biceps function was not achieved, appropriate investigations were undertaken, and a plan for surgical treatment was formulated [2, 3, 6].

Investigations:

Electrodiagnosis, which includes nerve conduction studies and electromyography, can provide valuable clinical information, although interpreting motor unit action potentials may prove challenging. Electrodiagnosis studies can address the following questions: What location and specific segment were involved? How extensive or severe was the condition (axonotmesis or neurotmesis), and was it preganglionic or postganglionic? Magnetic resonance imaging highly sensitive in detecting lesions of the peripheral nerves was done in severe cases only. MRN was localised the site and type of lesion either rapture of evolution of the roots. [4, 13]

Surgical treatment

Intra-plexus (primary) microsurgical procedures (Figure 1), such as neurolysis, excision of neuroma followed by nerve repair, nerve grafting, or neurotization (nerve transfer), were performed solely on those who had not recovered to a satisfactory level after 6 months of physiotherapy. Those who achieved satisfactory improvement in antigravity biceps power ($\geq$ M3) within 6 months but had some residual



Figure 1 Self-rehabilitation protocol executed by the mother

a) abduction, b) external rotation, c) elbow flexion, d) elbow extension with supination, e) wrist and finger extension, f) wrist and finger flexion. (Permission was taken from parents for using these pictures in publication)

deformities continued with physiotherapy and were planned for deformity correction (secondary surgery) through soft tissue release with muscle transfer procedures after 18 months of age (Figure 2). Michelow *et al.* assigned the indication for primary microsurgical procedures if a score of less than 3.5 out

of the highest possible score of 10 was recorded. A score between 0 and 2, where 0 denotes no function, 1 denotes partial function, and 2 denotes normal function, of the five motor functions (elbow flexion, wrist, finger, thumb extensions, and shoulder abduction) is assessed after three months of age. If the score exceeds 3.5, follow-up is recommended for up to 18 months; if any functional deficiencies are noted, secondary surgical procedures are advised to correct them. Conversely, a Mallet score of less than 13 out of 25 (five functions, each rated from one to five points, including shoulder abduction, external rotation, hand to mouth, hand to neck, and hand on spine) at three months of age also indicates the need for upper plexus surgery palsy [2,3,7,14].

Follow-up

The follow-up schedule consisted of monthly visits for the first six months, followed by bi-monthly visits for a further six months, and finally, quarterly visits until 30 months. The minimum required follow-up was 18 months; however, a follow-up period of at least 36 months is necessary to properly evaluate complete panpalsy cases. Functional improvement was evaluated using different scales. Typically, upper plexus palsy cases were assessed by the Mallet score, which evaluates shoulder and elbow function. The components include global external rotation, abduction, hand-to-mouth, hand-to-neck, and hand-to-spine movements. The highest possible score is 25, with scores ranging from 14 to 25 considered satisfactory and scores from 0 to 13 deemed unsatisfactory. The Raimondi score is used to assess hand and wrist function, where scores of 0-1 are considered unsatisfactory, scores of 2-3 are viewed as satisfactory, and overall muscle strength was assessed using the MRC scale, where $M \geq 3$ was considered satisfactory and $M \leq 2$ is deemed unsatisfactory [2,3,12,13].

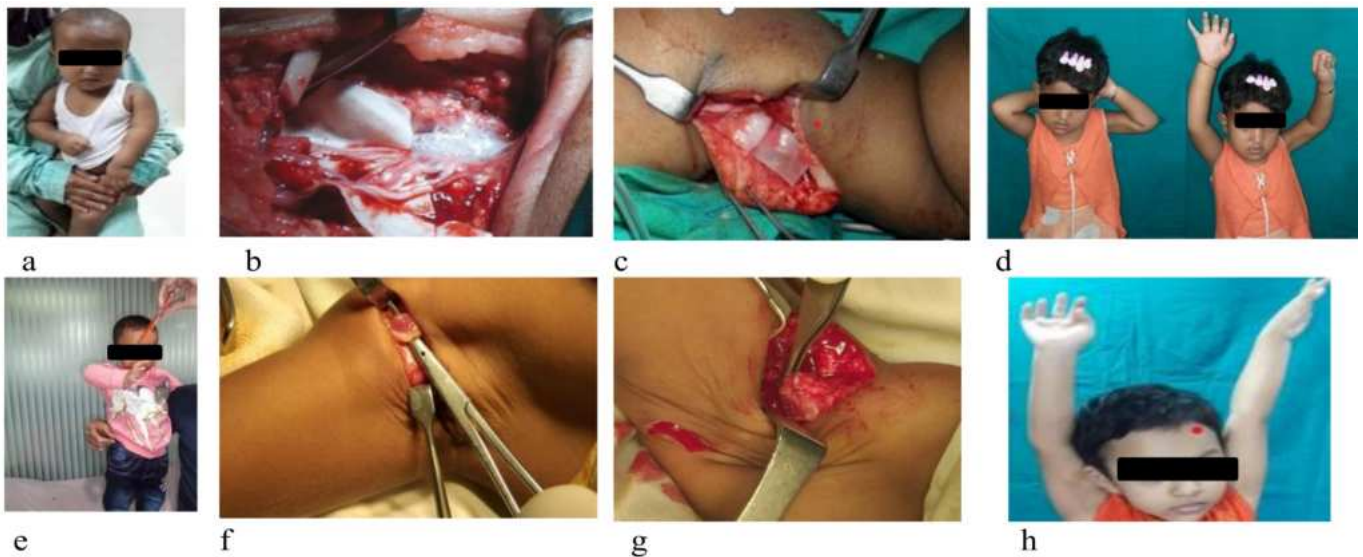


Figure 2 Primary and secondary surgeries

Upper panel: Primary surgery of a 6 months old girl, a) extended left-upper obstetrical brachial plexus (C5,6,7), b) cables nerve grafting, c) ulnar nerve fascicle transfer to biceps br. of MCN, d) excellent recovery of 24 months follow up abduction and external rotation of shoulder.

Lower panel: Secondary surgery of a 18 months old girl, e) adduction and internal rotation deformity of shoulder, f) release of pectoralis major, g) release of LD and transfer to teres minor, h) excellent recovery of 6 months follow up.

Table 1 Background status of the enrolled cases (n=200)

Background characteristics	Number (%)
Age at presentation (weeks) ^a	14.3 (9.2)
Gestational age at birth (weeks) ^a	37.5 (2.8)
Birth weight (grams) ^a	2,975.0 (825.0)
Sex	
Male	82 (41)
Female	118 (59)
Affected side	
Right	140 (70)
Left	54 (27)
Bilateral	6 (3)
Delivery type	
Normal vaginal delivery	152 (76)
Instrumental delivery	40 (20)
Cesarean section	8 (4)
Place of delivery	
Home delivery by traditional birth attendant	30 (15)
Hospital delivery by midwife	120 (60)
Hospital delivery by doctor	50 (25)
Prolonged labor	136 (68)
Presentation	
Cephalic	144 (72)
Breech	40 (20)
Transverse	16 (8)
Shoulder dystocia	136 (68)
Maternal diabetes	40 (20)
Maternal age (years) ^a	27.5 (6.8)
Parity of mother	
Primipara	156 (78)
Multipara	156 (78)

^aMean (standard deviation), all others are n (%)**Ethical consideration**

The therapeutic approaches employed are grounded in the standard practices of the division under the lead author (KPD). However, the procedure, risks, and benefits were explained to the patient's parents (or legal guardians), and written informed consent was obtained. Permission to disclose the patients' photo for research and publication purposes was secured. They were assured that all data would remain confidential and not be disclosed except for the education of students of the orthopaedics courses. All participants were guaranteed the full right to decline the surgical interventions.

Statistical analysis

Data analysis was performed using SPSS version 26.0. The categorical variables (sex, parity of mother, delivery type, presentation, etc.) are presented as numbers (percentages), while numerical variables (age at presentation, birth weight, etc.) were expressed as mean (standard deviation).

Results

Out of 200 enrolled cases of OBPP, 90% were referred from other centres and enrolled through the hand clinic, while the remaining 10% of cases were enrolled from the neonatology department. Only 25% of cases were identified during the neonatal period; the remaining 150 patients were enrolled within 6 months of birth injury. The mean age of presentation was 14.3 (standard deviation, 9.2) weeks, and the mean gestational age at delivery was 37.5 weeks. The mean birth weight was 2975 grams (**Table 1**). Twenty percent of mothers had diabetes, and their mean age was 27.6 years, with 78% being primipara. Normal vaginal delivery accounted for 76% of cases, instrumental delivery for 20%, while caesarean section delivery constituted only 4% of cases. Traditional birth attendants and midwives conducted 75% of the deliveries, whereas only 25% were carried out by doctors. Prolonged second stage of labour (68%) was the most common risk factor. Transverse presentation with shoulder dystocia (68%) was the most common presentation.

According to Narakas grading, 36% of cases were grade 1, presenting with C5,6 roots or upper trunk injury. Thirty two percent of cases were classified as grade 2 injury, with extended upper trunk involvement (C5,6,7). However, 25% of cases were identified as grade 3 injuries, which indicate pan-palsy or involvement of all five roots or trunk, while the remaining 7% were classified as grade 4, pan-palsy with Horner's syndrome. There was no substantial improvement in 40 cases (20%) (**Table 2**). Only in extensive injury cases where substantial improvement was not observed within six months were advised to undergo electrodiagnosis and magnetic resonance imaging studies.

Out of 40 cases with magnetic resonance imaging findings, neuroma in continuity was present in 20%, root ruptures were found in 25%, on the other hand, ruptures with avulsion were seen in 35%, and only root avulsion occurred in 20% of cases.

Overall, satisfactory rehabilitation improvement occurred in 65% of cases, mostly among those with Narakas type I and II palsy, with biceps motor recovery ($M \geq 3$) achieved within 3 months and wrist motor recovery at $M \leq 2$ level within 2 months.

Table 2 Evaluation of the rates of spontaneous (conservative treatment) recovery according to Narakas classification^b

Narakas classification	Total 200 (100%)	Grade 1 72 (36%)	Grade 2 64 (32%)	Grade 3 50 (25%)	Grade 4 14 (7%)
Complete recovery ^a	107 (54)	60 (83)	40 (63)	7 (14)	-
Near complete functional recovery but partial deformity ^a	22 (11)	5 (7)	10 (16)	6 (12)	1 (7)
Partial recovery with gross functional defect and deformity	31 (16)	7 (10)	13 (20)	10 (20)	1 (7)
No significant improvement	40 (20)	-	1 (1.5)	27 (54)	12 (86)

^aSatisfactory recovery^bGrade 1, C5, 6, 7 improvement; Grade 2, C5, 6, 7 improvement; Grade 3, panpalsy C5, 6, 7, 8, 9, Grade 4, panpalsy with Horner's syndrome.

Table 3 Satisfactory outcome of primary and secondary surgeries of obstetric brachial plexus palsies

Surgeries	Number (%)	Satisfactory outcomes n (%)
Primary surgery (n=24)		
Upper plexus	6 (25)	5 (83)
Pan-palsy	18 (75)	6 (33)
All	24 (100)	11 (46)
Secondary Surgery (n=26)		
Shoulder deformity	15 (58)	13 (87)
Wrist and forearm deformity	11 (42)	6 (54)
All	26 (100)	19 (73)
Primary and secondary surgery	50 (100)	30 (60)

Mallet score 14 to 25 or Raimondi score 2-3 or Medical Research grading >3 to 5.

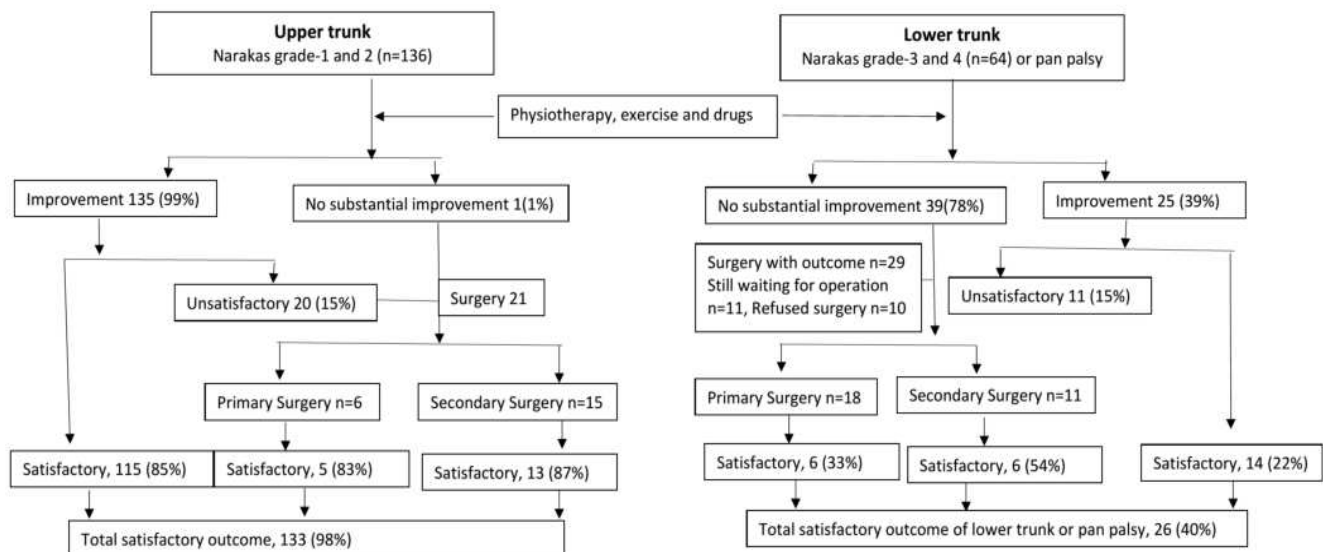
Conversely, only 22% of functional improvement was observed in Narakas type III and IV injuries. Furthermore, only 10% and 20% of patients with Narakas grade 1 and grade 2 injuries demonstrated partial improvement but presented with residual shoulder adduction and internal rotation deformities, while the partial improvement rates were 20% in grade 3 and 7% in grade 4 injuries. No significant improvement was noted in 20% of cases; among these, 2.5% were in grade 2, 67.5% in grade 3, and 30% in grade 4 injuries, with no cases in grade 1 injuries. These groups exhibited upper limb (shoulder, elbow, and hand) deformities, indicating the need for early surgical intervention.

After performing the primary intra-plexus surgery (neurolysis, nerve repair, grafting, and nerve transfer), cases of upper palsy and incompletely injured individuals showed a better outcome (satisfactory results at 83%) compared to those with lower palsy or complete palsy cases (satisfactory results at only 33%) (Table 3). In secondary surgeries (Figure 3), the satisfactory result was 87% for shoulder deformity correction and 54% for wrist and forearm deformity correction. Overall, (98%) satisfactory outcomes were achieved in upper trunk palsies compared to (41%) in the lower trunk palsies.

Discussion

Two-thirds of OBPP cases showed satisfactory improvement with physiotherapy alone, and after surgery, the satisfactory improvement rate was 80%. This indicates a Mallet score for shoulder function greater than 13 out of 25, a Raimondi score of 2-3 for hand function, and an MRC grading of muscle power greater than 3 out of 5. The satisfactory improvement was much higher (98%) in the upper trunk than the lower trunk (41%), with a follow-up of at least 18 months.

The reported rates of satisfactory recovery varied from 68-95%. Narakas grade 1 (upper trunk palsy) patients had a significantly better prognosis of 90% with conservative treatment, consistent with other series. In contrast, the satisfactory recovery rates for Narakas grade 2 (extended upper trunk palsy), grade 3 (pan-palsy/lower trunk palsy), and grade 4 (pan-palsy with Horner's syndrome) were 79%, 26%, and 7% of patients, respectively, in this series, leading to an overall rate of recovery were 50% in these three groups. This is relatively lower than the spontaneous recovery rates reported in other studies, likely because BSMMU is the only tertiary care referral centre treating all types of OBPP cases, with 90% of respondents referred from other centres. Additionally, the severe forms of injuries (grades 2, 3 and 4) comprised 64% of this study subjects, compared to 20%-30% in other Western studies, which may have influenced the spontaneous recovery rate. The mean age of presentation was 14.3 weeks, which is considered too late for early management and negatively impacted outcomes. Management of OBPP should commence within 6 weeks, and passive exercises for all joints of the affected upper limb should be initiated to prevent contracture and deformity formation, enabling the regenerated nerve to grow along its previous pathway and establish a healthy motor end plate for functioning muscle. However, only 30% of cases achieved this favourable condition.

**Figure 3** Flowchart of upper and lower trunk treatment outcomes

Exploration (surgery) between the 3rd and 6th months is advised for an infant exhibiting complete involvement with Horner's syndrome [3, 15, 16, 17]. However, cases were performed between 5 and 15 months (mean 8.4 months), somewhat longer than in reputed centres [3, 12]. Even in milder forms of injury, such as Narakas type I, if biceps power does not recover to M3 level within 3 months, some degree of residual deformity, including shoulder adduction and internal rotation, results; the more extensive the lesion, the greater the severity of the deformities produced, which require correction through secondary surgery for functional improvement. Secondary surgical interventions are recommended for children older than 18 months who have shoulder abduction and external rotation limitations, causing difficulties in daily activities [3, 6, 18]. Satisfactory outcomes from primary intra-plexus surgery were better 83% in incomplete and upper plexus palsy cases, which is significant and comparable to other studies [2, 13, 14]; however, satisfactory results in pan-palsy cases were only 33%, and overall satisfactory outcomes from primary surgery were 46%, which is not statistically significant, possibly due to short follow-up and severe injury patterns, aligning with findings from other studies [3, 15]. The satisfactory results of secondary surgery for shoulder deformity correction were 85%, while wrist and hand deformity corrections achieved 54%, both of which are statistically significant. However, in severe form of injury cases, parents were not interested to do the surgery in 16% of cases due to uncertainty of results.

Most respondents were classified as infants with a birth weight exceeding 3000 g. However, the mean weight in our study children was 2975 g, which is lower than the average birth weight reported in the literature for OBPP, yet higher than the average birth weight of 2565 g in Bangladesh. It has been reported that the risk of OBPP significantly increases with vaginal delivery in infants with a birth weight above 4000 g. Shoulder dystocia and high birth weight are two risk factors strongly associated with birth injury. Furthermore, it was observed that delivering infants with higher birth weights via caesarean section reduced the frequency of OBPP. Females are affected more than males, with right-sided involvement being more prevalent than left-sided, while bilateral involvement is rare. The number of patients born at home or in primary healthcare centres, regardless of whether assisted by a midwife or not, exhibited a high incidence of OBPP, with three-quarters of our patients being delivered at home or in primary healthcare centres by traditional birth attendants. Conversely, the frequency was significantly lower in better obstetric clinics when trained professionals or doctors performed births. Panpalsy and avulsion injury were also more prevalent in the lower roots, particularly associated with transverse lie or breech presentation. Assisted labour, such as the use of forceps and ventouse, not only heightened the risk but also led to permanent injury or panpalsy, with limited chances of spontaneous recovery [2, 3]. One-fifth of our patients had a history of assisted delivery; however, two-thirds of them presented with a severe pattern of injuries, a finding that aligns with other studies [3, 4].

The management, surgical or non-surgical, was done by a single team, for the first time in Bangladesh. One-fourth cases were treated within 4 weeks of age, and nine in ten cases were referred by other centres. The referred cases had inadequate background data. Physiotherapy initially was done by physician and followed by the patients' parents. There was mix of skills to get uniform results.

Finally, early detection, rehabilitation and appropriate surgical treatment is essential for better prognosis and can be ensured near normal function for most of the patients. Excellent recovery was ensured in incomplete and upper plexus palsy cases. Early surgery, even in severe (pan-palsy) cases can prevent complications and improved the quality of life but not ensure for recovery.

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Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data and drafting the work: KPD, RMC. *Drafting the work or reviewing it critically for important intellectual content:* KPD, RMC, SKM, MM, MS. *Final approval of the version to be published:* KPD, RMC, SKM, MM, MS. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* KPD, RMC.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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RESEARCH ARTICLE

Admission glycemic gap and other glycemic indices in assessing the need for mechanical ventilation among neurocritical patients with diabetes mellitus



Manas Kanti Mazumder¹ | Kazi Tuba-E Mozaffia² | Mostak Ahmed³ |
Mohammad Abdul Hannan¹ | AKM Habibullah¹ | Montosh Kumar Mondol¹

¹Department of Anesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (currently, Bangladesh Medical University), Dhaka, Bangladesh

²Department of Anesthesia and Intensive Care Unit, National Institute of Traumatology and Orthopaedic Rehabilitation, Dhaka, Bangladesh

³National Institute of Burn and Plastic Surgery, Dhaka, Bangladesh

Abstract

Background: We explored the value of admission glycemic gap (AGG) and other glycemic indices in determining the need for mechanical ventilation (MV) among neurocritical patients with diabetes mellitus.

Methods: We purposively included 60 adult neurocritical patients with diabetes mellitus and prospectively studied them for 30 days, or until discharge or death. These patients stayed in the intensive care unit for at least 24 hours and did not require MV within the first twelve hours of admission. The glycemic indices included admission blood glucose level, A1c (HbA1c) level, A1c-derived admission glucose, A1c level, and AGG. The need for initiation of MV was determined according to standard institutional guidelines.

Results: Among the 60 patients enrolled, 39 (65%) required MV. The need for MV was associated with female gender, ischemic stroke, history of insulin use, higher serum creatinine level, lower mean arterial pressure, higher AGG, admission blood glucose level, A1c, and A1c-derived admission glucose. A per unit rise of AGG (odds ratio (OR) 2.1; 95% confidence interval (CI) 1.4–3.1), and A1c (OR 2.6; 95% CI 1.2–5.4) had significant odds for the need for MV. AGG showed an optimal cut off value of 3.2 mmol/L, with a 79% and 81% sensitivity and specificity, respectively. The area under the curve was 0.79 (95% CI 0.66–0.91) for MV.

Conclusion: Among neurocritical patients with diabetes mellitus, all of the evaluated glycemic indices affect the need for MV. The AGG cut-off of 3.2 mmol/L is an acceptable value to predict the need for MV.

Key messages

Raised levels of admission glycemic gap, A1c-derived admission glucose, A1c, and admission blood glucose level are associated with a consequent need for mechanical ventilation among neurocritical patients with diabetes mellitus. An admission glycemic gap cut-off of 3.2 mmol/L can be considered acceptable to predict the need for mechanical ventilation.

Correspondence

Manas Kanti Mazumder
dr.manaskanti@gmail.com

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Tapati Basak
0000-0001-8052-061X

M Mostafa Zaman
0000-0002-1736-1342

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Introduction

There is an association between poor hospital outcomes with altered glycemic indices at the time of hospital admission [1–3]. Neurological conditions are among the most common reasons for intensive care unit (ICU) admission. Approximately 10-15% of all ICU patients are severely ill with major neurological or neurosurgical problems affecting the brain and spinal cord that necessitate life-sustaining care and close monitoring [2,4,5]. Most neurocritical patients presenting with at least one co-morbid illness, diabetes mellitus (DM) is the second most prevalent comorbidity after hypertension [6].

In the intensive care unit, among the patients with neurocritical illness, about 20% require mechanical ventilation (MV) [7]. While some patients do not require mechanical breathing right away, may need some MV subsequently [8]. Although the use of MV can be lifesaving, the decision to initiate it must not be a fast approach. Rather, it is advised to use a be made caecially, based on criteria to accurately predict which patients will most likely benefit from these interventions [9,10].

Altered glycemic indices are some of the risk variables linked to unfavorable outcomes in critically ill patients [3,11]. Patients with greater HbA1c (here-in-after denoted as A1c) have increased unfavorable outcomes, including raised mortality rates in the critical care unit [12]. However, chronic hyperglycemia could be associated with cellular mechanisms that buffer against injury induced by acute hyperglycemia amid severe illness [3,13]. Choosing the "optimal glycemic target" is therefore not the only consideration; other dimensions of glycemic management may also be more important. This is why adverse outcomes in critical illness have been linked to glycemic variability, which measures the extent of glycemic excursions during the day [3,14].

In critically ill patients, hyperglycemia may result from stress-induced hyperglycemia (SIH), which can occur with or without diabetes mellitus, or from the patient's preexisting diabetic condition [15]. Since many diabetic patients already have elevated blood glucose levels, the measurement of direct admission blood glucose indices may not be reliably related to stress levels. However, the admission glycemic gap (AGG) has been found to be a more accurate indicator of SIH than the other glycemic indices [16,17]. Other than exploring the relationship with SIH, in critically ill diabetic patients, AGG has also been used to assess the severity of the disease, forecast outcomes, including mortality. An assessment of AGG can minimize the confounding effect of persistent hyperglycemia on the evaluation of the severity of DM [17]. The AGG has been proposed as a predictor of various adverse outcomes in the ICU settings in various scientific works [2,3,11,12,15–17].

In this context, our primary objective was to investigate the role of AGG and other glycemic indices (admission blood glucose, A1c, and ADAG) at ICU admission on clinical outcomes, such as the need for MV in neurocritical patients with DM. Additionally, attempted to determine a cut-off value of glycemic indices, especially of AGG, that can effectively predict

the need for MV in the later stage of the same ICU admission. Another specific objective of the work was to evaluate how MV affects some other adverse clinical outcomes, such as survival, development of acute respiratory syndrome (ARDS), multi-organ dysfunction (MODS), and need for renal replacement therapy (RRT) in these patients.

Methods

Design, place, and population

For a duration of 12 months, from October 2022 to October 2023, this prospective observational case study was conducted in the intensive care unit (ICU) of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, under the auspices of the Department of Anesthesia, Analgesia, and Critical Care Medicine. The minimum sample size calculated, at 5% acceptable error and 80% power, for this study was 54. Sample size calculation was done using the area under the receiver operating characteristic curve (AUROC) value in the Medcalc software (MedCalc - version 23.1.1). AUROC of AGG for respiratory failure among ICU patients with DM (AUROC= 0.714) in the work of Donagaon and Dharmalingam, 2018 [2], was taken into consideration. However, all of the 60 patients with neurocritical illness who were admitted to the ICU during the stated timeframe and met inclusion criteria were purposively included. All study participants were older than 18 years, had a history of documented DM or an initial post-admission A1c >6.5% (patients who had no history of known DM, yet A1c was >6.5%, included as undiagnosed DM), had survived and spent a minimum of 24 hours in the ICU after admission, and had not required MV within 12 hours of ICU admission. This study excluded individuals who were on corticosteroids, pregnant women, known cases of chronic kidney disease (CKD), those with hemolytic anemia or known hemoglobin variations, hypoglycemic patients, and/or patients who were in hyperglycemic crises during ICU admission.

Data collection, biochemical measurements, and glycemic indices

A pre-tested, semi-structured questionnaire for obtaining data was created. The investigating team came to a consensus before finalizing the data collection instrument. Glasgow coma score, pulse, temperature, blood pressure (BP), mean arterial pressure (MAP), respiratory rate (RR), and partial pressure of oxygen in arterial blood (SpO₂) were among the initial patient assessments that were pertinent to this investigation at the time of admission. The enrolled participants' medical records were reviewed, and notes were made regarding their age, sex, place of residence, primary diagnoses, comorbidities, medication history, and duration of DM. All these variables were considered for this study, as our literature review prior to and during the study showed these as potential factors that affect the need for MV among ICU patients. Within 24 hours of ICU admission, laboratory investigations were sent to the Department of Biochemistry and Molecular Biology, BSMMU, including the arterial blood gas analysis (ABG), complete blood count, A1c (ion-exchange

HPLC method), and serum urea and creatinine, with results noted. The ABG was done using Easy Blood Gas Analyzer (MEDICA, USA), A1c with Abott premium (Hb 9210, USA), blood count with 6 MAX Auto Analyzer (Germany), and serum urea/ creatinine with Diamention Auto Analyzer (USA).

In the ICU, admission blood glucose level (ABGL) was measured from the capillary blood using a common glucometer (Accu check active, Germany, model 24697034). Before collecting data, glucometer and laboratory oxidase methods were compared in the pre-test, and the variation was less than 0.5 mmol/L. The glucometer reading was confirmed by double-checking a venous sample at the laboratory. The formula used to convert A1c to A1c-derived average glucose (ADAG) at admission was as follows: ADAG (mmol/L) = $(1.6 \times A1c) - 2.6$ [18]. Subtracting the ADAG level from the ABGL allowed for the calculation of the admission glycaemic gap (AGG). As a result, AGG = ADAG - ABGL [16,17].

The participants were all observed for 30 days, or until they were either discharged from ICU or moved to another unit or ward (classified as "survivor") or until death in the ICU (classified as "non-survivor"). The assessment and initiation of MV followed the standard ICU protocol of BSMMU.

Statistical analysis

Continuous data were expressed as mean (standard deviation), and categorical data were expressed as frequencies (percentages). Independent variables were compared between those who needed MV and those who did not. Analyses were performed using the 2-tailed Student's *t*-test for normally distributed continuous variables, or the Mann-Whitney U test for skewed data, and the Chi-square test or Fisher's exact test for categorical variables as appropriate. A logistic

regression analysis was performed on those independent variables found statistically significant in the above analysis. Predictor variables were entered as continuous variables, except RRT, which had a binary category and coded '0' for no and '1' for yes response. Receiver operating characteristic (ROC) curves were plotted to analyze the discernibility of the predictive indices, and the area under the curve (AUC) and its 95% confidence interval (CI) were calculated to quantify the discriminative ability of AGG in predicting these outcomes. Youden's index was used to calculate the best possible cut-off values of the glycemic gap, which can predict adverse outcomes. Data were analysed using STATA MP Version 16. A significance α level of 0.05 was used for statistical testing.

Ethics

The patients/ their consenting guardians were given an easy-to-understand explanation in the local language of the study's goals, risks, and advantages. Every participant/ their guardian was given the assurance that their treatment would not be hampered if they chose not to participate in the research or if they chose to withdraw at any point. Additionally, they received assurances that all information would be kept private and used only for the study.

Results

Overall population

Sixty ICU-admitted patients were included in the study, with a mean age (standard deviation) of 57.7 (2.0) years, and about half of them were from the 60 or more years' age group. The majority (63.3%) of the patients were male, and more than half (55.0%) were from rural residences. Ischemic stroke (35.0%), traumatic brain injury (21.7%), and hemorrhagic stroke (20.0%) were the prevalent diagnoses. Hypertension (65.0%) was the commonest comorbid condition.

Effect of primary and baseline features on MV

Baseline characteristics of patients were classified based on the provision of invasive MV. Among the 60 patients, 39 (65.0%) required MV. A significantly greater number of patients who were on MV were male and receiving insulin treatment (Table 1).

Clinical and laboratory variables

Among the clinical and laboratory findings, MAP was significantly lower in ventilated patients, while ABGL, A1c, ADAG, and serum creatinine were significantly higher in those patients. AGG of mechanically ventilated patients (4.9 (1.8) mmol/L) was considerably higher ($P < 0.01$) than that of non-ventilated patients (2.8 (1.5) mmol/L) (Table 2).

Adverse clinical outcomes associated with MV

The number of patients who developed MODS was higher among the mechanically ventilated patients ($P = 0.03$). Mechanically ventilated patients' survival rates were found to be significantly lower ($P = 0.01$) than those who did not require MV (Table 3).

Effect of AGG and other glycemic indices

Variables related to the primary outcome (MV) were screened out during univariate analysis. The logistic regression analysis revealed the statistically

Table 1 Baseline characteristics of neurocritical patients with diabetes mellitus based on the need for mechanical ventilation (MV)

Characteristics	Total (n=60)	Need for MV		P
		No (n=21)	Yes (n=39)	
Age (years) mean (SD)	57.7 (2.0)	62.5 (2.5)	55.3 (2.6)	0.07
Age group				0.18
<60 years	27 (45.0)	7 (33.3)	20 (51.3)	
≥60 years	33 (55.0)	14 (66.7)	19 (48.7)	
Sex				0.02
Female	22 (36.8)	12 (57.1)	10 (25.6)	
Male	38 (63.3)	9 (42.9)	29 (74.4)	
Residence				0.43
Rural	33 (55.0)	13 (61.9)	20 (51.3)	
Urban	27 (45.0)	8 (38.1)	19 (48.7)	
Primary diagnosis				
Ischemic stroke	21 (35.0)	11 (52.4)	10 (25.6)	0.04
Traumatic brain injury	13 (21.7)	2 (9.5)	11 (28.2)	0.11
Hemorrhagic stroke	12 (20.0)	3 (14.3)	9 (23.1)	0.51
Others ^a	14 (23.3)	5 (23.8)	9 (23.1)	0.95
Co-morbidities				
Hypertension	39 (65.0)	15 (71.4)	24 (61.5)	0.44
Asthma/COPD	8 (13.3)	3 (14.3)	5 (12.8)	0.99
Ischemic heart disease	4 (6.7)	1 (4.8)	3 (7.7)	0.99
Drug history				
Anti-hypertensive	35 (58.3)	13 (61.9)	22 (56.4)	0.68
Insulin	25 (41.7)	5 (23.8)	20 (51.3)	0.04
Oral anti-diabetic	33 (55.0)	14 (66.7)	19 (48.7)	0.18
Oral anticoagulant	4 (6.7)	2 (9.2)	2 (5.13)	0.61

Results are in number (%), unless indicated otherwise. COPD indicates chronic obstructive pulmonary disease; SD, standard deviation.
^aSubarachnoid hemorrhage, Guillain Barre Syndrome, motor neuron disease, and meningoencephalitis.

Table 2 Clinical and laboratory findings of neurocritical patients with diabetes mellitus according to the need for mechanical ventilation (MV)

Characteristics	Total (n=60)	Need for MV		P
		No (n=21)	Yes (n=39)	
Clinical Findings				
Pulse (beats/min)	91.4 (16.3)	90.1 (16.5)	92.0 (16.3)	0.67
Temperature				
<100.4º F	49 (81.7)	19 (90.1)	30 (76.9)	0.20
≥100.4º F	11 (18.3)	2 (9.5)	9 (23.1)	
Oedema	2 (3.3)	1 (4.8)	1 (2.6)	0.65
Glasgow coma score ^a	8 (5.5–11.0)	11 (6.0–14.0)	7 (5.0–10.0)	0.07
Respiratory rate (breaths/ min) ^a	20 (18.0–22.0)	20 (16.0–20.0)	20 (18.0–22.0)	0.24
Laboratory findings				
MAP (mmHg)	92.1 (14.7)	98.4 (13.6)	88.7 (14.3)	0.01
Oxygen saturation ^a	97 (95.5–98.0)	97 (95.0–98.0)	97 (96.0–99.0)	0.78
PaO ₂ : FiO ₂ ratio	263.9 (227.1)	288.4 (128.1)	250.7 (149.9)	0.33
ABGL (mmol/L)	13.6 (2.9)	11.4 (2.3)	14.7 (2.6)	<0.01
A1c (%) ^a	7.3 (6.9–8.1)	7 (6.6–7.2)	7.8 (7.0–8.2)	<0.01
ADAG (mmol/L) ^a	9 (8.4–10.3)	8.5 (7.9–8.9)	9.8 (8.5–10.4)	<0.01
AGG (mmol/L)	4.16 (1.9)	2.8 (1.5)	4.9 (1.8)	<0.01
Haemoglobin (g/dL)	11.7 (1.3)	11.6 (1.3)	11.7 (1.3)	0.98
WBC count (x10 ⁹ /L)	13.3 (4.0)	12.3 (3.5)	13.8 (4.2)	0.16
Platelet count (x10 ⁹ /L) ^a	210 (170.0–250.0)	210 (165.0–250.0)	210 (170.0–300.0)	0.52
pH ^a	7.5 (7.4–7.5)	7.5 (7.4–7.5)	7.5 (7.4–7.5)	0.90
Serum urea (mg/dL) ^a	39 (28.0–68.4)	35 (26.0–62.0)	40 (30.0–77.0)	0.59
Serum creatinine (mg/dL) ^a	1.0 (0.9–1.8)	0.9 (0.7–1.2)	1.0 (0.9–4.4)	<0.01

MAP, mean arterial pressure; ABGL, admission blood glucose level; ADAG, A1c derived average glucose; AGG, admission glycemic gap; TC, total count; PaO₂, partial pressure of oxygen in arterial blood; FiO₂, fraction of inspired oxygen; WBC, white blood cells

^aMedian (interquartile range), others are mean (standard deviation)

significant association of ABGL, A1c, ADAG, and AGG with MV. One unit increase in the variable was associated with a 2.1 times (95% CI 1.4–3.1) higher requirement for MV ($P < 0.01$). An increase of 1 mmol/L ADAG was associated with an 81% increase in the requirement for MV. Elevation of all four glycaemic indices (ABGL, A1c, ADAG, and AGG) significantly increased the risk of MV in neurocritical ICU patients with DM. A1c showed the greatest risk (OR 2.6; 95% CI 1.2–5.4) (Table 4).

Among the glycemic predictors evaluated, the AGG demonstrated good diagnostic performance with a Youden Index of 0.60, which indicates a moderate to good range for predictive performance, at a cut-off value of 3.2 mmol/L. This reflects a good overall sensitivity (79%) and specificity (81%), indicating its potential utility in predicting the requirement for invasive MV. The optimal cut-off value of the AGG was 3.2 mmol/L, with a maximum AUROC of 0.79 (95% CI 0.65–0.91) for MV (Figure 1 and Table 5).

Table 3 Association of adverse clinical outcomes of diabetic neurocritical patients with mechanical ventilation (MV), n (%)

Clinical outcomes	All patients (n=60)	Need for MV		P
		No (n=21)	Yes (n=39)	
Needed renal replacement therapy	13 (21.7)	2 (9.5)	11 (28.2)	0.11
Developed acute respiratory distress syndrome	19 (31.7)	4 (19.1)	15 (38.5)	0.15
Developed multiple organ dysfunction syndrome	30 (50.0)	5 (23.8)	25 (64.1)	0.03
Survival	25 (41.7)	15 (71.4)	10 (25.6)	0.01

Discussion

This study showed that 65% of neurocritical patients with DM needed MV in the ICU. The majority of our patients were elderly (>60 years) males. Male gender, ischemic stroke, and history of insulin were associated with the need for MV. Per unit raise of all glycemic indices significantly raised the risk of MV. An AGG cut-off value of 3.2 had an AUROC of 0.79 in the case of MV.

Table 4 Logistic regression analysis of the association between glycemic indices with mechanical ventilation (MV)

Predictors	OR (95% CI)
Admission blood glucose level (mmol/L)	1.8 (1.3–2.5)
Hemoglobin A1C (%)	2.6 (1.2–5.4)
A1C-derived admission glucose (mmol/L)	1.8 (1.1–2.9)
Admission glycemic gap (mmol/L)	2.1 (1.4–3.1)
Renal replacement therapy	3.7 (0.7–18.8)

All predictor variables were continuous except for renal replacement therapy, which was a binary category (coded '0' for no and '1' for yes). OR indicates odds ratio; CI, confidence interval

Evidence that altered glycemic indices at admission may be associated with major therapeutic events like the need for MV in neurocritical patients with DM in the ICU has scarcely been evaluated. Admission glycemic indices in these patients potentially affect the need for MV, and a probable cut-off to predict such an event can be of importance. As such, the predictors and cut-off values will essentially enable the clinician to identify, increase monitoring, and improve management of the most vulnerable patients in ICU setting.

The proportion of patients who needed MV in this study was very high, as other reports suggest that approximately 20% of the neurocritical patients in the ICU need MV [7]. The characteristics of our study population, study design, and study settings may be responsible for the much higher proportion of MV. We selected a study sample of patients who had at least one comorbid condition in addition to their neurological illness, such as DM, neurocritical patients in the general ICU rather than a dedicated ICU, and a 30-day-long observation duration, all of which might have contributed to the high rate of MV. The older patient pool of this study corresponds with Chentli, Azzoug, and Mahgoun [19], who explained that older patients with diabetes mellitus are at higher risk of morbidity and mortality through hyperglycemia-induced damage. Similarly, our sample being male-predominant mirrors the scientific conclusion that males are more likely victims of neuro-critical conditions [6,20,21].

Our finding associating ischemic stroke, CKD, history of insulin use, and male gender with MV is in line with the finding that neurological failure is a proven hazard that necessitates MV [22], that lung inflammation is modulated by insulin [23], and that men are more likely to need MV support [24].

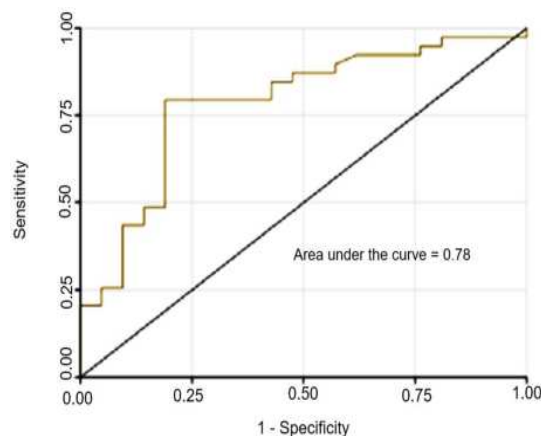
Acute-stress hyperglycemia is indicated by the glycemic gap, and patients with significant glycemic gaps have been shown to have higher mortality rates [25]. Hence we examined whether AGG can influence the requirement for MV and we discovered that AGG, ABGL, ADAG, and A1c all have the potential of predicting the need for MV in neurocritical patients

Table 5 Receiver operating characteristic curve and Youden index values of glycemic indices for prediction of mechanical ventilation

Predictors	Youden Index	Cut-off values	Sensitivity	Specificity	AUC (95% CI)
Admission blood glucose level (mmol/L)	0.63	>12.2	0.87	0.76	0.84 (0.72–0.96)
Hemoglobin A1C (%)	0.47	>7.4	0.62	0.86	0.75 (0.61–0.88)
A1C-derived admission glucose (mmol/L)	0.47	>9.1	0.62	0.86	0.75 (0.61–0.88)
Admission glycemic gap (mmol/L)	0.60	>3.2	0.79	0.81	0.79 (0.66–0.91)

AUC indicates area under the curve; CI, confidence interval

with DM. All these are in line with the report that hyperglycemia, glycemic gap, and glycemic variability affect and raise the possibility of requiring MV [3]. This may be due to the pathophysiological aspect that hyperglycemia is associated with diaphragmatic dysfunction and respiratory muscle weakness [26,27]. This study's finding of an increase in A1c showing the greatest odds of MV is interesting considering that elevated A1c showed the highest odds of MV in COVID-19 patients [28], was associated with ICU admission after surgery [29], and prolonged ICU stay after bypass graft in the coronary artery [30], etc.

**Figure 1** Receiver operating characteristic curve of admission glycemic gap to predict the need for mechanical ventilation

There are some limitations of this study. The sample size was modest, purposively selected, and carried out in a single general intensive care unit. Selection bias is, therefore, possible. Post-surgical neuro-critical patients did not participate in this investigation in large numbers, mostly because the ICU was not designed with post-surgical neurocritical patients in mind. A capillary sample was used to measure the first glucose level, which can vary from a venous sample. Therefore, our findings may not be generalized.

Conclusion

Findings from this study suggest that admission glucose level, A1c level, A1c-derived admission glucose, and AGG can predict the need for MV among the neurocritical patients with DM in the ICU. An AGG >3.2 mmol/L may be considered a marker to predict the need for MV in the defined patient pool.

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Author contributions

Conception and design: MKMa, KTM, MKMo, MA. *Acquisition, analysis, and interpretation of data:* MKMa, KTM, MKMo, MAH, AKMH, MA. *Manuscript drafting and revising it critically:* MKMa, KTM, MKMo, MAH, AKMH, MA. *Approval of the final version of the manuscript:* MKMa, KTM, MKMo, MAH, AKMH, MA. *Guarantor of accuracy and integrity of the work:* MKMa, KTM, MKMo, MA.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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RESEARCH ARTICLE

Swimming exercise on spatial memory performance and hippocampal oxidative stress in colchicine-induced memory-impaired male Long-Evans rats



Rokhsana Binte Amin¹ | Puspita Basak¹ | Fhamida Akter¹ | Md. Saiful Islam¹ |
Kazi Rafiqul Islam² | Taskina Ali¹ |

¹Department of Physiology, Bangabandhu Sheikh Mujib Medical University (currently Bangladesh Medical University), Dhaka, Bangladesh

²Department of Pharmacology, Bangladesh Agricultural University, Mymensingh, Bangladesh

Abstract

Background: Spatial memory is one of the necessary components of our typical day-to-day life. Therefore, its impairment should be alleviated or prevented. The purpose of this study was to assess the effects of swimming exercise on spatial memory performance and hippocampal oxidative stress in male Long-Evans rats with colchicine-induced memory impairment.

Methods: Thirty male aged 8 standard deviation (2) weeks; weight 225 (75) gm Long-Evans rats were assigned to normal control, sham control, colchicine control, pre colchicine swimming exercise and post colchicine swimming exercise groups. A memory-impaired rat model was established by administering colchicine intrahippocampally. Swimming exercise was performed before and after spatial memory impairment. For spatial reference and working memory performance evaluation, the Morris water maze test was used. Hippocampal malondialdehyde and glutathione peroxidase were estimated for oxidative stress assessment in all rats.

Results: Intrahippocampal colchicine administration significantly impaired spatial memory, and elevated malondialdehyde, decreased glutathione peroxidase level in the hippocampus of colchicine control rats. In contrast, both pre- and post-treatment with swimming exercise significantly improved learning and spatial memory retention and attenuated oxidative damage to nearly normal levels.

Conclusion: Swimming exercise prevents as well as alleviates colchicine-induced spatial memory impairment along with hippocampal oxidative stress in male Long-Evans rats. Moreover, this swimming exercise schedule is sufficient to reverse these alarming consequences to almost normal.

Correspondence

Rokhsana Binte Amin
rbinteamin@gmail.com

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M Mostafa Zaman
0000-0002-1736-1342

Reviewer

Niazur Rahman
0000-0002-0584-0792
Shelina Fatema Binte Shahid
0000-0001-8999-7115

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Introduction

Memory refers to the processes by which any learned knowledge is encoded, stored, and later retrieved [1]. In it, spatial memory plays a crucial role in helping us navigate and find our way to a specific destination [2]. According to WHO, currently, more than 55 million people have dementia worldwide [3] and spatial memory impairment is one of the critical components of dementia. Physical inactivity, a sedentary lifestyle, and a stressful lifestyle are linked with spatial memory impairment and many clinical conditions [4].

Currently, the long-term memory is known as reference memory (RM) [5]. Here, the information available for solving RM tasks remains constant throughout the trials and is reinforced by repeated training [6]. On the other hand, working memory (WM) is a form of short-term memory that retains information for a short period, usually while an individual plans an action based on it [7]. Both of these memories depend on the hippocampus, the most medial portion of the temporal lobe cortex. Neurodegeneration of the hippocampus can lead to memory impairment, and oxidative stress is one of the proposed mechanisms underlying this neurodegeneration [8]. Oxidative stress is caused by reactive oxygen species, which are part of a group of molecules called free radicals, and leads to cell injury [9]. Malondialdehyde (MDA), an end product of lipid peroxidation, is commonly measured as an indirect index of oxidative stress [10]. Superoxide dismutase, glutathione peroxidase (GPx) play a crucial role against oxidative injury as scavengers [9].

Physical exercises such as swimming exercise (SwE) that use oxygen more efficiently, [11] would be a good alternative for improving memory and reducing oxidative stress [12,13]. Reduction of oxidative stress and neuroinflammation, [14,15] as well as an increase in brain-derived neurotrophic factor [16] and choline acetyltransferase activity [17] in the hippocampus, are the suggested mechanisms for memory improvement by SwE. Therefore, SwE was applied either before [14] or after [18] or during [15] the brain damage in different experimental models. Various time schedules of SwE for 28 or 90 days [14,15,18] were applied in several studies.

The beneficial effects of SwE on memory impairment, as well as oxidative stress, before or after hippocampal damage remained unresolved [18]. However, the volume of information regarding the effects of SwE on memory impairment and oxidative stress is not enough for reaching any final inference. The present study has been designed to examine the effects of SwE on memory performance, as well as hippocampal oxidative stress markers, before and after colchicine-induced spatial memory impairment in male Long-Evans rats.

Methods

The experimental design

This experimental study was conducted at the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from March 2023 to February 2024. The sampling technique was purposive. Here, the specified difference between the two means was

compared to test the null hypothesis. So the formula, $n = [(u + v)^2 \times (\sigma_{12} + \sigma_{22})] / (\mu_1 - \mu_2)^2$, involving effect size was used to calculate the intended sample size for a group [19]. We used mean and standard deviation of 'escape latency in reference memory' version of the Morris Water Maze test, stated by Raghavendra *et al.* (2013) [20]. Thus, we used 30 rats.

Procurement and maintenance of animals

A total of 30 male Long-Evans rats aged 8 (standard deviation 2) weeks; weight 225 (75) gm were collected from the central animal house of BSMMU and were housed in standard laboratory environments (temperature: 27°C, 12/12 hour light-dark cycle). The rats were provided with free access to standard laboratory food [21] and cooled boiled water *ad libitum*. All the experiments were conducted according to the 'Guidelines for the Animal Experimentation Ethics Committee (AEEC, 15 May 2023) of the International Centre for Diarrhoeal Disease Research, Bangladesh and the advice of an expert veterinarian. All the experiments were performed during the daytime between 08:00 and 16:00 hours.

Experimental design and dose schedule

Rats were randomly divided into 5 groups (6 rats/group):

- Normal control (NC): No stereotaxic surgery (SS) + no normal saline (NS) + no swimming exercise (no SwE).
- Sham control (SC): SS + hippocampal infusion of 1 µl NS + no SwE.
- Colchicine control (ColC): SS + hippocampal infusion of 15 µg of colchicine in 1 µl NS + no SwE.
- Pre colchicine swimming exercise (Pre-SwE Exp): SwE for 28 days followed by SS + hippocampal infusion of 15 µg of colchicine in 1 µl NS.
- Post colchicine swimming exercise (Post-SwE Exp): SS + hippocampal infusion of 15 µg of colchicine in 1 µl NS followed by SwE for 28 days.

Swimming exercise protocol [14]

SwE was performed in a circular pool (150 cm X 50 cm) for 28 days in rats of Pre-SwE Exp and Post-SwE Exp groups. Treatment was conducted five days a week. During the initial two days, SwE was started at 10 minutes per day and gradually increased by 10 minutes every two days until reaching 1 hour per day by the 12th day. From that moment onward, training continued at a rate of one hour per day until day 26.

Hippocampal colchicine application by SS

According to previous research, [22-24] colchicine (Incepta Pharmaceuticals Ltd, Bangladesh) was administered into the rat hippocampus by SS. Each rat was deeply anesthetized with thiopental sodium (45 mg/kg, i.p.) and positioned in a stereotaxic apparatus (BioMed Easy Technologies Co., Ltd.). The scalp was incised and retracted. The rat was infused through a Hamilton microsyringe with 15 µg of colchicine in 1 µL of NS in each hippocampus. Controls that received the vehicle injection were utilised. The coordinates

were -3.6 mm anterior-posterior, ± 2 mm lateral-medial, and -3.4 mm dorso-ventral relative to bregma. All intra-hippocampal applications of colchicine and/or NS were infused very slowly over 1 minute, and the micro syringe was kept in place for the next minute before being slowly withdrawn. Gentamicin (5 mg/kg, i.p.) was administered postoperatively to prevent sepsis.

Spatial memory assessment by MWM test

Test tools and circumstances [25-27]

MWM was a large circular pool (150 cm x 50 cm) filled to a depth of 30 cm with water at 24 to 26 °C. This pool was arbitrarily divided into four quadrants: north-west (NW), north-east (NE), south-east (SE) and south-west (SW). A round platform (15 cm x 28 cm) was placed at the center of one quadrant, with its top 2 cm below the water's surface, and served as the only escape route for the rats from the water. To determine the start locations, eight points —north (N), south (S), east (E), west (W), northeast (NE), northwest (NW), southeast (SE), and southwest (SW) of MWM— were labelled. To prevent visual clues in the pool, the entire inner wall of the pool and platform was painted with a non-toxic black color. The pool was placed in a room containing extra maze cues that rats could use to assist them in navigating. Two distinct testing paradigms were sequentially employed to assess reference and working memory skills, as illustrated in the

[Supplementary file.](#)

Reference memory test

The rats swam without a platform for 3 minutes over three consecutive days to acclimatise and habituate themselves to the reference memory version. Then, during the acquisition phase, all rats underwent four trials each day for six consecutive days, with the platform consistently placed in the NE quadrant. In every trial, the rats were released from different starting points in a predetermined sequence each day and given 60 seconds to locate the platform and climb onto it. A 50-second inter-trial time (20 seconds on the platform and 30 seconds for self-drying) was allowed. The time taken for the rat to find the platform, also known as the mean escape latency (EL), was measured using a stopwatch to assess the rat's learning ability. On the first trial each day, the rats found the platform by chance, which served as the information stage. The subsequent trials necessitated matching to the new position each day, as the platform remained in the same place for 6 days. The average EL of the 5th and 6th acquisition days was measured to assess memory consolidation. Approximately 24 hours after the last trial on day 6, the platform was removed from the pool, and a final spatial probe trial was conducted to assess the strength of learning and retrieval. In this probe trial, rats swam freely for 60 sec during which target crossings (TC; number of passing the quadrant made by rats within 60 sec after the platform was removed) and time spent in target (TT; the time spent in the quadrant from where the platform was removed during the same 60 sec period) were measured [28].

Working memory test

A testing paradigm adapted from Sarihi *et al.* [25] was used to conduct the working memory version of the test approximately 48 hours following the probe trial.

Here, the 6-day acquisition phase of the reference memory test was considered as the pre-training phase of the working memory test. Then, a training and test phase was conducted over four consecutive days, with four trials each day. Here, the platform position was altered daily but remained the same for the four trials. However, during the four daily trials, each rat was released from four distinct starting points, all of which were far from the platform position. Rats randomly arrived at the platform on the first trial of each day, which served as the information stage. The following trials needed to be matched to the new position for that day, as the platform was changed daily. The mean escape latency in the training and test phases was recorded as above to assess learning ability and savings (the difference in latency scores between trials 1 and 2, expressed as the percentage of savings increased from trial 1 to trial 2) was measured to assess learning efficiency [28, 29].

Hippocampal oxidative stress marker assessment

Rats were euthanised through decapitation under diethyl ether anesthesia, 24 hours following the final behavioral test [15]. Then the brain tissues were swiftly taken out, and the hippocampal tissues were promptly isolated. They were then carefully rinsed with ice-cold Phosphate-Buffered Saline (PBS) (0.1 M, pH 7.4) to ensure complete removal of excess blood. The tissue pieces were weighed and homogenised in PBS using a glass homogeniser on ice, maintaining a ratio of weight (g) to volume (mL) of 1:4. Next, the homogenate underwent centrifugation at 3500 rpm for 10 minutes to obtain the supernatant. The supernatant was collected for the estimation of MDA and GPx levels by ELISA according to the manufacturer's protocol (Elab Science Biotechnology, USA). If any unintended delay occurred, the supernatant was stored in a laboratory at -20 °C.

Statistical analysis

Data were expressed as mean (standard error) of the study variables and statistically analysed using ANOVA followed by the Bonferroni post hoc test (between groups) using SPSS (version 25.0), $P < 0.05$ was considered statistically significant.

Results

Effect of SwE on spatial memory impairment induced by hippocampal colchicine

For reference memory performance

ColC rats showed significantly ($P < 0.01$) higher mean EL than those of SC rats. However, SwE improved learning ability performance, as evidenced by statistically significant ($P < 0.01$) differences in mean EL of our ColC and experimental (Pre-SwE Exp and Post-SwE Exp) rats. Notably, the differences in this variable between experimental and NC rats were found to be statistically non-significant on the last acquisition day. However, the differences of mean EL between Pre-SwE Exp vs Post-SwE Exp rats were found statistically non-significant in all acquisition days (Table 1). These data demonstrated that the learning ability of reference memory was impaired by colchicine, and this impairment was reversed almost to normal by SwE.

Table 1 Mean (standard errors) escape latency, in seconds and average escape latency (5th and 6th acquisition days, in seconds) in the acquisition phase of the Morris water maze test in five groups of rats

Mean escape latency of acquisition day	Groups				
	NC	SC	ColC	Pre-SwE Exp	Post-SwE Exp
Days					
1 st	26.2 (2.3)	30.6 (2.4)	60.0 (0.0) ^b	43.2 (1.8) ^b	43.8 (1.6) ^b
2 nd	22.6 (1.0)	25.4 (0.6)	58.9 (0.5) ^b	38.6 (2.0) ^b	40.5 (1.2) ^b
3 rd	14.5 (1.8)	18.9 (0.4)	56.5 (1.2) ^b	34.2 (1.9) ^b	33.8 (1.0) ^b
4 th	13.1 (1.7)	17.5 (0.8)	53.9 (0.7) ^b	35.0 (1.6) ^b	34.9 (1.6) ^b
5 th	13.0 (1.2)	15.9 (0.7)	51.7 (2.0) ^b	25.9 (0.7) ^b	27.7 (0.9) ^b
6 th	12.2 (1.0)	13.3 (0.4)	49.5 (2.0) ^b	16.8 (1.1) ^b	16.8 (0.8) ^b
Average of acquisition days					
5 th and 6 th	12.6 (0.2)	14.6 (0.8)	50.6 (0.7) ^b	20.4 (2.1) ^a	22.4 (3.2) ^a

NC indicates normal control; SC, Sham control; ColC, colchicine control; SwE, swimming exercise exposure.

^a $P < 0.05$; ^b $P < 0.01$.

The mean value of the average EL on the 5th and 6th acquisition days was significantly ($P < 0.01$) higher in ColC rats than in SC rats (Table 1). Moreover, SwE showed significantly ($P < 0.05$) lower average EL in both groups of our experimental rats than in the ColC rats. On the contrary, the differences in this variable between our NC and experimental rats, as well as between Pre-SwE Exp and Post-SwE Exp rats, were found to be statistically non-significant. This result indicated that colchicine induced consolidation disability in our ColC rats and SwE improved it similar to normal.

Table 2 Target crossings, in frequency/minute and time spent in target, in seconds/minute in probe trial of Morris water maze test in five groups of rats

Variables in probe trial day	Groups				
	NC	SC	ColC	Pre-SwE Exp	Post-SwE Exp
Target crossings	8.0 (0.3)	7.3 (0.3)	1.7 (0.2) ^a	6.0 (0.3) ^a	5.8 (0.4) ^a
Time spent in target	18.0 (0.4)	16.2 (0.7)	5.8 (0.8) ^a	15.3 (0.7) ^a	15.2 (0.9) ^a

NC indicates normal control; SC, Sham control; ColC, colchicine control; SwE, swimming exercise exposure.

^a $P < 0.01$.

Moreover, ColC rats showed retrieval impairment, as evidenced by significantly lower TC and TT ($P < 0.01$) compared to those of SC rats. SwE caused significantly higher TC and TT in our experimental rats compared to ColC rats ($P < 0.01$). However, statistical analysis revealed that the differences in these variables between our two experimental groups were not significant. However, when these variables were compared between NC and experimental rats, TC showed a significant difference ($P < 0.01$), but TT did not (Table 2). From these findings, we inferred that

Table 3 Mean (standard deviation) escape latency, (seconds) and savings (%) in training and test phase of Morris water maze test in five groups of rats

Trials	Groups				
	NC	SC	ColC	Pre-SwE Exp	Post-SwE Exp
1	20.8 (0.6)	22.1 (1.8)	41.1 (1.3) ^b	31.9 (1.9) ^b	32.9 (1.8) ^{a, b}
2	10.9 (0.6)	14.9 (1.7)	37.4 (1.1) ^b	24.9 (2.0) ^b	26.8 (2.5) ^b
3	8.4 (0.5)	9.9 (2.0)	32.8 (1.2) ^b	22.0 (1.4) ^b	21.0 (1.4) ^b
4	7.8 (0.5)	10.4 (1.3)	27.6 (1.1) ^b	12.8 (1.2) ^b	13.0 (1.4) ^b
Savings (%) ^c	47.7 (3.0)	33.0 (3.0)	10.0 (0.9) ^b	23.6 (2.7) ^b	18.9 (5.3) ^b

NC indicates normal control; SC, Sham control; ColC, colchicine control; SwE, swimming exercise exposure.

^a $P < 0.05$; ^b $P < 0.01$.

^cThe difference in latency scores between trials 1 and 2, expressed as the percentage of savings increased from trial 1 to trial 2

learning strength (retrieval) was hampered by colchicine and was both prevented and alleviated by our 28-day SwE; however, our exercise schedule was not sufficient to fully utilise the complete retrieval power.

For working memory performance

Here, colchicine caused significantly higher mean EL ($P < 0.01$) and lower savings ($P < 0.01$) in the training and test phases in ColC rats compared to those in SC rats. However, both of our experimental rats showed significantly lower mean EL [Pre-SwE Exp ($P < 0.01$ in trial 1; $P < 0.01$ in trial 2, 3 and 4) and Post-SwE Exp ($P < 0.05$ in trial 1; $P < 0.01$ in trial 2; $P < 0.01$ in trial 3 and 4)], but not savings, when compared to those of ColC rats. Moreover, when we compared these variables between our experimental and NC rats, mean EL was found to be statistically non-significant in trial 4, except for savings. Furthermore, no statistically significant difference was observed in any of these variables between Pre-SwE Exp and Post-SwE Exp rats (Table 3). Therefore, based on these findings, it is evident that our 28-day SwE could improve the learning disability of colchicine-induced WM impairment in our rats, although not entirely and efficiently.

Effect of SwE on hippocampal oxidative status induced by colchicine

We observed that our ColC rats showed significantly higher ($P < 0.01$) hippocampal MDA levels and lower GPx levels compared to those of the SC rats. However, SwE caused a significantly lower MDA and higher GPx in Pre-SwE Exp ($P < 0.01$) as well as in Post-SwE Exp ($P < 0.01$) rats in comparison to those of ColC rats. Strikingly, there were non-significant differences between NC vs Pre-SwE Exp and NC vs Post-SwE Exp as well as Pre-SwE Exp vs Post-SwE Exp rats (Table 4). These data indicate that colchicine causes hippocampal oxidative stress, and our SwE can prevent and alleviate this stress to nearly normal levels.

Discussion

In our research, we examined the effects of SwE on spatial memory and hippocampal oxidative stress in a colchicine-induced memory-impaired rat model. The present study demonstrated that both pretreatment and posttreatment with SwE were able to ameliorate spatial memory impairment and the marked diminution of oxidative stress.

Here, the intrahippocampal colchicine may bind to microtubule-binding proteins (tubulin), depolymerising microtubules and blocking axoplasmic flow, cellular growth, and cellular differentiation, leading to damage to hippocampal granule and pyramidal neurons [22]. Moreover, this microtubule-disrupting agent might also induce direct nitric oxide (NO) production by activation of inducible nitric oxide synthase (iNOS) enzyme [30]. This NO might react rapidly with superoxide anions (a reactive oxygen species, ROS) to form peroxynitrite (ONOO-) (a reactive nitrogen species, RNS), resulting in oxidative stress and hippocampal neuronal death. In addition, this neurotoxic agent may elevate glutamate binding site [22] in α -amino-3-hydroxy-5-methyl-4-

Table 4 Hippocampal malondialdehyde and glutathione peroxidase in five groups of rats

Hippocampal oxidative stress markers	Groups				
	NC	SC	ColC	Pre-SwE Exp	Post-SwE Exp
Malondialdehyde (ng/mg protein)	8.0 (1.4)	8.3 (0.6)	17.3 (2.0) ^b	9.7 (1.4) ^b	11.7 (2.0) ^a
Glutathione peroxidase (pg/mg protein)	316.2 (28.9)	258.3 (14.6)	121.8 (6.4) ^b	308.8 (22.2) ^b	296.0 (26.2) ^b

NC indicates normal control; SC, Sham control; ColC, colchicine control; SwE, swimming exercise exposure.

^aP < 0.01; ^bP < 0.001.

isoxazolepropionic acid (AMPA) and N-methyl-D-aspartate (NMDA) receptors in hippocampal neurons, causing excess Ca²⁺ influx. This process might be responsible for mitochondrial stress, ROS production, oxidative stress [31] and neuronal death in the hippocampus. Moreover, this marked increase in ROS and RNS might affect the double bonds of polyunsaturated fatty acids in neuronal cell membranes (lipid peroxidation) [9] and elevate hippocampal MDA levels in our memory-impaired rats [24]. In addition, this increase in oxidants may cause an increased consumption of GPx [9] for maintaining oxidative balance and a decreased GPx concentration [24] in hippocampal neurons.

In our study, SwE may cause an increase in brain-derived neurotrophic factor (BDNF), [16] an important marker of memory and cognition [32]. As a consequence, BDNF might activate neurogenesis, [33] synaptogenesis [34] and hippocampal volume increment, [35] to replenish the microtubule-disrupted neuronal death in our experimental rats. Moreover, SwE may reduce glutamate concentration, followed by regulation of Ca²⁺ influx through the NMDA receptor [18]. In addition, our 28 days SwE might stimulate the hippocampal ROS induced metabolic adaptation, [36, 37] enhancement of the activity of nuclear erythroid 2 – related factor 2/antioxidant response element (Nrf2/ARE) signal transduction pathway and formation of GPx [14, 38-40] in our experimental rats. This increased GPx might mitigate the increased MDA level in both our pre- and post-exercise treated experimental rats.

Limitations

This study was done using manual stereotaxic apparatus and manually operated memory performance tests. Here, only two variables related to reference memory retrieval were measured, and only two oxidative stress markers from the hippocampus were assessed.

Conclusion

Findings of this study suggest that swimming exercise may be equally effective in preventing as well as alleviating colchicine-induced spatial memory impairment, along with hippocampal oxidative stress, in male Long-Evans rats. Moreover, this swimming exercise schedule might be sufficient to reverse these alarming consequences to almost normal.

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Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data and drafting the work: RBA, TA, PB, FA, MSI, KRI. *Drafting the work or reviewing it critically for important intellectual content:* RBA, TA, PB, FA, MSI, KRI. *Final approval of the version to be published:* RBA, TA, PB, FA, MSI, KRI. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* RBA.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

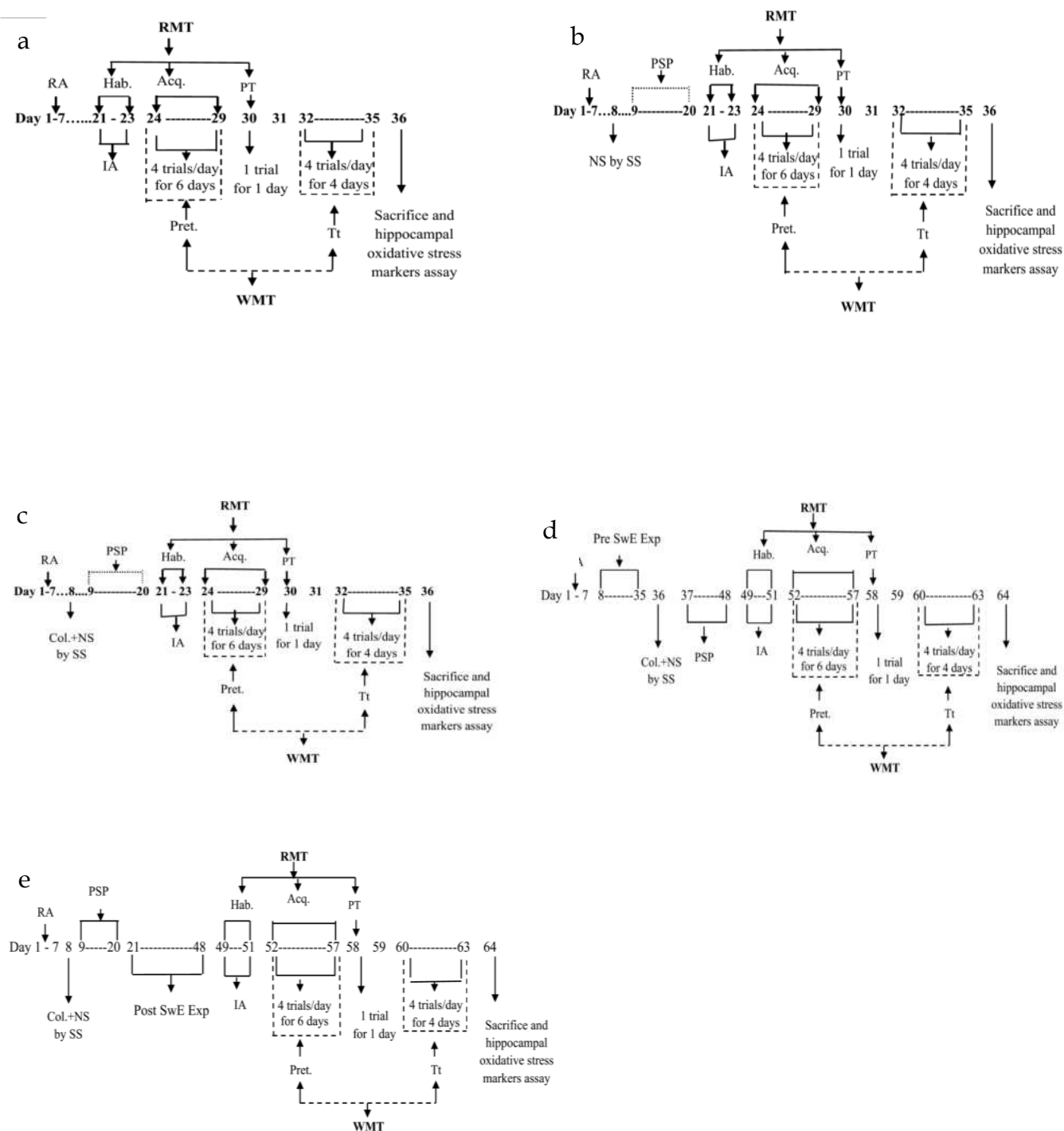
Yes

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Supplementary file 1 Working plan for rats*



*a) normal control, b) sham control, c) colchicine control, d) Pre colchicine swimming exercise, e) Post colchicine swimming exercise.

RMT: Reference memory test; WMT: Working memory test; RA = Room acclimatization; PSP=Post-surgical period; Hab.=Habituation; Acq.=Acquisition; PT=Probe trial; IA=Instrumental acclimatization; Pret.=Pretraining; Tt=Training and test; NS=Normal saline; SS=Stereotaxic surgery; Col.=Colchicine; Pre SwE Exp=Pre colchicine swimming exercise; Post SwE Exp=Post colchicine swimming exercise.

RESEARCH ARTICLE

Internet addiction and its association with life satisfaction among university students in Bangladesh



Md. Abdul Hannan Mondal¹ | Tahmina Khatun¹ | Moynul Haque² | Md. Nazrul Islam Mondal² |
Md. Golam Hossain³ |

¹Department of Clinical Psychology, University of Rajshahi, Rajshahi, Bangladesh

²Department of Population Science and Human Resource Development, University of Rajshahi, Rajshahi, Bangladesh

³Department of Statistics, University of Rajshahi, Rajshahi, Bangladesh

Abstract

Background: Internet addiction (IA) is a serious issue for students because it hampers their daily activities and academic performance negatively impacting mental health. Therefore, this study aimed to determine the prevalence of IA and the factors associated with it among university students.

Methods: A total of 1,168 students of four Bangladeshi universities (50.2% males, 49.8% females, mean age 22.7 and standard deviation 2.2 years) were collected using multistage cluster sampling for this cross-sectional study. The Bangla-adapted Young's Internet Addiction Test (IAT) was used to assess the presence of IA.

Results: A total of 78% of individuals had IA. The key factors associated with IA were marital status, self-reported physical health condition, sleep quality, physical exercise, social engagement, and life satisfaction. Students who reported dissatisfaction with life were more likely to have IA than those who were satisfied (92.8% versus 69.8%). Unmarried individuals were more likely to experience IA compared to married individuals (83.9% versus 63.2%). Respondents with poor physical health status exhibited higher IA rates than those with good physical health status (91.5% versus 62.1%). Higher IA was found to be more prevalent among individuals with poor sleep quality than those with good sleep (89.2% versus 59.8%). Individuals who did not engage in social activities were more likely to have IA than those who engaged in social activities (81.6% versus 71.8%). Multiple logistic regression analysis supported these relationships.

Conclusion: IA is widely prevalent among university students, with nearly three-fourths of them being addicted. Therefore, university administrators and relevant authorities should take necessary measures to mitigate the adverse effects of IA.

Key messages

Internet addiction affects 78% of university students of Bangladesh, with key risk factors including marital status, physical health, sleep quality, exercise, social engagement, and life satisfaction. Unmarried students, along with those in poor health, experiencing inadequate sleep, and exhibiting low social engagement, are more vulnerable to internet addiction, while life dissatisfaction further increases the risk. Given its high prevalence and negative impact, universities should implement measures to address internet addiction and support students' well-being.

Correspondence

Md. Abdul Hannan Mondal
abhannanru.ac.bd@gmail.com

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M Mostafa Zaman
0000-0002-1736-1342

Reviewers

Sifat E Syed
0000-0003-3075-0294

Md. Faisal Ahmed
0000-0001-7190-8591

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Not applicable

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Introduction

The internet is essential to modern life, with users and online time increasing exponentially [1]. Globally, the number of internet users has been rising [2], and in July 2024, the number of internet users reached 5.45 billion [3].

In Bangladesh, mobile internet subscribers numbered 117.5 million in February and 125.15 million in April 2024 [4]. Thus, it is evident that each month the internet use rate has been growing presumably, the prevalence of internet addiction (IA) is also increasing. A study conducted in 2020 found that 27.1% of young adults in Bangladesh experienced IA [5].

Many studies have shown that gender [6, 7] and marital status [7] can influence the IA of university students. Other studies have also found that physical health status [8], sleep quality [7, 9], and physical exercise [6, 7, 9, 10] are important factors in predicting IA. These factors not only predict IA but also have a detrimental effect on mental health issues like depression, anxiety, and chronic physical health problems such as diabetes and high blood pressure [5, 7, 9, 10]. Engagement with other organisations (debating club, science club, research society, various research groups, etc.) increases social support, which decreases IA [11]. Life satisfaction externalises people's psychological necessities [12]. A Chinese study reported that individuals who are satisfied with their lives are more likely to have their mental needs met in real life than on the internet, making them less prone to IA compared to those who are not satisfied [13]. Lower life satisfaction and IA lead to anxiety, depression, suicidal behaviors, and aggressiveness [14].

Several studies were conducted to determine the prevalence of IA in Bangladesh [5, 9]. Two studies identified the prevalence of IA in college students and adolescents [15, 16]. Previous studies also indicated that IA leads to physical and mental health problems among university students [7, 8]. Therefore, the objective of the study was to determine the prevalence of IA and its association with life satisfaction and other factors among university students.

Methods

Study design and study settings

This is a cross-sectional study, and data were collected from four universities located in four divisions of Bangladesh from November 2023 to January 2024. The universities are Dhaka University, Rajshahi University, Khulna University, and Begum Rokeya University. These universities have approximately 1,30,000 students from various regions of Bangladesh.

Sample size and sampling method

Using the equation, $(z^2pq)/d^2$ [17], where $z=1.96$ (95% CI); p = prevalence estimate (0.271) [5]; $q=1-p$; and $d=10\%$ of 0.027 the calculated sample size was 1,033. Multistage clustered sampling was used to select the sample for the study. Firstly, we randomly selected four divisions from the eight divisions. Secondly, we

randomly selected one university from each division. Thirdly, eight halls from Dhaka University (four males and four females) and Rajshahi University (four males and four females), two halls each from Khulna University (one male and one female) and the Begum Rokeya University (one male and one female), were randomly selected from all halls of the respective universities. The simple random sampling technique was applied to select 60 participants from each hall. We randomly drew participants from a list of all students residing in the male and female halls, ensuring diverse representation of the student population from each hall. Finally, the total selected sample was 1200 (600 males and 600 females), but 24 (nine males and 15 females) students did not agree to provide their data, and eight (five males and three females) students did not correctly fill in the socio-demographic information and questionnaire. Therefore, they were not included in this study. Consequently, the final sample size was 1,168 students from four universities. We considered Bangladeshi regular students but excluded students from other countries, and evening M.Phil and Ph.D. courses.

Risk factors

We considered age, sex, marital status (married or unmarried), and self-reported sleep quality (poor, average, and good), physical health status (poor, average, and good), physical activity (average minutes spent daily), social engagement (engaged or not engaged), and life satisfaction (not satisfied or satisfied).

Measuring instruments

The Internet Addiction Test (IAT)

IAT developed by Dr. Kimberly S. Young in 1998, is a 20-item self-report tool designed to measure the severity of internet dependency and its effects on daily life, including productivity, social interactions, and emotional well-being [18]. A validated Bangla version of the IAT is available that has been culturally adapted and psychometrically tested to ensure its reliability and validity among Bangladeshi populations [19]. The Bangla IAT retains the original 20-item structure and assesses the extent of problematic internet use across dimensions such as emotional well-being, time management, and interpersonal relationships. Each statement is scored from 1 to 5 (never to very often). The total score ranges from 20 to 100. For this scale, scores under 50 are considered no IA (coded 0), and scores above 50 are indicated as IA (coded 1). In this study, Cronbach's alpha for this scale was 0.86, reflecting good internal consistency.

Satisfaction with life scale (SWLS)

The SWLS was developed by Diener *et al.* [20] to measure individuals' overall life satisfaction using 5 items rated on a 7-point scale ranging from 1 (extremely dissatisfied) to 7 (highly satisfied). The total scores, which range from 5 to 35, reflect a person's global life satisfaction, and the scale has demonstrated good reliability and validity across diverse populations. The Bangla-adapted version of the SWLS was validated in Bangladesh by Shahnaz

Table 1 Descriptive characteristics and associated factors of internet addiction among university students

Variables	Participants, number (%)			Internet addiction, number (%)		
	Overall (n=1,168)	Males (n=586)	Females (n=582)	Overall (n=911)	Males (n=443)	Females (n=468)
Life satisfaction						
Not satisfied	416 (35.6)	202 (34.5)	214 (36.8)	386 (92.8) ^a	189 (93.6) ^a	197 (92.1) ^a
Satisfied	752 (64.4)	384 (65.5)	368 (63.2)	525 (69.8)	254 (66.2)	271 (73.6)
Marital status						
Married	84 (7.2)	34 (5.8)	50 (8.6)	45 (53.6) ^a	19 (55.9) ^a	26 (52.0) ^a
Unmarried	1084 (92.8)	552 (94.2)	532 (91.4)	866 (79.9)	424 (76.8)	442 (83.1)
Self-reported physical health status						
Poor	211 (18.1)	95 (16.2)	116 (19.9)	205 (91.5) ^a	91 (95.8) ^a	107 (92.2) ^a
Average	826 (70.7)	414 (70.7)	412 (70.8)	624 (76.8)	309 (74.6)	328 (89.6)
Good	131 (11.2)	77 (13.1)	54 (9.3)	82 (62.1)	43 (55.8)	33 (61.1)
Self-reported sleep quality						
Poor	345 (29.5)	163 (27.8)	182 (31.3)	321 (89.2) ^a	156 (95.7) ^a	173 (95.1) ^a
Average	677 (57.9)	338 (57.7)	339 (58.2)	489 (76.5)	255 (75.4)	268 (79.1)
Good	146 (12.6)	85 (14.5)	61 (10.5)	101 (59.8)	32 (37.7)	27 (44.3)
Physical exercise (in minutes)						
<15	629 (53.9)	295 (50.3)	334 (57.4)	532 (84.6) ^a	249 (84.4) ^a	283 (84.7) ^a
15-30	471 (40.3)	249 (42.5)	222 (38.1)	339 (72)	168 (67.5)	171 (77.0)
>30	68 (5.8)	42 (7.2)	26 (4.5)	40 (58.8)	26 (61.9)	14 (53.9)
Social engagement						
Engaged	433 (37.1)	213 (36.4)	220 (37.8)	311 (71.8) ^a	151 (70.9) ^b	160 (72.7) ^a
Not engaged	735 (62.9)	373 (63.6)	362 (62.2)	600 (81.6)	292 (78.3)	308 (85.1)

^a $P < 0.01$; ^b $P < 0.05$ (comparisons are overall-and sex-specific).

and Karim [21]. This study involved translating the scale and assessing its psychometric properties among university students. It was found that the Bangla version exhibited good internal consistency and construct validity, confirming its reliability in measuring life satisfaction in the Bangladeshi context. A higher score indicates greater life satisfaction. Here, scores of 5-20 are considered not satisfied (coded 0), while scores of 21-35 are deemed satisfied (coded 1), and this SWLS has shown good psychometric properties [22]. In this study, the Cronbach's alpha for this scale was 0.81, reflecting good internal consistency

Ethical considerations

Data collection was started after obtaining ethical approval. Purpose of the study was explained to all participants, and informed consent was obtained. All data were anonymised and kept confidential.

Statistical analysis

The characteristics of the participants were summarised using descriptive statistics. The chi-square test was utilised to examine the association between the outcome variable (IA) and the independent variables. Variables significantly associated with the IA were included as independent variables in the binary logistic model to identify the predictors of IA independent of other variables. We performed sex-stratified analysis also. The multicollinearity of the variables selected for the model was tested prior to their entry into the model. All statistical analyses were conducted using SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Statistical significance was established using a 95% confidence interval, with a 5% significance level.

Results

Participants' background and IA prevalence

All characteristics of the participants are presented in (Table 1). This study recruited 1,168 respondents. About half (50.2%) were male, and 7.2% were married. According to participants' self-reports, 19.2% had poor physical health, and 30.8% had poor sleep quality. More than six in ten (62.9%) had no social engagement. Only 5.8% spent over 30 minutes on physical activity per day. More than one-third (35.6%) did not have life satisfaction.

Overall, 78% students had IA of (males, 75.6%; females, 80.4%). Most students (92.8%) who were unsatisfied with their lives had IA compared to those satisfied with their lives (69.8%) ($P < 0.01$). Similarly, IA was significantly greater among females (80.4%), unmarried students (79.9%), those with poor physical health (91.5%), those who had poor sleep quality (89.2%), those who were not socially engaged (81.6%), and those who were sedentary (84.6%). A sex-stratified analysis also showed similar results.

Predictors of IA

A multivariate logistic regression analysis was done using all variables presented in Table 1. Results are presented in (Table 2). Individuals who were unsatisfied with life had 2.2 times (95% confidence interval (CI) 1.4 – 3.5) more IA than those who were satisfied with their lives. Unmarried individuals had 3.4 times (95% CI 2.2 – 5.4) more IA than married individuals. Individuals with poor and average physical health status had 5.9 times (95% CI 2.9 – 11.9) and 2.3 times (95% CI 1.5 – 3.6) more IA than those who rated their health as good. Similar results were found for poor sleep quality, sedentary lifestyle, and non-engagement in social activities. Social

Table 2 Adjusted odds ratios (95% confidence intervals) as obtained by multiple logistic regression analysis

Variables	Adjusted odds ratios (95% confidence intervals)		
	Overall (n=1,168)	Males (n=586)	Females (n=582)
Life satisfaction (Ref. Satisfied)			
Not satisfied	2.2 (1.4 – 3.5) ^a	2.4 (1.2 – 4.9) ^a	1.9 (1.0 – 3.6) ^a
Gender (Ref. Male)			
Female	1.2 (0.9 – 1.7)	-	-
Marital status (Ref. Married)			
Unmarried	3.4 (2.2 – 5.4) ^a	2.6 (1.3 – 5.3) ^a	4.5 (2.5 – 8.3) ^a
Self-reported physical health status (Ref. Good)			
Poor	5.9 (2.9 – 11.9) ^a	9.1 (2.8 – 29.5) ^a	4.6 (1.8 – 11.7) ^a
Average	2.3 (1.5 – 3.6) ^a	2.2 (1.2 – 3.9) ^a	2.5 (1.3 – 4.9) ^a
Self-reported sleep quality (Ref. Good)			
Poor	18.3 (9.4 – 35.7) ^a	22.2 (8.3 – 59.7) ^a	15.7 (6.3 – 39.4) ^a
Average	5.1 (3.3 – 7.9) ^a	5.0 (2.8 – 9.0) ^a	5.1 (2.7 – 9.6) ^a
Physical exercise (in minutes) (Ref. >30)			
<15	1.9 (1.0 – 3.5) ^a	1.9 (0.8 – 4.5)	2.0 (0.8 – 5.0)
15-30	1.3 (0.7 – 2.4)	1.1 (0.5 – 2.5)	1.7 (0.7 – 4.3)
Social engagement (Ref. Engaged)			
Not engaged	1.7 (1.2 – 2.4) ^a	1.4 (0.8 – 2.3)	2.1 (1.3 – 3.4) ^a

^aP < 0.05

engagement in male participants was however not statistically significant.

Discussion

The current study found a higher prevalence of IA and identified the associated factors among university students. This study revealed that 78% of participants were classified as addicted internet users, which is more than double that of the pre-COVID-19 studies [5, 9]. However, studies conducted post-COVID-19 have reported comparable rates 63% [15] and 88% [16], among adolescents and college students. The COVID-19 pandemic might have sparked overuse of the internet among university students, leading to a higher level of mental health problems [7].

The higher prevalence of IA in our study, compared to previous reports, may be due to the living conditions of the university students in our sample, who reside in hostels without familial supervision. Unlike students living with families, those in hostels in Bangladesh often experience greater independence, social isolation, and unstructured routines, which can lead to increased internet use for academic, entertainment, and social purposes [5, 23]. Previous studies in Bangladesh have shown that living with family provides more regulatory control and alternative social activities, which help reduce excessive internet use [5, 24].

The current study found that unmarried students were more likely to be addicted than married students, similar to previous studies [7]. Poor health status was a significant predictive factor of IA [8]. The present study found that poor health status was also associated with addictive internet usage. Individuals with poor sleep quality were more likely to be addicted to internet usage than good sleepers [9]. Those who engaged in physical activity for less than 25 minutes daily were more likely to have IA than those who exercised for more than one hour. This suggests that physical activity significantly decreases IA [9, 10].

Social engagements reduce isolation and introduce new friends who can enhance social support. Involvement with any organisation allows

students to achieve various goals, thereby increasing their interaction and fostering strong social support. However, studying IA is critical because it contributes to various physical health-related issues, such as high blood pressure, diabetes, headaches, and pain [8, 10], as well as mental health issues, such as depression and anxiety [7].

Strengths and limitations

Face-to-face interviews may reduce misunderstandings in answering the self-reported data, which may create advantages over the data collected online. Multistage cluster sampling gives advantages over convenience sampling. However, some limitations were in the present study: (i) the study was cross-sectional, so establishing a causal relationship was impossible; (ii) this study used self-reported data, which creates the chance of information bias or social desirability bias.

Conclusions

The results showed a significant increase in IA among Bangladeshi university students in recent years. University students with life satisfaction are less likely to experience IA. This study identifies other influential factors related to internet addiction, such as being unmarried, having poor physical health, experiencing poor sleep quality, engaging in less physical activity, and lacking social engagement. Effective interventions could be planned based on these findings

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Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: MAHM, TK, MH, MNIM, MGH. *Drafting the work or reviewing it critically for important intellectual content:* MAHM, TK, MH, MNIM, MGH. *Final approval of the version to be published:* MAHM, TK, MH, MNIM, MGH. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* MAHM.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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RESEARCH ARTICLE

Effect of concurrent chemoradiation with cisplatin versus concurrent chemoradiation with carboplatin in locally advanced carcinoma cervix: A quasi-experimental study



Syed Md. Asadul Hoque | Uday Kumar Sarkar | Mohammad Rahamatullah

Newton Kumar Sarker | Md Jamal Uddin | Md Abdul Bari

Department of Clinical Oncology, Bangabandhu Sheikh Mujib Medical University (currently, Bangladesh Medical University), Dhaka, Bangladesh

Abstract

Background: The standard approach for locally advanced cervical cancer is concurrent chemoradiation with platinum agents, preferably cisplatin. This study was aimed at comparing the treatment response and toxicity of carboplatin-based versus cisplatin-based concurrent chemoradiation in locally advanced carcinoma of the cervix.

Methods: This quasi-experimental study was conducted from September 2022 to August 2023 on 80 patients with locally advanced carcinoma cervix. Patients were divided evenly between the two arms (40 in each Arm). Arm A received weekly cisplatin 40 mg/m², while Arm B received weekly carboplatin with an area under the curve equal to 2 during external beam radiation. Then all the patients in both arms were treated by intracavity brachytherapy. Each patient was evaluated weekly during treatment and three months after the completion to assess treatment response and treatment related acute toxicities.

Results: After three months of completion of treatment, the response was statistically similar between arms [Arm A, 35 (87.5%) versus Arm B, 37 (92.5%), $P=0.71$]. In terms of toxicity, Arm B had significantly less anaemia ($P=0.03$), vomiting ($P=0.05$), and renal toxicity ($P=0.03$) than Arm A. Other toxicities such as leucopenia, thrombocytopenia, nausea, hyponatremia, radiation-induced dermatitis, cystitis, proctitis, and diarrhea were similar between arms.

Conclusion: Concurrent chemoradiotherapy with carboplatin had a similar therapeutic response to concurrent chemoradiotherapy with cisplatin in locally advanced cervical cancer. Furthermore, the carboplatin arm had lesser toxicity than the cisplatin arm in terms of anaemia, vomiting, and renal toxicity.

Key messages

In the case of locally advanced carcinoma cervix, the use of concurrent chemoradiation with carboplatin had a similar treatment response to cisplatin-based concurrent chemoradiation. Concurrent chemoradiation with carboplatin had less chance of anaemia, vomiting, and renal toxicity. Toxicities such as leucopenia, thrombocytopenia, nausea, hyponatremia, radiation-induced dermatitis, cystitis, proctitis, and diarrhea were similar between carboplatin and cisplatin-based concurrent chemoradiotherapy.

Correspondence

Syed Md. Asadul Hoque
asadulhoque85@yahoo.com

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M Mostafa Zaman
0000-0002-1736-1342

Reviewers

Md. Jahirul Islam
0000-0002-8825-1319
Anonymous
Md.Nazmul Hasan
0000-0002-5737-5124

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Declaration

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Introduction

Cervical carcinoma is the most common gynecological malignancy and is considered a major global health problem for women. It is the eighth most common cancer in the world, with an anticipated 6,04,127 cases and 3,41,831 deaths in 2020, according to the Global Cancer Observatory (GLOBOCAN) 2020 database. The incidences of cervical cancer are significantly higher in underdeveloped countries such as Sub-Saharan Africa and Southeast Asia [1]. In Bangladesh, according to the hospital cancer registry report (2018-2020), carcinoma cervix is the 2nd most common malignancy among the female population of Bangladesh [2]. The three most prevalent histologies of cervical cancer are squamous cell carcinoma (SCC), adenocarcinoma (AC), and small cell neuroendocrine carcinoma. SCC accounts for approximately 80% and AC accounts for approximately 20% of all cervical cancers [3].

Asian countries exhibit a higher prevalence of locally advanced carcinoma cervix (LACC) [4]. According to a Bangladeshi study, the majority of these patients had stage IIB disease [5]. The treatment options for cervical cancer are composed of surgery, radiotherapy, and/or chemotherapy according to the stage and performance status of patients. Radiotherapy plays a vital role in the management of LACC. Both external beam radiation therapy (EBRT) and intracavitary brachytherapy (ICRT) are used as radiotherapy. According to the National Comprehensive Cancer Network (NCCN) guideline, the recommended treatment choice for locally advanced carcinoma cervix is concurrent chemoradiation (CCRT), which includes pelvic external beam radiotherapy concurrent with platinum agents, preferably cisplatin, followed by intracavity brachytherapy [6]. Cisplatin-based CCRT is the preferred treatment option because of its established benefits in terms of overall survival and progression-free survival compared to radiotherapy alone [7, 8].

Cisplatin is a platinum complex that acts as DNA cross-linkers and reacts preferentially with N-7 guanine and blocks DNA replication, RNA transcription, and protein synthesis. Despite its proven benefit, cisplatin-induced toxicity such as nausea, vomiting, nephrotoxicity, and neurotoxicity are common, and a specific hydration policy is needed to be maintained during cisplatin administration. Carboplatin, on the other hand, is another platinum-based chemotherapy that has a similar mechanism of action as cisplatin. Compared to cisplatin, carboplatin rarely causes nephrotoxicity or severe nausea or vomiting; instead, its dose-limiting toxicity is myelosuppression, primarily thrombocytopenia [9]. In a Thai study, carboplatin showed equivalent outcomes to cisplatin in concurrent chemoradiation for locally advanced cervical cancer. Furthermore, carboplatin was associated with higher compliance and lower rates of anemia, neutropenia, and nephrotoxicity [10]. Therefore, carboplatin is often used instead of cisplatin in patients who are unable to tolerate cisplatin-related toxicity or the aggressive hydration that needs to be avoided. Since no previous study was carried out to compare the effectiveness of these two-platinum based anticancer drugs during concurrent chemoradiation of cervical cancer in our

country's perspective, the present study may aid in optimising the concurrent chemoradiation schedule in cervical cancer in Bangladesh. The objective of the study was to compare the treatment response and toxicity of concurrent chemoradiation with carboplatin to concurrent chemoradiation with cisplatin in LACC.

Methods

Design and sample size calculation

This was a quasi-experimental study and the total sample size was 84. We need 36 patients in each arm according to the following formula:

$$n = \frac{p1(1-p1) + p2(1-p2)}{(p1-p2)^2} \times (Z_{\alpha} + Z_{\beta})^2$$

where, $p1 = 0.35$, $p2 = 0.066$, $Z_{\alpha} = 1.96$, $Z_{\beta} = 1.28$ [10, 11, 12]. With 10% allowance for lost to follow up, final sample size was 40 in each arm.

Selection criteria of patients

Criteria for inclusion

Biopsy-proven squamous cell carcinoma or adenocarcinoma of the cervix in a locally advanced stage (Stage IIB to IVA).

Criteria for exclusion

Age below 20 and above 70 years old; other epithelial tumors of the cervix, including neuroendocrine tumors; patients with an Eastern Co-operative Oncology Group (ECOG) performance status of three or above; prior chemotherapy or pelvic radiation or surgery; uncontrolled concurrent medical condition; and pregnant or lactating patients were excluded.

Study design and treatment

The study was conducted from September 2022 to August 2023 at Bangabandhu Sheikh Mujib Medical University (BSMMU), Delta Hospital Limited, and Ahsania Mission Cancer and General Hospital in Dhaka, Bangladesh. At first, a total of 91 patients of LACC was assessed for eligibility. Seven patients were excluded as they did not meet selection criteria. Finally, following the application of inclusion and exclusion criteria, 84 patients were equally divided between two arms (42 patients in Arm A and 42 patients in Arm B) using purposive sampling (Figure 1). Two patients from each arm were either dropped or lost to follow up. Finally, 40 participants in each arm were analysed.

Patients of Arm A were treated by concurrent chemoradiation (CCRT) with weekly cisplatin at a dose of 40 mg/m² intravenously. Patients of Arm B were treated by concurrent chemoradiation (CCRT) with weekly carboplatin intravenously at a dose of Area Under the Curve (AUC) equal to 2 using the Calvert formula. As a part of CCRT, all patients received pelvic radiotherapy to the primary tumor and pelvic lymph nodes at a total dose of 50 Gy in 25 fractions by the three-dimensional conformal radiation therapy technique. After pelvic radiation with EBRT, all the patients of both arms were treated with ICRT. Three insertions (one insertion per week) of ICRT and 7 Gy for each insertion were given.

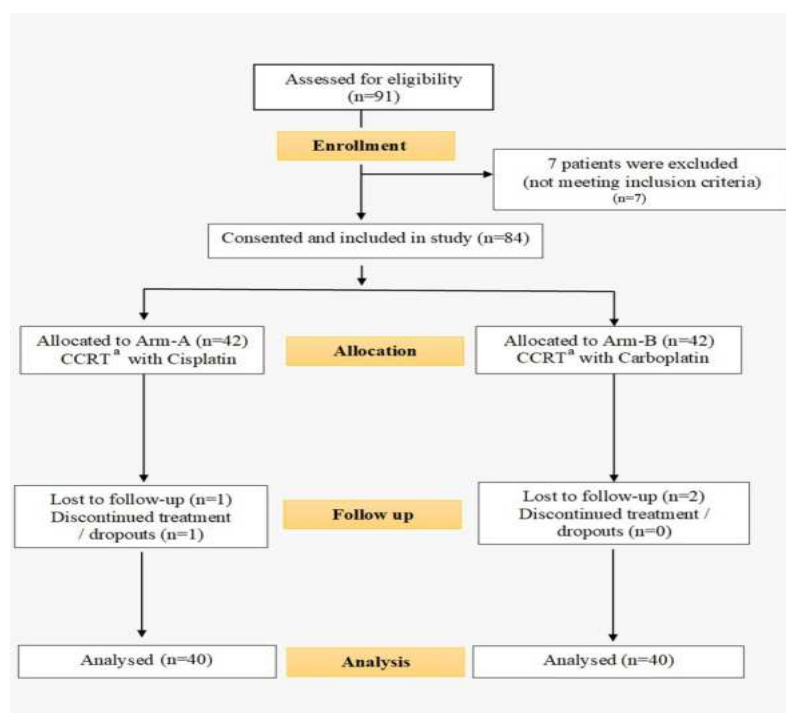


Figure 1 Concurrent chemoradiative patient enrollment, allocation, follow-up, and analysis

^aCCRT indicates concurrent chemoradiation

Assessment and data collection

In this study, outcome variables are treatment responses and acute toxicities. Patients of both arms were assessed weekly during CCRT, starting from the onset of radiotherapy. Response evaluation was done during and after treatment. The final responses were documented 3 months after completion of all therapy. To assess the tumor response to the radiotherapy treatment, Response Evaluation Criteria in Solid Tumors (RECIST) were followed [13]. According to RECIST criteria, if there is complete disappearance of all target lesions, it is mentioned as complete response

Table 1 Characteristics of the concurrent chemoradiative patients

Characteristics	Total (n=80)	Arm A (CCRT ^a with Cisplatin) (n=40)	Arm B (CCRT ^a with Carboplatin) (n=40)	P
Age (years), mean (SD) ^a	51.5 (9.1)	52.0 (8.8)	50.9 (9.4)	0.59
ECOG Performance Status				
ECOG 0	62 (77.5)	32 (80.0)	30 (75.0)	0.84
ECOG 1	14 (17.5)	6 (15.0)	8 (20.0)	
ECOG 2	4 (5.0)	2 (5.0)	2 (5.0)	
Stage				
Stage IIB	44 (55.0)	23 (57.5)	21 (52.5)	0.96
Stage IIIA	3 (3.8)	2 (5.0)	1 (2.5)	
Stage IIIB	7 (8.8)	3 (7.5)	4 (10.0)	
Stage IIIC	9 (11.3)	4 (10.0)	5 (12.5)	
Stage IVA	17 (21.3)	8 (20.0)	9 (22.5)	
Histological type				
Squamous cell carcinoma	73 (91.3)	37 (92.5)	36 (90.0)	0.99
Adenocarcinoma	7 (8.8)	3 (7.5)	4 (8.8)	
Histological differentiation				
Well differentiated	11 (13.8)	5 (12.5)	6 (15.0)	0.87
Moderately differentiated	60 (80.0)	31 (77.5)	29 (72.5)	
Poorly differentiated	9 (11.3)	4 (10.0)	5 (12.5)	

^aAge in mean and standard deviation, all others are number (%). ^aCCRT indicates concurrent chemoradiation

(CR), if there is 30% or more reduction of size of all target lesions it is mentioned as partial response (PR), 20% or more increase size of target lesions is mentioned as progressive disease (PD) and finding in-between PR and PD is stated as stable disease (SD). Acute and late hematological toxicities (both hematological and non-hematological), if present, were recorded using toxicity criteria of the radiation therapy oncology group [14]. To gather information, a data collection sheet was employed.

Ethical considerations

After Institutional Review Board (IRB) approval from BSMMU, permission was taken from Department of Clinical oncology, BSMMU, Delta Hospital Limited, and Ahsania Mission Cancer and General Hospital in Dhaka, Bangladesh. The study was carried out in line with the Helsinki Declaration and good clinical practice guidelines. All patients were given an explanation of the study, including the risks and benefits. They were also informed that if any complication arises due to the intervention, they will avail treatment for that particular complication free of cost. It was also explained to them that they have the right to refuse or accept to participate in the study. Before each patient's involvement in the study, signed informed consent was obtained from them. All data obtained during the study period from the patient was kept confidential.

Table 2 Assessment of treatment response at three months after completion of treatment

Treatment Response	Total (n=80)	Arm A (CCRT ^a with Cisplatin) (n=40)	Arm B (CCRT ^a with Carboplatin) (n=40)	P
Complete Response ^a	72 (90.0)	35 (87.5)	37 (92.5)	0.71
Partial Response ^b	8 (10.0)	5 (12.5)	3 (7.5)	

^aComplete disappearance of all target lesions as per RECIST criteria; ^b30% or more reduction of size of all target lesions as per RECIST criteria; ^cCCRT indicates concurrent chemoradiation

Statistical analysis

Data analysis was done according to the objectives of the study using the SPSS (Statistical Package for Social Science) software program for Windows, version 26.0. In this study, quantitative variables (age) were compared by the *t* test and qualitative variables were compared by fisher's exact test. The results of the test were *P* less than 0.05 was considered statistically significant. Two patients in each arm did not complete the treatment or were lost to follow up (Figure 1). Therefore, 40 patients were analysed per-protocol in each arm.

Locally advanced carcinoma cervix

According to the International Federation of Gynecology and Obstetrics (FIGO), LACC is defined as stages IIB–IVA, which is assessed by clinical examination, imaging and pathological findings.

Results

The mean (standard deviation) of age of the 80 participants in both arms was 51.5 (9.1) years. In Arm A, the mean age was 52 (8.8) years, while in Arm B, the

Table 3 Assessment of treatment response at 3 months after completion of treatment

GIT toxicity	Total (n=80)	Arm A (CCRT ^a with Cisplatin) (n=40)	Arm B (CCRT ^a with Carboplatin) (n=40)	P
Nausea				
Grade 0	58 (72.5)	25 (62.5)	33 (82.5)	0.06
Grade 1	15 (18.8)	9 (22.5)	6 (15.0)	
Grade 2	7 (8.8)	6 (15.0)	1 (2.5)	
Vomiting				
Grade 0	71 (88.8)	32 (80.0)	39 (97.5)	0.046
Grade 1	6 (7.5)	5 (12.5)	1 (2.5)	
Grade 2	3 (3.8)	3 (7.5)	0 (0)	
Proctitis				
Grade 0	71 (88.8)	35 (87.5)	36 (90.0)	0.99
Grade 1	5 (6.3)	3 (7.5)	2 (5.0)	
Grade 2	4 (5.0)	2 (5.0)	2 (5.0)	
Diarrhea				
Grade 0	67 (83.8)	33 (82.5)	34 (85.0)	0.82
Grade 1	8 (10.0)	5 (12.5)	3 (7.5)	
Grade 2	5 (6.3)	2 (5.0)	3 (7.5)	

^aCCRT indicates concurrent chemoradiation

mean age was 50.9 (9.4) years. Nearly two-thirds of all participants (77.5%) had an ECOG performance status score of 0. The majority of the patients in both arms were at stage IIB, with 57.5% in Arm A and 52.5% in Arm B. The vast majority of the patients in both arms were diagnosed with squamous cell carcinoma: 92.5% and 90% for Arms A and B, respectively. Most of the patients in both arms had the histology of a moderately differentiated tumor (77.5% and 72.5% in Arms A and B, respectively) (Table 1).

Final treatment response was evaluated 3 months after completion of treatment by using RECIST criteria. In the final evaluation, a complete response was seen in 35 patients of Arm A and 37 patients of Arm B. Five patients in Arm A and 3 patients in Arm B

had partial responses. There was no statistical difference between these treatment responses in both arms ($P=0.71$) (Table 2).

Regarding hematological toxicity, the severity of anaemia was higher in Arm A compared to Arm B. Seven, 9, and 2 patients in Arm A developed grade 1, grade 2, and grade 3 anaemia, respectively, whereas 6 and 2 patients in Arm B developed grade 1, grade 2 anaemia, respectively. This finding was statistically significant between the two arms ($P=0.03$). Regarding leucopenia and thrombocytopenia, Arm A had a higher prevalence of leucopenia of all grades, whereas Arm B had a higher prevalence of thrombocytopenia. However, these findings were not statistically significant between the two arms.

In terms of Gastrointestinal tract (GIT) toxicity, there was a higher prevalence of nausea and vomiting in Arm A. Three patients and 5 patients in arm A experienced grade 1 and grade 2 vomiting, respectively. One patient experienced grade 1 vomiting in Arm B. There were no grade 2 vomiting episodes in Arm B. This finding was statistically significant between the two arms ($P=0.046$). Proctitis and diarrhea were two other GIT toxicities that were observed in both groups; however, the findings did not reach statistical significance (Table 3).

In respect of renal toxicity, Grade 1 renal toxicity was seen more in Arm A. 8 patients in Arm A and 1 patient in Arm B developed grade 1 renal toxicity. This finding was statistically significant between the two arms ($P=0.03$). On the other hand, there was almost the same distribution of dermatitis, cystitis, and hyponatremia in both groups (Table 4).

Discussion

CCRT with cisplatin is the current standard in the treatment of LACC because it showed therapeutic benefits compared to radiotherapy alone in various clinical trials [15, 16, 17]. However, many patients cannot receive cisplatin, especially due to pre-existing renal impairment. Therefore, several chemotherapeutic agents that have less nephrotoxicity, including carboplatin, has been investigated during CCRT. In this study, we compared the treatment response and toxicity of carboplatin with cisplatin during CCRT in LACC patients.

In our study, we found that treatment responses in LACC patients were similar in both arms at 3 months after completion of treatment. The complete response rate in Arm A was 87.5%, whereas the complete response rate in Arm B was 92.5%. Several studies showed that carboplatin and cisplatin based CCRT had comparable locoregional control [10, 18, 19]. A retrospective observational study involving 250 patients, 121 in the carboplatin- and 129 in the cisplatin-based CCRT, was carried out by Valdiviezo *et al.* in 2016. They observed that the cisplatin arm had a complete response rate of 85%, while the carboplatin arm had a complete response rate of 71% [20]. A study conducted by Katanyoo *et al.* on 148 carcinoma cervix patients found that carboplatin-based CCRT had a complete response rate of 95.9% [21]. Both studies used the same dose of carboplatin concurrently with EBRT as our study used.

The main reason to consider carboplatin over cisplatin during CCRT is its toxicity profile. Cisplatin, a platinum drug, can produce severe nephrotoxicity,

Table 4 Non-GIT toxicities during treatment in both arms

Hematological toxicities	Total (n=80)	Arm A (CCRT ^a with Cisplatin) (n=40)	Arm B (CCRT ^a with Carboplatin) (n=40)	P
Anaemia				
Grade 0	54 (67.5)	22 (55.0)	32 (80.0)	0.03
Grade 1	13 (16.3)	7 (17.5)	6 (15.0)	
Grade 2	11 (13.8)	9 (22.5)	2 (5.0)	
Grade 3	2 (2.5)	2 (5.0)	0 (0.0)	
Leucopenia				
Grade 0	55 (68.8)	24 (60.0)	31 (77.5)	0.16
Grade 1	12 (15.0)	6 (15.0)	6 (15.0)	
Grade 2	10 (12.5)	8 (20.0)	2 (5.0)	
Grade 3	3 (3.8)	2 (5.0)	1 (2.5)	
Thrombocytopenia				
Grade 0	62 (77.5)	35 (87.5)	27 (67.5)	0.11
Grade 1	14 (17.5)	4 (10.0)	10 (25.0)	
Grade 2	4 (5.0)	1 (2.5)	3 (7.5)	
Hyponatremia				
Grade 0	70 (85.0)	34 (85.0)	36 (90.0)	0.78
Grade 1	7 (10.0)	4 (10.0)	3 (7.5)	
Grade 2	3 (5.0)	2 (5.0)	1 (2.5)	
Renal toxicity				
Grade 0	71 (88.8)	32 (80.0)	39 (97.5)	0.03
Grade 1	9 (11.3)	8 (20.0)	1 (2.5)	
Dermatitis				
Grade 0	73 (91.3)	37 (92.5)	36 (90.0)	0.99
Grade 1	4 (5.0)	2 (5.0)	2 (5.0)	
Grade 2	3 (3.8)	1 (2.5)	2 (5.0)	
Cystitis				
Grade 0	75 (93.8)	38 (95.0)	37 (92.0)	0.99
Grade 1	5 (6.3)	2 (5.0)	3 (7.5)	

^aCCRT indicates concurrent chemoradiation

nausea, vomiting, and myelosuppression [22]. Carboplatin, another platinum drug, is widely used to substitute cisplatin due to its comparable mechanism of action but reduced rates of toxicity, notably nephrotoxicity. In this study, we observed that carboplatin-based CCRT had significantly less anaemia, vomiting, and renal toxicity compared to cisplatin-based CCRT, while leucopenia, thrombocytopenia, nausea, hyponatremia, dermatitis, cystitis, proctitis, and diarrhea were not statistically different between two arms. A study conducted by Tharavichitkul *et al.* found that carboplatin significantly reduced anaemia and nephrotoxicity compared to cisplatin during CCRT, which is consistent with our findings. However, the trial found almost similar incidences of vomiting between the two groups, which does not correlate with our observation, possibly due to different antiemetic protocols prior to chemotherapy administration [10]. According to Kim *et al.*, carboplatin showed a higher rate of thrombocytopenia compared to cisplatin [22]. In our study, we also observed that thrombocytopenia developed more commonly in the carboplatin arm than the cisplatin arm, though this finding was not statistically significant between the two arms. Three patients in Arm A and two in Arm B experienced a one-week treatment interruption during CCRT due to toxicities. In cases of treatment interrupted patients, a gap correction of the planned radiotherapy schedule was done.

This study has some limitations. As the period of study was one-year, overall survival or late toxicities could not be evaluated. It was an unblinded, non-randomised, and quasi-experimental study so that selection bias could not be avoided.

Conclusion

In this study, the use of CCRT with carboplatin resulted in a comparable treatment response to cisplatin in LACC. In terms of toxicity, the carboplatin arm showed considerably lower rates of anaemia, vomiting, and renal toxicity than the cisplatin arm. Therefore, carboplatin-based concurrent chemoradiotherapy could be considered as an alternative option, particularly where cisplatin is contraindicated.

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Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: SMAH, MAB, UKS, MR, NKS, MJU. *Drafting the work or reviewing it critically for important intellectual content:* SMAH, MAB, UKS, MR, NKS, MJU. *Final approval of the version to be published:* SMAH, MAB, UKS, MR, NKS, MJU. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* SMAH.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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RESEARCH ARTICLE

Neutrophil gelatinase-associated lipocalin is a urine-based biomarker for diagnosing active lupus nephritis



Anthony Chakma¹ | Debatosh Paul¹ | Sheuly Ferdoushi¹ |

Minhaj Rahim Choudhury² | Md. Saiful Islam¹ |

¹Department of Laboratory Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

²Department of Rheumatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Abstract

Background: Lupus nephritis is one of the most serious complications of systemic lupus erythematosus (SLE). Urinary neutrophil gelatinase-associated lipocalin (NGAL) is a non-invasive biomarker that may aid in diagnosing active lupus nephritis. This study seeks to evaluate NGAL as a urine-based biomarker to diagnose active lupus nephritis.

Methods: This cross-sectional study was conducted in the Department of Laboratory Medicine, Rheumatology, and Nephrology at Bangabandhu Sheikh Mujib Medical University. Urine samples were collected to estimate NGAL levels using the ELISA method in the Department of Laboratory Medicine. Participants were divided into three groups: patients with SLE and active lupus nephritis, patients without nephritis, and healthy controls. Each group was comprised of 24 individuals. Patients with active lupus nephritis were classified into six categories (I to VI). ANOVA was performed to compare urinary NGAL values across the groups or categories. A receiver operating characteristic curve was created to establish the cut-off point for NGAL.

Results: The mean urinary NGAL level was 19.5 (SD 6.9), 7.2 (3.8), and 1.7 (6.5) ng/mL in SLE patients with active lupus nephritis, SLE patients without active lupus nephritis, and healthy individuals, respectively. Increasing mean levels were observed across the classes of lupus nephritis. The cut-off point for urinary NGAL in active lupus nephritis was 11.6 ng/mL, demonstrating a sensitivity of 83.3% and a specificity of 93.8%.

Conclusion: The level of urinary NGAL was elevated in SLE patients with active lupus nephritis. It could serve as a valuable biomarker for diagnosing active lupus nephritis.

Key messages

Lupus nephritis is a major cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). We observed elevated levels of urinary neutrophil gelatinase-associated lipocalin (NGAL) in patients with SLE and active lupus nephritis compared to those without lupus nephritis and healthy individuals. Urinary NGAL serves as a valuable biomarker for identifying active lupus nephritis in SLE patients.

Correspondence

Anthony Chakma
anthonychakma117@gmail.com

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M Mostafa Zaman
0000-0002-1736-1342

Reviewers

Arifa Akram
0000-0001-8829-9817
Rijwan Bhuiyan
0000-0003-0005-8889

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Introduction

SLE is a complex, multisystem autoimmune disease characterised by the production of numerous autoantibodies to cellular components and marked by complicated manifestations, ranging from detectable laboratory abnormalities to multi-organ inflammation and failure [1]. SLE predominantly affects women of childbearing age, particularly those between 15 and 44 years old [2]. It is one of the most gender-differentiated autoimmune disorders, with a female predominance of 9:1 [3].

The estimated global incidence of SLE is 5.14 per 100,000 population annually, and the estimated prevalence is 43.7 per 100,000 population [4]. In the Asia-Pacific region, the incidence of SLE ranges from 0.9 to 3.1 per 100,000 population annually, while the prevalence varies from 4.3 to 45.3 per 100,000 population annually [5]. Lupus nephritis is one of the most severe manifestations of SLE [6]. It affects up to 70% of children, and between 30% and 60% of adult SLE patients [7]. Approximately 40% of SLE patients in Bangladesh are affected by lupus nephritis [8]. It is a major cause of morbidity and mortality in SLE. It is an important predictor of poor outcomes and is often difficult to categorise [9].

Renal biopsy is considered the gold standard for diagnosing and grading lupus nephritis. This invasive procedure requires repeated testing to assess disease activity in lupus nephritis [7]. Urinary NGAL is a highly sensitive and early biomarker for kidney injury [10]. It is a 25 kDa lipocalin derived from human neutrophils [11]. As an acute-phase glycoprotein released in small amounts by neutrophils, renal tubular cells, epithelial cells, macrophages, hepatocytes, and neurons under physiological conditions, its production significantly increases in response to cellular stress [12].

Elevated urinary NGAL demonstrated a sensitivity of 95% and a specificity of 100% in diagnosing active lupus nephritis [13]. The urinary NGAL exhibited a sensitivity of 92% and a specificity of 75% when detecting active lupus nephritis in SLE patients [14]. Urinary NGAL has not been established as a global diagnostic marker for active lupus nephritis. No studies on urinary NGAL in lupus nephritis patients have been conducted in Bangladesh. This study aims to assess NGAL as a urine-based biomarker to diagnose active lupus nephritis.

Methods

Study design

This cross-sectional study was conducted from September 2023 to August 2024 in the Department of Laboratory Medicine in collaboration with the

Department of Rheumatology and Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka.

Sample and sampling of subjects

Seventy-two patients were purposively selected from the inpatient and outpatient departments of Rheumatology and Nephrology at BSMMU. They were grouped as Group I: SLE patients with active lupus nephritis, Group II: SLE patients without active lupus nephritis, and Group III: healthy individuals. SLE patients were diagnosed according to the 2019 EULAR and American College of Rheumatology criteria. Patients with diabetes mellitus, metabolic disorders, malignancies, drug-induced lupus, overlap syndrome, renal stones, urinary tract infections, those undergoing haemodialysis, or with a history of renal transplantation were excluded from this study.

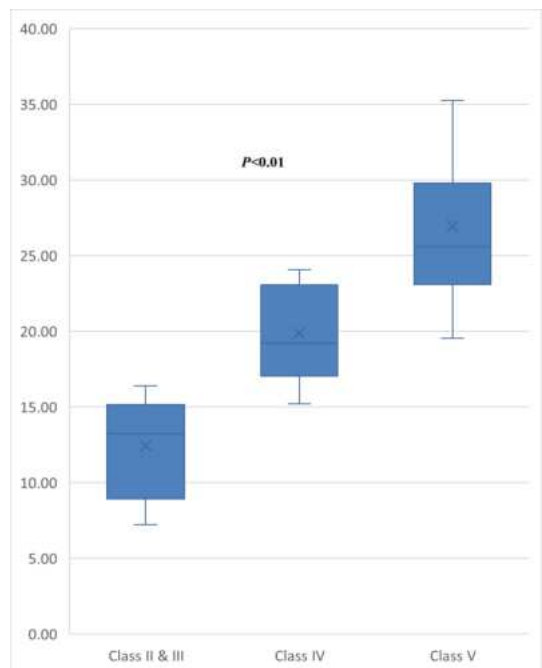


Figure 1 Comparison Urinary neutrophil gelatinase associated lipocalin according to International Society of Nephrology (ISN)/Renal Pathology Society (RPS) (2003) classification of lupus nephritis (n=24)

Class I: Minimal mesangial lupus nephritis; Class II: Mesangial proliferative lupus nephritis; Class III: Focal lupus nephritis; Class IV: Diffuse lupus nephritis; Class V: Membranous lupus nephritis; Class VI: Advanced sclerotic lupus nephritis.

The ethical standards of the Helsinki Declaration were upheld. A structured questionnaire was developed in both English and Bangla. A comprehensive investigation was carried out, and written consent was obtained from each patient. Subsequently, clinically suspected patients of active lupus nephritis were selected for renal biopsy by the nephrologists. Renal tissue was preserved in 10% formalin and sent to the Department of Pathology at BSMMU. The renal tissue was stained using hematoxylin and eosin. A histopathologist prepared the biopsy reports for lupus nephritis.

Measurement of urinary NGAL

A Random urine sample (10 mL) was collected from each participant at the Department of Laboratory

Table 1 Comparison of age and urinary neutrophil gelatinase-associated lipocalin (NGAL) among the three groups^a of participants

Variables	Group I (n=24)	Group II (n=24)	Group III (n=24)	P
Age (years), mean (SD) ^b	30.2 (13.1)	28.0 (7.6)	33.3 (9.8)	0.10
Urinary NGAL in ng/ml, median (IQR) ^c	19.2 (14.5–24.1)	6.5 (4.4–10.0)	3.98 (2.9–5.1)	<0.01

^aGroup I: SLE patients with active lupus nephritis; Group II: SLE patients without lupus nephritis; Group III: Healthy Individuals; ^bSD indicates standard deviation; ^cIQR indicates interquartile range.

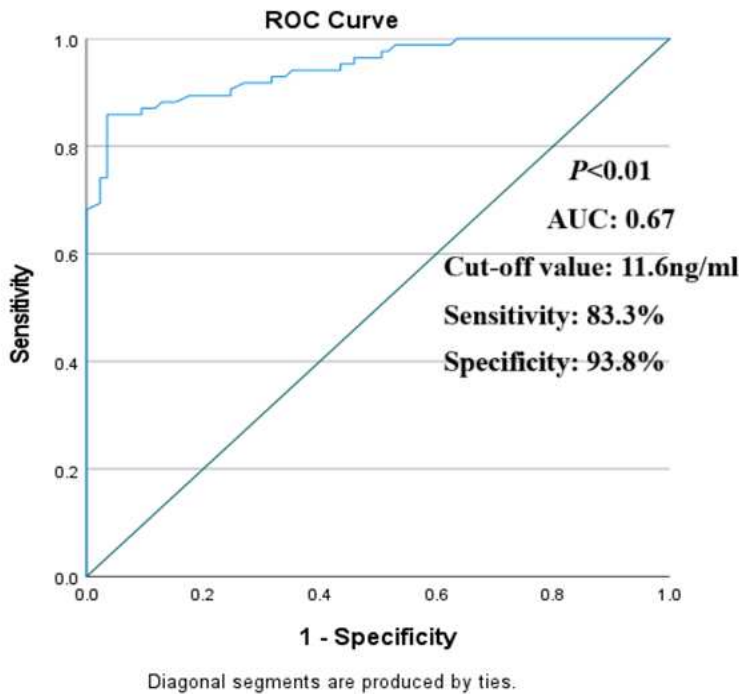


Figure 2 Receiver operating characteristic curve of urinary neutrophil gelatinase-associated lipocalin for detecting active lupus nephritis

Medicine, BSMMU. The samples were then centrifuged at 3000 rpm for 5 minutes. One millilitre of the urine supernatant was placed in an Eppendorf tube and stored at -20°C until the analysis was conducted. The urinary NGAL level was measured using the direct Sandwich-ELISA principle. The optical density of each well was determined immediately using a microplate reader set to 450 nm within 10 minutes.

Statistical analysis

Data were processed and analysed using SPSS version 27. Means, medians, and standard deviations were employed to express quantitative data. The NGAL values among three groups of participants and six classes of active lupus nephritis (I to VI) were compared using ANOVA. Urinary NGAL sensitivity and specificity for identifying biopsy-proven nephritis were calculated, and a receiver operating characteristic (ROC) curve was constructed. A $P < 0.05$ was deemed statistically significant.

Results

The mean age of the participants was 30, 28 and 33 years in groups I, II and III, respectively ($P = 0.10$). Median of urinary NGAL was 19.2 ng/ml, 6.5 and 3.9 ng/mL in groups I, II and III, respectively ($P < 0.01$) (Table 1). There were no classes I and VI in the active SLE patients. There was one patient in class II. Therefore, they were merged with class III before they were compared with classes IV and V. The NGAL showed an increasing level with the classes ($P < 0.01$) (Figure 1).

The area under the receiver operating characteristic curve of urinary NGAL was 0.67 (95% confidence interval, 0.28–0.99) ($P < 0.01$). The best cut-

off point of urinary NGAL level for detecting active lupus nephritis in SLE patients was 11.6 ng/mL. This cut-off point showed a sensitivity of 83.3% and a specificity of 93.8% (Figure 2).

Discussion

We report that urinary NGAL levels remain elevated in patients with active lupus nephritis compared to those without lupus nephritis and healthy controls. These findings provide an opportunity for the early detection of lupus nephritis, helping to prevent its progression to end-stage renal disease. NGAL demonstrates high sensitivity and specificity in predicting lupus nephritis in SLE. It is well known that early detection and treatment of lupus nephritis can enhance long-term survival in SLE [9]. The confirmatory test for lupus nephritis is a renal biopsy, which may pose risks to patients [7]. Therefore, a urinary biomarker like NGAL is easily obtainable without the risk of invasion to the patient. It can even be conducted in primary care settings of low-resource countries such as Bangladesh because it is cheaper [10]. NGAL has high potential for detecting renal injury from various aetiologies [10].

It is well established that SLE is predominantly found in females [15], much like our findings. The current study demonstrated significantly higher levels of NGAL in SLE patients with active lupus nephritis than those without. This result aligns with other studies [14]. We noted the best performance of the NGAL test at cut-off points of 11.6 ng/mL. However, a similar study indicated a cut-off point of 13.7 ng/mL [14]. Their sensitivity (92%) and specificity (75%) were comparable to our results.

The present study has inherent limitations due to a small sample size. We obtained the NGAL measurement at a single point in time. Serial measurements, along with indicators of disease activity, could provide greater insight. Understanding its response to treatment(s) would be beneficial.

Conclusion

Urinary NGAL levels are elevated in patients with SLE and active lupus nephritis compared to patients without active lupus nephritis and healthy individuals. Therefore, it may be considered a potential candidate biomarker for detecting active lupus nephritis in patients with SLE, serving as an adjunct to renal biopsy.

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Author contributions

Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: AC, DP, MRC, SF. *Drafting the work or reviewing it critically for important intellectual content:* AC, DP, SF, MSI. *Final approval of the version to be published:* DP, SF. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* AC.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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RESEARCH ARTICLE

Mental health status and associated factors prevailing among the patients having orofacial clefts in Bangladesh: A mixed method study



Tanzila Rafique¹ | Gazi Shamim Hassan¹ | Fariha Haseen²

¹Department of Orthodontics, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

²Department of Public Health and Informatics, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Abstract

Background: Patients with craniofacial anomalies endure various psychological distress. This study assessed the mental health status and related factors among the patients with cleft lip and/or palate in Bangladesh.

Methods: This case-control study was conducted at the Department of Orthodontics, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, over a four-year period. Treated and untreated patients were recruited. A validated Depression Anxiety Stress Scale 21(DASS-21) questionnaire was used to determine the depression, anxiety and stress levels. In-depth and key informants' interviews included 16 and 7 participants, respectively. Participants were taken purposively from Bangabandhu Sheikh Medical University, Dhaka, Bangladesh; Sheikh Hasina National Institute of Burn and Plastic Surgery, Dhaka, Bangladesh, and Bangladesh Specialised Hospital, Dhaka, Bangladesh.

Results: Among the 105 cleft patients, 55 were treated, and 50 were untreated. The overall (Median and interquartile range) depression rate was 2 (0–6) versus 28 (24–32), anxiety 4 (0–6) versus 16 (12–18), and stress 6 (4–8) versus 20 (16–24) in treated and untreated groups ($P < 0.01$). Untreated patients had significant association of poor mental health status (depression, anxiety, and stress), female gender (anxiety), postgraduate education (anxiety), Peri-urban/rural living areas (depression, and anxiety). Qualitative evidences supported these study findings.

Conclusion: Treated patients with cleft lip and/or palate have a better mental health status compared to those remained untreated.

Key messages

Patients with cleft lip or palate who received partial or complete treatment exhibited lower levels of depression, anxiety, and stress compared to those who did not receive any treatment. Females and individuals with higher educational attainment experienced higher levels of anxiety than males. Furthermore, patients from peri-urban and rural regions reported greater levels of depression and anxiety.

Correspondence

Tanzila Rafique
tanzila_rafiq@bsmmu.edu.bd

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M Mostafa Zaman
0000-0002-1736-1342

Reviewers

Helal Uddin Ahmed
0000-0003-4106-218X
Anonymous

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Trial registration number

Not applicable

Introduction

Oral clefts, also known as cleft lip and/or palate (CL/P), are frequent congenital disabilities. Birth abnormalities affect approximately 0.45 in 1,000 live births globally [1]. Seventy percent of newborns with CL/P have an isolated phenotype and do not have any other severe structural problems [2].

Persons with CL/P experience difficulties with eating, hearing, breathing, and speaking, and some of these also have psychological effects. The affected person reported more behavioral problems, depression, anxiety, low self-esteem and poor interpersonal skills than the unaffected people [3].

The knowledge provided by the numerous research studies conducted on various aspects of cleft lip and palate is inadequate. Cleft lip palate individuals are predicted by studies to suffer from some psychosocial functioning issues, yet little is known regarding how severe and long-lasting such problems might affect [4]. A range of physiological and sociocultural factors influence psychosocial disorders among individuals with any kind of facial abnormalities. It seems that being physically attractive is a positive attribute at every stage of life [5].

The current study assessed the mental health status among the adult treated and untreated groups of CL/P patients in Bangladesh and factors related to these issues. Data were collected from three tertiary-level hospitals located in Dhaka City, Bangladesh.

Methods

Study design and settings

This case-control study was conducted by the Department of Orthodontics at Bangabandhu Sheikh Medical University (BSMMU) for four years, 2021–2024. Samples were collected from the Department of Orthodontics of BSMMU, Sheikh Hasina National Institute of Burn and Plastic Surgery, Bangladesh and Bangladesh Specialised Hospital, Dhaka, Bangladesh. The World Health Organization's Study on Global Ageing and Adult Health (SAGE) provided the sociodemographic questions [6]. Mental health statuses of the participants were assessed by validated Bangla version of Depression Anxiety Stress Scale 21 questionnaire [7]. The reliability of the tool has been reported in terms of Cronbach's alpha. We utilised data from a qualitative study, which included key informant interviews (KII) and in-depth interviews (IDI), to support the findings of the quantitative study.

Participants

Fifty-five treated and 50 untreated adult patients, aged 15 to 30, with CL/P, were selected using purposive sampling methods, considering the inclusion and exclusion criteria. Patients with medically handicapping conditions and unwilling to participate in the study were excluded. IDIs were carried out with 16 adult treated and untreated cleft lip and cleft palate patients. KIIs were conducted with 7 key informants who were connected to the cleft care services. The interview sessions were continued until the last saturation point was reached to achieve sufficient data.

Key variables ascertainment

The data collection was initiated after a pilot study involving 15 patients. Pretesting of the qualitative interview guidelines was carried out.

Cleft lip and cleft palate

An opening or split in the upper lip that results from an unborn baby's developing facial tissues unable to close fully is called a cleft lip. An opening in the roof of the mouth known as a cleft palate develops when tissue fails to fuse during fetal development [8].

SAGE

The demographic information of SAGE, including age, sex, residence (rural or urban), marital status, level of education, and socioeconomic variables, was collected from the HDSS (Health and Demographic Surveillance System) surveillance data and verified during the interview [6].

DASS-21

It's a shorter form of the DASS-42, a self-report instrument designed for assessing negative emotional states like stress, anxiety, and depression. The Bangla version of the DASS-21 questionnaire was employed in this study to determine the participants' mental health statuses [7]. The DASS assesses the three related states of stress, anxiety, and depression, and then evaluates them clinically. There are 21 questions on it.

To indicate how much each statement applied to them over the previous week, the patient is asked to read each statement and circle a number 0, 1, 2, or 3, which indicates how much the statement applied to them over the past week. There are no correct or incorrect responses [7]. The rating scale is as follows:

0 Did not apply to me at all.

1 Applied to me to some degree, or some of the time.

2 Applied to me to a considerable degree or a good part of time.

3 Applied to me very much or most of the time.

Depression

Depressive disorder is characterised by a persistently low mood, loss of enjoyment, or disinterest in activities [9].

Anxiety

These emotions are frequently accompanied by physical tension. Anxiety disorders disrupt everyday routines and can negatively impact a person's social, familial, academic, and professional lives [9].

Stress

A feeling of anxiety or tension brought on by a challenging circumstance is known as stress. It is a normal human reaction to confront obstacles and dangers in life [10].

Ethical considerations

Ethical clearance to conduct the study was obtained from the Institutional Review Board of BSMMU. Informed written consent was obtained from each participant, explaining the purposes of the study, goals, minimal risks, and benefits. A separate identification number was given to each patient to

maintain confidentiality. Participation in the survey was voluntary, and participants had the complete right to withdraw from the study at any time without affecting their regular treatment procedures.

Statistical analysis

Data were analysed using SPSS, version 20.0. The characteristics of the study participants were expressed as percentages. The dependent variables were depression, anxiety, and stress. Fisher's exact tests assessed the distribution of depression, anxiety, and stress levels. The DASS-21 scale assessed the average score of depression, anxiety, and stress. Cronbach's alpha assessed the reliability of the test. We have conducted Kruskal-Wallis tests to check the association of depression, anxiety, and stress indicators with the characteristics of the individuals. As the three key outcome variables were categorised, we conducted logistic regression models to understand the factors influencing depression, anxiety, and stress levels.

For the IDIs and KIIs, interview sessions were scheduled and conducted with each participant, continuing until a sufficient amount of data was collected. After recording, immediate transcription was carried out. After that, the coding of transcribed data was completed, and themes were identified. Finally, data were analysed by thematic analysis procedures.

Results

a. Quantitative study findings

Out of 105 study participants, 55 were from the treated group and 50 from the untreated group. The highest proportion of patients was 25 years and above in the treated group and up to 24 years in the untreated group. The percentages of female patients in the treated and untreated groups were 38.2% and 44.0%, respectively, and those of male patients were 61.8% and 56.0%, respectively. The percentage of unmarried patients in the untreated group was 80.0. In the untreated group, 72.0% of the participants were

students, and in the treated group, this proportion was 65.5%. Most of the patients had completed college or higher education. Most of the patients in both groups were from urban areas (Table 1).

The depression, anxiety, and stress score were significantly lower among the treated patients compared to that of untreated. Untreated patients found significant association of mental health status' (depression, anxiety, stress), male gender (anxiety), postgraduate (anxiety), peri urban/rural living areas (depression, anxiety) (Table 2).

Multivariable logistic regression model for assessing the association of depression, Anxiety, and Stress score of DASS 21 items with treatment status of cleft patients after adjusting with other covariates. Depression was found to be significantly higher, by 11 times, among the untreated patients compared to the treated patients. Those who were divorced or widowed had higher depression levels compared to those who were married. Those who had completed secondary education were significantly more depressed compared to the patients who had up to the primary level of education. Patients living in urban areas had significantly higher depression scores by 3.2 times than those living in rural/peri-urban areas (Table 3).

The findings from the second model on anxiety showed that untreated patients had significantly higher anxiety levels, 6.4 times higher compared to the treated. Females had 2.1 times higher anxiety, which was statistically significant, compared to males. Patients who had postgraduate level education had significantly more anxiety compared to the patients having up to secondary level of education.

The findings from the third model on stress showed that untreated patients experienced significantly more stress than treated patients, a 3.2-fold increase. Patients in higher education had a significantly higher level of stress compared to patients at the secondary level. Other socioeconomic factors did not have a significant influence on stress levels. Patients living in urban areas had significantly higher stress levels, 3.2 times higher than those living in rural or peri-urban areas. A significant association ($P < 0.01$) of depression, anxiety, and stress with untreated CL/P patients was observed when the multiple logistic regression was done, adjusting for covariates (Table 4).

b. Qualitative study findings

Saturation for the qualitative IDIs was reached with 16 participants, comprising 8 participants who were treated and 8 participants who were untreated. Out of them, 50% were male and 50% were female in each group. KIIs included 7 participants from 3 organisations.

Eating difficulties

Some patients shared their experiences of difficulty in incising foods with their teeth. As one mentioned, "My cleft makes it difficult for me to chew or swallow hard things like fish bones, meat, or medication like tablets. I usually prefer syrup over tablets when I suffer from a fever or cold type symptoms."

Table 1 Characteristics of treated and untreated patients with cleft lip and/or palate, n (%)

Characteristics	Total (n=105)	Treated (n=55)	Untreated (n=50)	P
Age (years)				
≤24	52 (49.5)	14 (25.5)	38 (76.0)	<0.01
≥25	53 (50.5)	41 (74.5)	12 (24.0)	
Sex				
Female	43 (41.0)	21 (38.2)	22 (44.0)	0.55
Male	62 (59.0)	34 (61.8)	28 (56.0)	
Marital status				
Unmarried	73 (69.5)	33 (60.0)	40 (80.0)	0.03
Married/divorced/widowed	32 (30.5)	22 (40.0)	10 (20.0)	
Education				
Up to secondary school	51 (48.6)	13 (23.6)	38 (76.0)	<0.01
College completed and above	54 (51.4)	42 (76.4)	12 (24.0)	
Occupation				
Student/unemployed	72 (68.6)	36 (65.5)	36 (72.0)	0.34
Employed	33 (31.4)	19 (34.5)	14 (28.0)	
Living area				
Urban	67 (63.8)	36 (65.5)	31 (62.0)	0.83
Peri-urban/rural	38 (36.2)	19 (34.5)	19 (38.0)	

Table 2 Median (interquartile range) score of depression, anxiety, and stress scale of DASS 21 by characteristics of the treated and untreated patients with cleft lip and/or palate

Characteristics	Depression		Anxiety		Stress	
	Treated (n=55)	Untreated (n=50)	Treated (n=55)	Untreated (n=50)	Treated (n=55)	Untreated (n=50)
Overall	2 (0–6)	28 (24–32) ^b	4 (0–6)	16 (12–18) ^b	6 (4–8)	20 (16–24) ^b
Age group (years)						
≤24	1 (0–8)	29 (26–34) ^b	3 (0–4)	17 (14–18) ^b	6 (4–8)	20 (16–26) ^b
≥25	2 (0–6)	25 (17–27)	4 (2–6)	11 (8–14)	6 (4–8)	18 (15–19)
Gender						
Female	4 (0–10)	32 (24–35)	4 (2–6)	18 (15–20) ^a	6 (4–8)	20 (16–26)
Male	0 (0–2)	26 (24–28)	0 (0–4)	12 (10–14)	4 (4–8)	18 (16–22)
Marital status						
Unmarried	2 (0–2)	28 (24–32)	4 (0–4)	16 (12–18)	6 (4–8)	20 (18–22)
Married/divorced/widowed	2 (0–6)	28 (24–34)	4 (2–6)	15 (10–18)	5 (4–8)	16 (14–18)
Education						
Up to secondary school	6 (2–8)	29 (24–34) ^b	4 (2–6)	16 (12–18) ^b	6 (4–8)	18 (16–24) ^b
College completed or above	1 (0–4)	26 (18–28)	4 (0–6)	14 (9–17)	6 (4–8)	20 (18–23)
Occupation						
Student/unemployed	2 (0–9)	29 (25–34)	4 (2–6)	17 (18–13)	6 (4–8)	20 (17–25)
Employed	0 (0–2)	26 (20–28)	4 (0–4)	12 (14–8)	4 (4–8)	18 (16–20)
Living areas						
Urban	0 (0–2)	26 (20–30) ^b	2 (0–4)	14 (10–18)	4 (4–8)	20 (18–26)
Peri-urban/ rural	8 (4–16)	32 (26–36)	4 (4–6)	18 (14–20)	8 (4–8)	16 (16–24)

^aP<0.05; ^bP<0.01 obtained by Kruskal-Wallis test

Speaking difficulties

Speech difficulty is one of the most problematic issues for these patients. Due to the nasal voice associated with their speaking issues, they frequently face mockery from their classmates when communicating. A patient mentioned, “Since I can't speak clearly, I used to suppress myself a lot.” I keep myself sit down. I always apprehend whether everyone will understand me or not. I might have to repeat it again. I should remain silent.”

There were also a few patients who believed that it was a God-given issue, beyond their control. They desire to resolve these issues by becoming self-reliant through education.

Table 3 Odds ratio (95% confidence interval) for treatment status obtained by multiple logistic regression analyses for depression, anxiety, and stress^a using three separate models adjusted for covariates, n=105

Characteristics	n (%)	Depression	Anxiety	Stress
Patients type				
Treated	55 (52.3)	Reference	Reference	Reference
Untreated	50 (47.6)	11.0 (6.1–19.9) ^c	6.4 (4.4–9.3) ^c	3.2 (2.6–3.9) ^c
Age group (years)				
≤24	52 (49.5)	Reference	Reference	Reference
≥25	53 (50.4)	1.6 (0.8–3.1)	1.1 (0.8–1.6)	0.8 (0.6–1.1)
Gender				
Male	43 (40.9)	-	Reference	-
Female	62 (59.0)	-	2.1 (1.5–2.9) ^c	-
Marital status				
Unmarried	73 (69.5)	Reference	-	Reference
Married/ divorced/widowed	32 (30.5)	0.67 (0.4–1.1)	-	0.9 (0.7–1.2)
Education				
Up to secondary school	51 (48.6)	Reference	Reference	Reference
University/college completed	34 (32.4)	0.7 (0.4–1.2)	0.9 (0.7–1.3)	0.9 (0.7–1.2)
Postgraduate	20 (19.0)	0.9 (0.4–2.0)	1.5 (1.0–2.4) ^b	1.1 (0.9–1.5)
Living area				
Urban	67 (63.8)	Reference	Reference	-
Peri-urban/rural	24 (36.1)	3.2 (1.8–5.6) ^c	1.4 (1.1–1.9) ^c	-

^aDetermined using DASS-21 items scale; ^bP<0.05; ^cP<0.01

Orthodontic problems

Another common difficulty reported by patients was orthodontic issues. Practically all patients feel depressed about their outward attractiveness and aesthetic beauty.

One of the participants mentioned, “One thing I often hear is, ‘Hey! Your teeth are crooked; when will you address this issue?’ ”

Stigma related to health conditions

Emotional experiences

The patients' feelings about their facial anomaly were found to be uneasiness, sadness, shock, confusion, and guilt, and over time, they tried to adapt to it in their way.

According to a participant, “People often ask me about the abnormality of my appearance; I try to explain it to them normally.” It's true that I feel a lot of pain inside and become upset with the thought of why this has happened to me and feel bad about myself.”

Reactions from family, friends or the public

The majority of respondents reported having experienced some form of cruelty from friends, neighbors, family members, or relatives.

One of the patients mentioned, “My grandparents and relatives, teased me as disabled and commented that I became more handicapped looking after having my cleft surgeries and not able to hear properly. They never realise these make me sad.”

Another patient shared her experience as, “People not only imitated my way of speaking, they also try to make the shape of my lip by altering their lip position.”

Anxiety for the future, especially marriage

Though the majority of the patients were concerned about their future self-esteem and self-image, the primary concern of female patients was marriage. When the issue of marriage arises, the issue of appearance also comes into play. Demanding dowry from the bride's side is very common, as they are often considered to be esthetically compromised.

Table 4 Distribution of depression, anxiety, and stress scale by treated and untreated cleft patients, n (%)

Level of sub-scales (range)	Total (n=105)	Treated (n=55)	Untreated (n=50)	P
Depression				
Normal (0–9)	44 (42.4)	45 (81.8)	1 (2.0)	<0.01
Mild (10–13)	4 (4.2)	3 (5.5)	1 (2.0)	
Moderate (14–20)	11 (10.5)	7 (12.7)	8 (16.0)	
Severe (21–27)	12 (11.5)	0 (-)	12 (24.0)	
Extremely severe (28+)	28 (26.8)	0 (-)	28 (56.0)	
Anxiety				
Normal (0–7)	54 (49.0)	50 (90.9)	4 (8.0)	<0.01
Mild (8–9)	8 (15.3)	4 (7.3)	4 (8.0)	
Moderate (10–14)	17 (33.5)	1 (1.8)	16 (32.0)	
Severe (15–19)	17 (34.0)	0 (-)	17 (34.0)	
Extremely severe (20+)	9 (18.0)	0 (-)	9 (18.0)	
Stress				
Normal (0–14)	60 (57.3)	54 (98.2)	6 (12.0)	<0.01
Mild (15–18)	19 (18.1)	1 (1.8)	18 (36.0)	
Moderate (19–25)	15 (14.3)	0 (-)	15 (30.0)	
Severe (26–33)	10 (9.7)	0 (-)	10 (20.0)	
Extremely severe (34+)	9 (8.6)	0 (-)	9 (18.0)	

A patient stated, "When my relatives discuss my marriage issue, they advise me that you have to sacrifice than others because you have a problem."

Key informants' experiences related to the patients' mental health status

According to most KIs, mental health status largely varies according to the patient's health conditions, severity of the clefts, socioeconomic status, social and cultural norms, beliefs and level of education. They found the most frequent causes for the lower mental health were the scheduled treatment process, lack of treatment facilities in the peripheral areas, lack of awareness and proper information regarding the available treatment options, social classes, lack of financial support, travel costs, lack of information and health system responsiveness.

A KI from the speech therapy department of BSMMU stated that "There might be some prejudices among patients from the upper class of our society, who believe that spending more money will provide them with better services, and vice versa."

One KI stated that one of the participants shared her mother's griefs by mentioning that, "My relatives often tell my mother that, this is a God gifted condition and you will commit sin by altering this condition of your child. Leave it as it is, and keep faith in your destiny."

People from higher societal levels tend to exhibit relatively high mental strength and believe that these events are actually things that happen by God to test people and that everything is going according to God's plan, as one KI stated.

A common experience was shared by all KIs that female patients experience more worries and anxieties about their conditions and face more socio-cultural difficulties compared to the males. Almost all patients who seek treatment believe that undergoing functional and cosmetic treatments will enable them to achieve an attractive look, ultimately enhancing their overall quality of life.

Discussion

Physical attractiveness plays a significant role in social settings, such as developing relationships at various stages of life. Within the current study, a considerable difference was found between the treated and untreated patients. Overall mean depression, anxiety, and stress scores were lower among the treated patients compared to the untreated patients using DASS 21, which is a validated tool. However, since the tool was not previously used among these groups, the validity of the tools was checked by CA. Depression among the patients was significantly related to gender, marital status, education, occupation and family income. Anxiety among patients with cleft lip was significantly associated with sex, marital status and occupation. Stress was significantly related to treatment status and education level. A study conducted among the Chinese CL/P patients found that the difference in proportions of depression groups was statistically significant between the CL/P group and control group. This study also found that CL/P patients suffered from severe depression [11].

The first model of regression analysis found that depression was significantly higher by 23.5 points among the untreated patients compared to the treated patients. Compared to the unmarried patients, depression was lower among the married patients by 3.5 points; however, it was significant at a 10% level of significance. Patients who had secondary incomplete education at university/college and postgraduate level of education had significantly more anxiety compared to the patients having up to primary level education. Unemployed patients had significantly higher depression scores by 6 points compared to the students. Compared to the patients living in the urban areas, patients in the peri-urban areas had significantly higher depression scores by 4.7 points.

From the qualitative IDIs, a similar scenario was also observed, where a respondent mentioned that despite having a cleft child, she did not face any comments from neighbors or relatives, as they live in a place like Dhaka city, where nobody seems to care about such issues. One of the KIs from the Sheikh Hasina National Burn and Plastic Surgery Institute, Bangladesh, mentioned that patients usually visit there, ranging from day laborers to upper-class society, and the majority of patients are from the lower and middle classes. Therefore, their physical and mental health status also varies accordingly.

The findings from the second model of regression on anxiety showed that untreated patients had significantly higher anxiety levels by 12.1 points compared to the treated patients. Females had significantly higher anxiety compared to males. In general, females' depression, anxiety and stress levels were at the extreme severe level as compared to their male counterparts. The tremendous social pressure these patients face from society makes them vulnerable [12]. From our qualitative findings, it was also evident that the primary concern and anxiety among the female patients were regarding their marriage. The KIs of every organisation shared a common experience: female patients experience more worries and anxieties about their conditions and face more socio-cultural difficulties compared to male patients.

The findings from the third model of the regression analysis showed that untreated patients experienced significantly more stress than treated patients, by 15.5 points. Patients with higher education had significantly higher levels of stress compared to those who completed primary education or less.

A cultural meta-analysis by Kathleen Hutchinson reported that people with cleft lip and palate have less psychological development than people without it, regardless of age, gender, or culture [13].

The majority of respondents often experienced cruelty from friends, neighbors, family members or relatives. One KI from the Orthodontics Department of BSMU stated that patients' social status, level of education, and presence of stigmas have profound impacts on their mental health status and treatment-seeking behaviors.

From our qualitative IDIs, it was also found that teasing was a strong predictor of lower psychosocial functioning and was more common among people with cleft lip and/or palate. Almost all patients who seek treatment believe that undergoing functional and cosmetic treatments will result in an attractive appearance, ultimately enhancing their overall social status, self-esteem, and physical and emotional well-being, as stated by the KIs.

This study will help generate evidence-based information regarding the mental health status of adult CL/P patients with associated factors by using the standard tools. Although the findings from this study cannot support the study conclusion regarding actual causal relationships, as it was based on cross-sectional data, they can be useful for establishing preliminary evidence of a causal relationship.

Conclusion

This study found a lower mental health status among the untreated CL/P patients compared to the treated group. A multifaceted approach is needed, including addressing psychological challenges, promoting positive self-esteem, and ensuring access to comprehensive medical and psychological support, as well as family support. Future studies would need to investigate causal effects using a causal effect research design.

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Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

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RESEARCH LETTER

Analysis of strengths, weaknesses, opportunities, and threats: Analytical hierarchy process based dental waste management in Odisha



Somalee Mahapatra¹ | Manoranjan Dash² | Subhashis Mohanty³

¹ Department of Prosthodontics, Institute of Dental Sciences, Siksha O Anusandhan, Bhubaneswar, Odisha, India

² Department of Information Systems and Operation Management, Institute of Business and Computer Studies, Siksha O Anusandhan, Bhubaneswar, Odisha, India

³ Department of Pathology, SUM Ultimate Medicare, Bhubaneswar, Odisha, India

Correspondence

Somalee Mahapatra
somaleemahapatra@soa.ac.in

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Tahniyah Haq
0000-0002-0863-0619

Reviewers

Prince Kerketta
0000-0003-1119-8000
Kaushik Mitra
0000-0002-8865-373X
Shamsul Gafur Mahmud

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Biomedical and dental waste includes biohazardous, hazardous, pharmaceutical, and non-hazardous materials [1]. Improper disposal poses serious health risks, including infections from Hepatitis B, Hepatitis C, and HIV. In India, approximately 300 dental hospitals and 65,000 dental clinics generate an estimated 0.33 million tons of dental waste annually, with inadequate waste management exacerbating environmental and public health concerns. The COVID-19 pandemic further underscored the need for efficient dental waste management (DWM) strategies [2].

This cross-sectional study employs a structured, data-driven SWOT-AHP (Strengths, Weaknesses, Opportunities, Threats-Analytical Hierarchy Process) approach to assess and prioritize improvements in DWM practices in Odisha. Thirty experts-including dental practitioners, hospital administrators, and public health professionals from urban and rural clinics-were selected through purposive sampling. A structured questionnaire was used to identify SWOT factors in the existing DWM system, and pairwise comparisons based on Saaty's 1–9 scale was conducted to evaluate their relative significance. The AHP method was applied to assign weights and rank the influence of each factor, ensuring logical consistency through consistency ratio (CR) calculations, with values below 0.1 deemed acceptable. The findings highlight key strengths such as regulatory compliance and skilled personnel, while underscoring weaknesses including financial constraints, inadequate segregation, and logistical

issues. Opportunities for improvement-such as digital waste tracking technologies and stronger policy support-were explored, though their lower weight in the analysis indicates underutilization. While purposive sampling was effective for capturing expert insights, the limited sample size restricts generalisability [3]. Future research should consider larger, randomised samples and incorporate real-world DWM performance data to enhance external validity and practical relevance. SWOT analysis categorises internal (strengths and weaknesses) and external (opportunities and threats) factors, while AHP ranks them based on expert evaluations. A purposive sampling technique was employed, involving 30 experts, including academics and dental practitioners. Pairwise comparisons were conducted to assess the significance of various factors, with weights assigned using the AHP method [4, 5].

The SWOT analysis revealed strengths such as administrative support, legal compliance, and trained personnel, especially in tertiary institutions. Weaknesses included inconsistent waste segregation, lack of training at the grassroots level, and high costs of disposal services. Opportunities exist in leveraging digital tracking systems, tapping into public-private partnerships, and adopting newer eco-friendly technologies. However, significant threats remain: limited waste storage space in small clinics, lack of coordination between local bodies, and high initial investment costs for newer waste processing technologies.

Key messages

The study assesses dental waste management in Odisha using a SWOT-based approach. Strengths play a key role, while financial and logistical challenges hinder efficiency. Opportunities remain underutilized. Strong management, regulatory compliance, and strategic resource allocation are essential. Future research should refine decision-making for sustainable waste disposal and reduced health risks.

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Table 1 SWOT analysis with key factors and weights

Category	Key Factors	Weight
Strengths	Strong management support, skilled workforce, compliance with legal regulations	0.338
Weaknesses	Logistical complexity, inadequate segregation, financial constraints	0.13
Opportunities	Industry collaboration, environmental policies, new technology	0.094
Threats	Limited space, lack of coordination, high investment risk	0.329

Technological innovations such as real-time waste tracking systems, barcode-based segregation, and automated auditing tools can significantly enhance DWM efficiency. Policy-level initiatives, including stricter enforcement of biomedical waste rules and incentives for eco-friendly disposal units, offer systemic reform possibilities. The inclusion of these elements could lead to scalable improvements. The SWOT-AHP analysis revealed that strengths had the highest weight (0.338), highlighting their dominant role in DWM effectiveness. Threats (0.329) and weaknesses (0.13) were notable concerns, while opportunities (0.094) had the least impact. AHP-based ranking identified financial issues (GW: 0.15), data incompleteness (GW: 0.148), and logistical complexities (GW: 0.14) as the most pressing challenges requiring immediate attention.

The results warrant strong management and regulatory compliance, which is crucial for sustainable DWM. Weaknesses such as financial and logistical constraints hinder effective waste disposal. Opportunities include leveraging technology for waste tracking and fostering industry-government partnerships [1, 6, 7]. Enhancing waste segregation and logistics is essential for reducing health and environmental risks. Global best practices, such as efficient waste management systems, can be adapted to improve Odisha's waste management. The SWOT-AHP approach offers a structured framework for evaluating and refining the process. While strengths provide a strong foundation, weaknesses and threats present key challenges. Strategic resource allocation based on this analysis can enhance waste management practices [1, 6, 7]. Future research should consider additional variables and explore advanced methodologies to improve decision-making policies.

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Data availability statement

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CASE REPORT

Barraquer–Simons syndrome: A case report

Mita Dutta¹ | Munira Afroz Siddika¹ | Mohammad Aminul Islam² | Hurjahan Banu¹ ¹Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh²Department of Endocrinology, National Academy for Planning and Development, Dhaka, Bangladesh

Correspondence

Mita Dutta

mitadutta42@gmail.com

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0000-0002-0863-0619

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Introduction

Barraquer-Simon syndrome (BSS) is an acquired partial lipodystrophy characterised by bilateral symmetrical loss of fat from the upper extremities [1]. Although mutations in the lamin B2 gene have been reported, they are not definitive for diagnosis [2]. These patients exhibit less pronounced features of insulin resistance compared to other lipodystrophies [3]. Diagnosis of this rare condition can be done by the presence of the essential component of the disease along with other supporting evidence [4].

Case description and management

A 23-year-old Bangladeshi female, the second offspring of healthy, non-related parents, was referred to the endocrinology department for facial fat loss. She had oligomenorrhea since the onset of her menarche. At puberty, she noticed a gradual decline in her facial adipose tissue. Apart from viral illness in her teen years, she had no significant family or drug history. On physical examination, she had large zygomatic arches and disappearance of buccal fat pads (Figure 1). She had mild hirsutism, mild acanthosis nigricans, and umbilical hernia. Her waist and hip circumference were 69 and 90 cm, respectively. There were no features of autoimmune disorders, clitoromegaly or hepato-splenomegaly. Her routine blood, urine tests, and hormonal profiles were within normal limits. Her antinuclear antibody was also negative. She had dyslipidemia in the form of low high-density lipoprotein (cholesterol (40 mg/dL), high low-density lipoprotein cholesterol (230 mg/dL), and a marginally elevated triglyceride level (351 mg/dL). Her complement C3 level was low at 0.767 g/L

(reference ranges 0.9-1.8 g/L). Although her glycemic profiles were within normal limits, she had elevated fasting insulin level of 35.36 micro U/mL (reference values: 3.21-16.32 micro U/mL) and an elevated homeostatic model assessment for insulin resistance of 6.37 (reference ranges: <1.9). Fat mass was measured using a dual-energy X-ray absorptiometry scan. She was treated with pioglitazone to improve the distribution of fat in her body. Rosuvastatin was started to treat her dyslipidemia. She was also counseled about diet, exercise, and lifestyle changes.

As this young woman was facing distress due to her facial appearance, we referred her to a plastic surgeon for facial fat grafting to enhance her appearance. We kept her on regular follow-up to monitor her metabolic and renal parameters as there is an increased chance of development of chronic kidney disease due to membranoproliferative glomerulonephritis.

Discussion

BSS is rarely observed in Asian countries, with only 250 cases reported in the literature [3, 5, 6]. To our knowledge, no comparable cases have been recorded from Bangladesh thus far.

BSS has a female preponderance, with a median age of presentation at 25 years [4]. This disease is believed to have originated from unknown causes, but it exhibits implications of viral illnesses, such as chickenpox and measles, as well as autoimmune associations with systemic lupus erythematosus (SLE), vasculitis, and other conditions. Although 80% of cases are associated with autoimmune diseases, most cases can develop them many years after the initial diagnosis of lipodystrophy (systemic lupus

Key messages

Barraquer–Simons syndrome is a rare condition characterised by the loss of upper body fat and hypertrophy of lower body fat, along with pronounced psychological stress due to facial fat loss but less pronounced features of insulin resistance and its complications. Pioglitazone and cosmetic surgery are the primary treatment options.

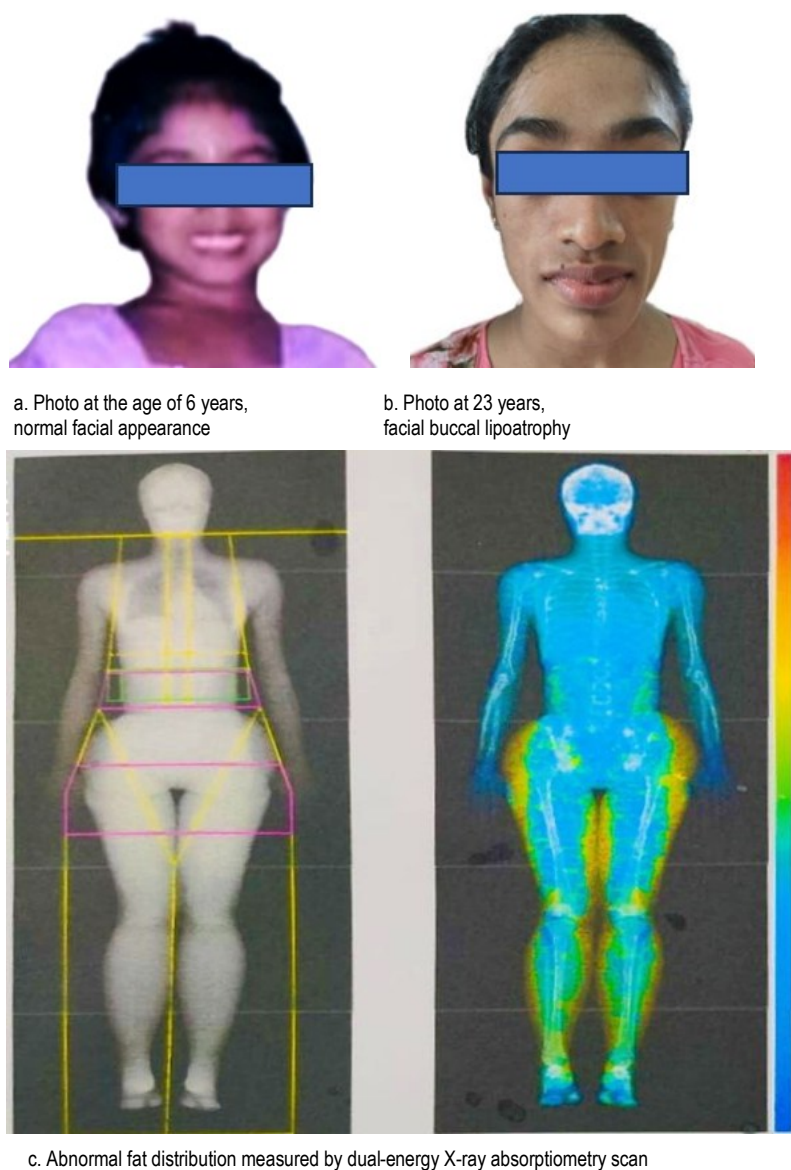


Figure 1 Characteristic features of Barraquer-Simons syndrome.

Yellow color represents increased fat mass in lower body.

erythematosus, 4–37 years; vasculitis, 17–28 years) [4]. BSS is atypical from other lipodystrophies. Although the predominant abnormality is hypertriglyceridemia, hypercholesterolemia can be present in a minority of cases [4].

The diagnosis of BSS was made using the recognised standards of Mishra *et al.*, in which the hallmark feature is the loss of fat from the face and chest, accompanied by the deposition of excess fat in the hips, thighs, and legs. These physical findings can be confirmed by the imaging results of a dual-energy X-ray absorptiometry scan, which is considered the gold standard for measuring body fat [4]. Evidence of insulin resistance and hypocomplementemia enhances further confirmation. Most authors suggested a finding of low complement in the cases of BSS [4, 5].

In cases of BSS, patients mainly raise concern about their facial appearance. This finding is absent

in cases of facial puffiness due to chronic kidney disease as there is an association with membranoproliferative glomerulonephritis [4]. However, only 22% of cases developed it after a median of 8 years following the onset of lipodystrophy [4].

Pioglitazone has particular importance in cases of acquired partial lipodystrophy as it improves fat distribution and is associated with a reversal of chronic inflammation and insulin resistance [5]. Cosmetic restoration through autologous fat grafting is a promising treatment option, with sustained positive outcomes observed in follow up among patients with BSS [6].

BSS is a rare condition that has profound psychological and clinical effects; therefore, the authors emphasise the importance of detecting and evaluating patients with acquired partial lipodystrophy.

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We confirm that the data supporting the findings of the study will be shared upon reasonable request.

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CASE REPORT

Percutaneous epidural balloon decompression and neuroplasty by ZiNeu catheter in lumbar spinal stenosis patient in Bangladesh: A case report

Rajat Shuvra Das¹ Sanjoy Kumar Saha¹ Panna Lal Saha²Jin-Woo Shin³AKM Akhtaruzzaman¹

¹Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (currently, Bangladesh Medical University), Dhaka, Bangladesh

²Department of Anaesthesiology, Critical Care and Pain Medicine, National Institute of Burn and Plastic Surgery, Dhaka, Bangladesh

³Department of Anaesthesiology and Pain Medicine, Asan Medical Center, Seoul, South Korea

Correspondence

Rajat Shuvra Das
rajatsdas1351@gmail.com

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Md Nahiduzzamane Shazzad
0000-0002-8535-4259

Reviewers

Taslim Uddin
0000-0002-2884-9212
Seong-Soo Choi
0000-0002-2333-0235
Kazi Mahzabin Arin
0009-0004-0064-3847

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Introduction

Epidural adhesions, often resulting from surgery, spinal stenosis, or disc herniation, restrict spinal nerve movement and increase neural sensitivity causing pain. Percutaneous epidural adhesiolysis (PEA), particularly beneficial for patients resistant to conservative treatments, breaks these adhesions and delivers drugs directly to the affected area [1]. Utilising RacZ or ZiNeu catheters, PEA enhances drug distribution effectiveness hindered by adhesions [2]. PEA proves more effective than traditional epidural steroid injections in lumbar spinal stenosis [3]. Percutaneous epidural balloon neuroplasty (PEBN), combining balloon decompression and neuroplasty, has shown significant pain reduction and functional improvement with minimal complications [4]. We report a case of percutaneous balloon decompression and neuroplasty with a ZiNeu catheter for lumbar spinal canal stenosis, confirming its safety and effectiveness. So far literature search, no cases of combined balloon decompression and epidural neuroplasty with the ZiNeu catheter have been reported in our country.

Case description and management

A 22-year-old female presented with a three-year history of lower back pain and right leg tingling that worsened after walking for 5 minutes and improved with rest or forward flexion. Physical examination revealed bilateral sacroiliac joint tenderness, positive

straight leg raise, at right side, Patrick's, sacral thrust, and Kemp tests. Laboratory findings showed elevated erythrocyte sedimentation rate (40 mm/hour) and C-reactive protein 8, pelvic radiography (modified Ferguson view) indicated bilateral grade 2 sacroiliitis.

MRI showed L4-L5 right paracentral disc protrusion and L5-S1 diffuse disc bulge, compressing L4-L5 traversing nerve roots, resulting in right-sided foraminal stenosis at L4-L5 and bilateral neural foraminal stenosis at L5-S1. The diagnosis was lumbar spinal canal stenosis at L4-L5 and L5-S1 caused by right paracentral disc protrusion and spondyloarthropathy. The patient received oral ibuprofen, acetaminophen, pantoprazole, and duloxetine, along with oral tofacitinib and physical exercise based on specialists' recommendations.

After one month, with minimal improvement, the patient underwent percutaneous epidural balloon decompression and neuroplasty. The procedure performed under C-arm guidance with American Society of Anesthesiologists Monitoring System, involved an 18-gauge IV line in the right arm and a 10-gauge caudal epidural needle from the ZiNeu (02) 1.55 mm catheter set up to S3 in caudal epidural space. The skin was infiltrated with 1% lidocaine before needle insertion. A mixture of 10 ml iohexol contrast dye and 1% lidocaine (1:1) identified filling defects at L5-S1 anterior epidural space and bilateral foramen and L4-L5 anterior epidural space (Figure 1). A ZiNeu balloon catheter was guided to both the anterior and posterior epidural space at the sites of

Key messages

This case demonstrates the efficacy of percutaneous epidural balloon neuroplasty with a zineu catheter for lumbar spinal stenosis in patients unresponsive to conservative treatment. This procedure facilitates adhesiolysis, reduces venous congestion, and enables localised drug delivery, resulting in pain relief and functional improvement. It may also serve as an alternative to surgical intervention or conventional epidural steroid injections.

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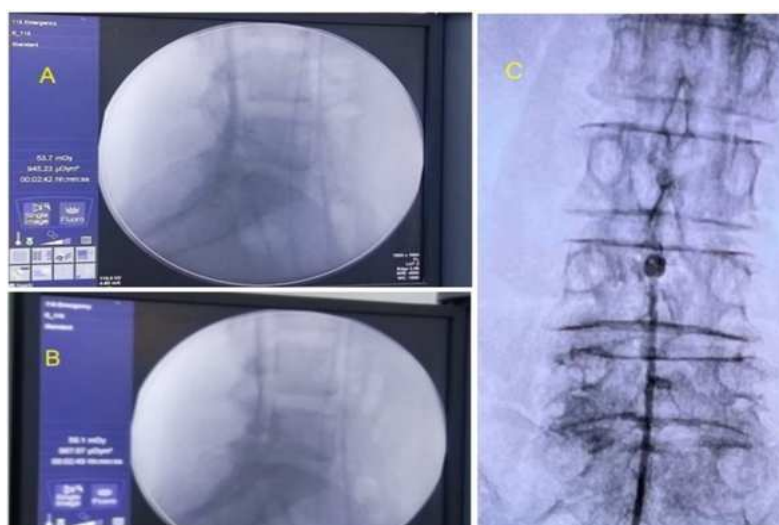


Figure 1 a) Epidurogram before percutaneous balloon decompression; b) Epidurogram after percutaneous balloon decompression; c) ZiNeu catheter at posterior epidural space with inflated balloon.

the filling defect mentioned above and, balloon was inflated with 0.1 ml iohexol dye for adhesiolysis and repeated for up to a maximum of 5 seconds at each site. Dexamethasone (3 mg) was injected into L4-L5 and L5-S1. Severe adhesions in the L5-S1 anterior epidural space necessitated 1500 units of hyaluronidase.

Although an epidurogram showed dye spread to the anterior epidural space and right L5-S1 neural foramen, balloon decompression could not be done at the L4-L5 anterior epidural space. An epidural catheter was placed in the right L4-L5 lateral canal, and 5 ml of plain 1% lidocaine was administered postoperatively. Thirty minutes later, 4 ml of 5.0% NaCl was injected after confirming the absence of motor block. The patient was discharged after one hour of satisfaction. Follow-ups over one month showed reduced pain, tingling, numbness, and improved mobility, with scores of 2/11 on the numerical rating scale, 8/35 on Paindetec, and 4 on PHQ9. The patient was able to walk for 30-40 minutes without neurogenic claudication. Physical examination revealed negative straight leg raise, and Kemp tests on the right side.

Discussion

Lower back and lower extremity pain unresponsive to conservative treatments is often linked to post-surgery syndrome, spinal stenosis, or disc herniation [5]. For patients unsuitable for or unresponsive to surgery and epidural injections, percutaneous adhesiolysis may be an effective alternative [6]. PEA alleviates pain and improves function by disrupting epidural adhesions and restoring nerve mobility.

Studies show PEA's efficacy in managing lumbar spinal stenosis, chronic disc herniation, and post-lumbar surgery syndrome [7]. The ZiNeu catheter's balloon technology aids adhesiolysis and decompression, enhancing epidural drug delivery and expanding stenotic areas. This intervention increases nerve root mobility and reduces neurogenic claudication symptoms [8].

Epidurography is crucial for identifying filling defects from adhesions and assessing procedural efficacy. A study reported transforaminal balloon treatment increased epidural space in the intervertebral foramen by 28% and lumbar foramen canal volume by 98% [9]. Research shows significant pain relief and functional improvement with balloon decompression. In our case, improvement confirmed the safety and effectiveness of this minimally invasive procedure.

The combined balloon decompression and adhesiolysis approach using the ZiNeu catheter offers a promising alternative for managing chronic lumbar spinal stenosis, providing long-term relief and functional recovery while minimising risks.

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Author contributions

Manuscript drafting and revising it critically: RSD, SKS, AKMA. *Approval of the final version of the manuscript:* RSD, SKS, PLS, JWS, AKMS. *Guarantor accuracy and integrity of the work:* RSD, SKS, PLS, JWS, AKMA.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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CASE REPORT

Conversion disorder with psychogenic vomiting and coexisting organic etiology in an adolescent: A case report



Tanbir Ahmed¹ | Sifat E Syed¹ | Afsana Benta Anowar² | Syeda Rawnak Jahan¹ | Nahid Mahjabin Morshed¹

¹Department of Psychiatry, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

²Department of Psychiatry, National Institute of Mental Health, Dhaka, Bangladesh

Correspondence

Tanbir Ahmed
tanbir200@gmail.com

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Handling editor

Tahniah Haq
0000-0002-0863-0619

Reviewer

Md Rashedul Islam
0000-0003-2101-9694
Md Nahiduzzaman Shazzad
0000-0002-8535-4259

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Introduction

Psychogenic vomiting is an uncommon, often overlooked condition linked to psychosocial stressors, without an obvious organic cause [1]. The most common diagnosis for patients with habitual postprandial or irregular vomiting is major depressive disorder (MDD), whereas conversion disorder is the most common diagnosis for patients with chronic vomiting [1, 2]. Unfortunately, psychogenic vomiting is not well addressed in the Diagnostic and Statistical Manual of Mental Disorders -5th Edition (DSM-5) and International Classification of Diseases-11th Revision (ICD-11), creating diagnostic challenges [3].

This case study examines an adolescent girl with persistent vomiting who, after diagnostic challenges, responded well to psychiatric intervention.

Case description and management

A 13-year-old eighth grader presented to the Department of Gastroenterology at Bangabandhu Sheikh Mujib Medical University following 3 months of recurrent vomiting and fatigue. She started off with infrequent but increasingly frequent episodes of vomiting, which would happen 10-15 times daily, usually in the hours following a meal or drink. The vomitus consisted of freshly consumed food, with no blood or bile, and did not improve with medication. There were no other gastrointestinal symptoms, headache, or weight loss. She had regular menstrual cycles with moderate flow. Her body mass index was

18.6 kg/m², placing her at the 50th percentile. Upon examination, the patient was normotensive, with tachycardia and mild dehydration. There were no signs of skin hyperpigmentation, calluses on knuckles, and tooth erosion. Her neurological examination was normal. Despite consulting multiple specialists, none of the treatments provided significant relief. She was also using salbutamol and fluticasone inhalers for her bronchial asthma, diagnosed five years earlier and currently in remission.

The findings of laboratory testing, such as a complete blood count, electrocardiogram, metabolic panel, and radiographic investigations (including barium swallow), were normal. Endoscopic assessment showed non-specific gastritis. Initial laboratory results showed low adrenocorticotrophic hormone (ACTH) (3.55 pg/ml) and basal cortisol (8.30 µg/dl), with cortisol levels rising to 9.5 µg/dl one hour after ACTH injection. Other hormone reports were normal.

Glucocorticoid-induced adrenal insufficiency, which was discovered upon referral to endocrinology, was probably brought on by her previous use of steroids. The clinician initially ordered hydrocortisone injection; however, this was later changed to oral hydrocortisone. One month later, hydrocortisone was stopped when cortisol levels were 14.32 µg/dl. However, her vomiting persisted, and suddenly, within 24 days of admission, she developed frequent asynchronous limb movements without bladder or bowel involvement. Neurological

Key messages

This case report highlights the diagnostic and therapeutic challenges associated with conversion disorder overlapped with organic causes in an adolescent presenting with psychogenic vomiting. The report emphasizes the importance of early identification and holistic management of conversion disorder, utilizing multi-disciplinary intervention, drugs, psychotherapy, and stress management techniques, based on clinical criteria and psychological assessment.

evaluations identified psychogenic non-epileptic seizures (PNES). Symptomatic treatment offered no improvement.

Despite improvements in adrenal function and gastritis management, her symptoms worsened. This suggested that a complex psychological or functional component may be contributing.

A psychiatry consultation eventually diagnosed her with conversion disorder, presenting with a combination of symptoms according to DSM-5. Psychiatric assessment highlighted preoccupation with illness, feelings of helplessness, and moderate stress, with no significant family history of psychiatric disorders. She never self-induced the vomiting and thought her weight was ordinary. The treatment plan combined pharmacotherapy with supportive psychotherapy, relaxation techniques, stress management, and cognitive restructuring. Psychoeducation was provided to both the patient and her mother. No adverse events were reported during treatment.

After 2 months of treatment, the patient's symptoms improved. She returned to full-time school attendance and demonstrated improved social interactions and emotional well-being. Follow-up sessions confirmed sustained symptom remission.

Discussion

The case report outlines the process of excluding other causes of vomiting through laboratory tests and evaluations. Organic causes were ruled out through gastroenterologist, endocrinologist, and neurologist assessments, with no signs of eating disorders or metabolic conditions in the patient.

Psychogenic vomiting is typified by the following symptoms: nausea in generalized-anxiety disorder, habitual postprandial or irregular vomiting in MDD and mixed anxiety-depressive disorder, self-induced vomiting in obsessive-compulsive disorder, and continuous vomiting in conversion disorder [2, 4], as demonstrated here. The Rome-III criteria distinguishes it from persistent idiopathic nausea, and cyclical vomiting syndrome [1, 5]. Most of the group suffer from a serious mental illness, mainly conversion disorder or MDD [2, 6]. Previous studies align with the finding that psychogenic vomiting often manifests in adolescence and may involve academic stress, perfectionism, and emotional dysregulation [1, 6]. Some patients show more than just emotional difficulties. Vomiting can develop into a habit and be regarded as a learned behavior, even though it may start as an organic or functional problem [2] (Figure 1) [7, 8]. Furthermore, since they may influence treatment choices, metabolic factors should be taken into account [5].

Corticosteroid therapy for asthma may have predisposed the patient to glucocorticoid-induced adrenal insufficiency, contributing to her initial vomiting [9]. This also links to the unstable connection between cognition, emotion, and motor control in PNES, which frequently associates with a range of psychological, psychiatric, and physical symptoms [10]. The interplay between these factors underscores the complex nature of the patient's condition.

This case illustrates the complexity of psychogenic vomiting when associated with other concomitant conditions. Early recognition of psychological influences is crucial for timely and comprehensive management, highlighting the need for a multidisciplinary approach.

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Conflict of interest

We do not have any conflict of interest.

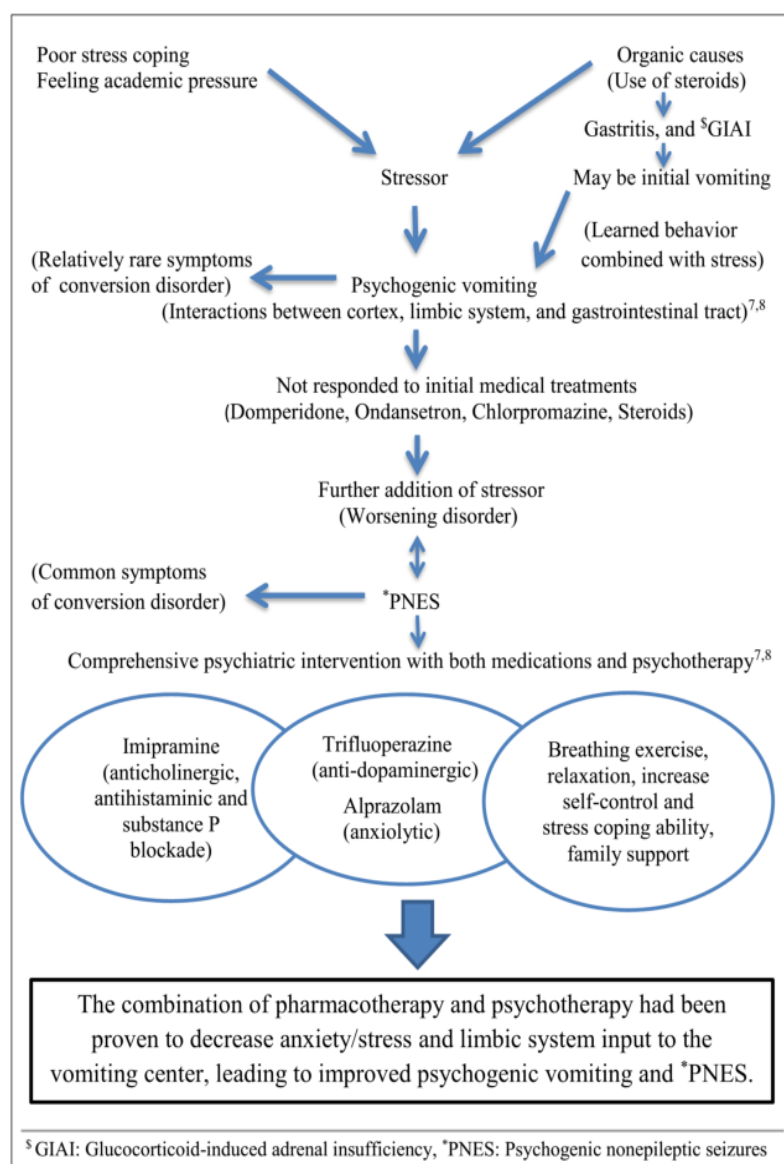


Figure 1 Flowchart of the patient's clinical event

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

None

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CASE REPORT

Dermatofibrosarcoma protuberans of the foot in a 72-year-old man: A case report



Saurabh Vighe¹ | Amritasingh Chauhan¹ | Rajesh Deshmukh¹ | Chandrashekhar Mankar²

¹Department of Pathology, Datta Meghe Institute of Higher Education and Research, Sawangi Meghe, Wardha, India

²Department of Medical Radiology and Imaging Technology, Datta Meghe Institute of Higher Education and Research, Sawangi Meghe, Wardha, India

Correspondence

Saurabh Vighe
saurabhvighe2001@gmail.com

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Handling editor

Tahniyah Haq
0000-0002-0863-0619

Reviewer

Lubna Khondker
0000-0002-7186-3749

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Introduction

Dermatofibrosarcoma protuberans (DFSP) was characterized as a keloid sarcoma by Taylor in 1890. Ferrand subsequently recognised it as a recurring dermatofibroma. Hoffman, in 1924, used the term DFSP. The 2012 National Comprehensive Cancer Network guidelines state that 'typical' DFSP is a rare low to intermediate grade sarcoma originating from fibroblasts [1, 2]. It is an intermediate-level soft tissue sarcoma that arises in the dermal layer of the skin and has the potential to infiltrate deeper structures. [3] The chromosomal translocation t(17;22)(q22;q13) between chromosomes 22 and 17 causes its cytogenetic growth, forming the fusion protein COL1A1-PDGFB [4, 5]. The standard treatment involves complete surgical removal, typically achieved through wide local excision, ensuring a tumour-free margin. In rare cases, amputation may be necessary [6].

Case description and management

A 72-year-old male presented to the surgical outpatient department of Acharya Vinoba Bhave Rural Hospital with a primary complaint of a non-healing ulcer on the left great toe for 2 months. He had no previous history of asthma, diabetes, hypertension, or tuberculosis. His family history did not reveal any significant medical conditions. Eleven months prior, the patient had noticed a non-healing ulcer on his left foot featuring everted margins, without any active discharge or bleeding. He underwent a ray amputation of the left great toe, along with prior debridement of the ulcer, followed by two sessions of platelet-rich plasma (PRP) therapy.

The ulcer healed after the operation. During examination, a single 4×4 cm ulcer was noted at the site of the left great toe amputation. No active bleeding was observed; however, slough was present alongside healthy granulation tissue. There was no local rise in temperature, and lymphadenopathy was absent. The dorsalis pedis and posterior tibial pulses were palpable. A neurological examination of the lower limbs indicated normal muscular tone and power, except for the left foot, which exhibited slight weakness. All other motor and sensory evaluations were normal. Routine investigations were within normal limits, including complete blood count, blood glucose levels, and renal and liver function tests.

Ray amputation of the metatarsal joint of the left great toe was performed. The specimen measured 8×6.5×5 cm (Figure 1). On sectioning, whitish, diffuse, homogeneous areas were identified, extending to the inferior aspect of the superior border of the great toe. Histopathological examination of the whitish area within the soft tissue revealed features suggestive of a borderline fibrohistiocytic tumour (DFSP). He was advised to maintain proper local wound hygiene, undergo daily wound dressing, and consume a high-protein diet. Regular follow-ups were recommended every six months for the next 5–6 years to monitor his recovery.

Discussion

DFSP is a rare, low-grade malignant soft tissue tumour that originates in the dermis and progressively extends to subcutaneous tissues and muscles [1]. It predominantly affects the trunk (40–50%), proximal limbs (30–40%), and head and neck

Key messages

A rare dermatofibrosarcoma protuberans (DFSP) case in a 72-year-old man underscores the challenges in diagnosing and treating this slow-growing sarcoma. Despite previous amputation, recurrence required further surgical intervention. Histopathological confirmation was essential for an accurate diagnosis. This case highlights the significance of early detection, surgical treatment, and long-term monitoring in preventing recurrence and metastases.

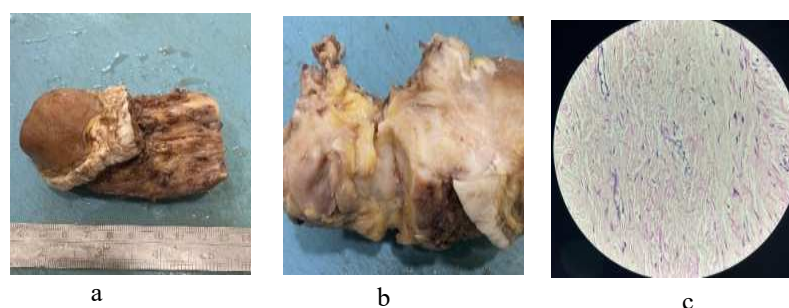


Figure 1 a) Amputated left great toe, b) Gross image of the amputated left great toe measuring 8x6.5x5 cm, c) Spindle-shaped cells arranged in a storiform pattern on a high-power field.

(10–15%); however, it can also arise in uncommon locations such as the perineum [7]. DFSP is characterised by slow growth and local invasiveness, with a low metastatic potential of less than 5% [7, 5]. When metastasis occurs, it is typically following multiple recurrences and primarily affects the lungs, while regional lymph node involvement is exceedingly rare, occurring in only 1% of cases. The overall incidence of DFSP is estimated at 6.3 cases per million people, with a slight predominance among women [8, 9]. The disease primarily affects adults between the ages of 20 and 50, while there are fewer reported cases among geriatric patients [6]. According to epidemiological reports, DFSP in the feet remains rare [5], usually involving the great toe with a long disease duration. It is difficult to diagnose and has the potential to metastasise from untreated DFSP [7, 10].

This study meaningfully contributes to the research on DFSP by presenting a rare case of an elderly patient who responded well to treatment through ray amputation. Given the low incidence of DFSP in older adults, this case underscores the importance of considering DFSP in the differential diagnosis of soft tissue tumours within this population. The successful use of ray amputation highlights its effectiveness in achieving complete tumour excision while preserving functional outcomes.

Patients frequently receive incorrect diagnoses of their soft tissue neoplasms due to confusion with conditions such as myxoid sarcoma, keloids, Bednar tumours, angiosarcoma, dermatofibromas, and spindle cell melanoma [5]. A secure diagnosis relies on testing tissue samples and conducting immune cell tests to differentiate DFSP from other diseases. The survival expectancy for patients diagnosed with DFSP remains highly favourable, as their predicted ten-year survival rate reaches 99.1%. When patients present with metastatic disease, doctors estimate their survival period to be approximately two years from the time of diagnosis.

Histopathological assessment combined with extended patient monitoring is essential for managing DFSP. Maintaining a comprehensive differential includes atypical cases of DFSP in elderly patients, as these situations require urgent medical attention. Ray amputation has proven successful in treating DFSP for this patient, as evidenced by its effectiveness in such circumstances.

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Conflict of interest

We do not have any conflict of interest.

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We confirm that the data supporting the findings of the study will be shared upon reasonable request.

Supplementary file

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COMMENTARY

When leaders fail: Exploring the role of dysfunctional leader cells in autoimmune disease pathogenesis



Falah Hasan Obayes AL-Khikani  

Department of Medical Laboratory Technology, College of Medical Technology, The Islamic University, Najaf, Iraq

Correspondence

Falah Hasan Obayes AL-Khikani
falahgh38@gmail.com

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M Mostafa Zaman
0000-0002-1736-1342

Reviewers

Chandan Kumar Roy
0000-0003-1679-9454

Sheuly Ferdoushi
0009-0009-4037-3833

Afzalun Nessa
0000-0002-4474-9836

Umme Shahera
0000-0002-8811-578X

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The concept of 'leader cells'—specialised cells orchestrating collective cell behaviours during development, tissue repair, and cancer progression—offers a compelling, yet relatively unexplored lens for examining the pathogenesis of autoimmune diseases [1]. These cells are crucial for maintaining tissue homeostasis and integrity, coordinating complex processes through mechanical force generation, signaling molecule secretion, and intercellular communication [1, 2]. Dysfunction within these critical leader cells, potentially arising from genetic predispositions, environmental insults, or pathogen interactions, can profoundly disrupt tissue equilibrium [2]. We hypothesise that such leader cell dysfunction represents a significant factor in the breakdown of self-tolerance and the subsequent development of autoimmune pathology, potentially linking tissue-level dysregulation to immune system activation, a concept often explored through mechanisms like molecular mimicry [3].

The precise mechanisms by which dysfunctional leader cells could trigger or perpetuate autoimmunity are likely multifaceted. Aberrant tissue repair responses represent a key pathway; failure of leader cells to properly orchestrate repair can lead to chronic inflammation, excessive release of damage-associated molecular patterns (DAMPs), and inappropriate exposure of self-antigens, providing triggers for autoreactive immune responses [4, 5]. Furthermore, dysfunctional leader cells might alter the local immune microenvironment through

dysregulated production of cytokines, chemokines, or extracellular vesicles, shifting the balance towards a pro-inflammatory state and impairing regulatory immune cell function [6, 7]. Specific leader cell populations have been implicated in tissues prone to autoimmune attack. For instance, in the pancreas, specialized 'hub' or 'leader' beta cells that normally coordinate islet responses could, if dysfunctional, contribute to the inflammatory milieu and beta cell destruction seen in Type 1 Diabetes [8, 9]. Similarly, compromised leader cell function during repair in epithelial tissues like the gut or skin could impair barrier integrity, potentially driving conditions like inflammatory bowel diseases or psoriasis [7, 10].

This leader cell perspective complements established autoimmune mechanisms like genetic susceptibility and environmental triggers [3]. However, significant challenges remain. Distinguishing whether leader cell dysfunction is a primary cause or a secondary consequence of the autoimmune process (cause or effect) is crucial. Experimental hurdles include the precise identification and specific manipulation of leader cells in vivo within complex tissue environments. Furthermore, the potential overlap in mechanisms between leader cells in repair and cancer necessitates caution when considering therapeutic interventions [1].

Future research employing advanced techniques like single-cell multi-omics and lineage tracing in relevant animal models is needed to dissect the role of leader

Key messages

Leader cell dysfunction, disrupting tissue repair and immune communication, presents a novel and potentially crucial mechanism contributing to autoimmune disease pathogenesis. Elucidating the specific roles and dysfunctions of leader cells in various autoimmune conditions could unveil new therapeutic targets, although significant challenges in research and therapeutic implementation remain.

cells [10]. Investigating whether enhancing leader cell function or restoring their communication with immune cells can mitigate autoimmune responses may offer novel therapeutic strategies, despite the inherent challenges [7]. Targeting strategies must be highly specific to avoid unintended consequences like promoting malignancy. In conclusion, leader cell dysfunction, disrupting tissue repair and immune communication, presents a novel and potentially crucial mechanism contributing to autoimmune disease pathogenesis. Elucidating their specific roles could unveil new therapeutic targets, although significant research and implementation challenges remain.

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I do not have any conflict of interest.

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COMMENTARY

Implementation of a pedagogical skills training programme in postgraduate medical education at Bangabandhu Sheikh Mujib Medical University: Lessons and outcomes



Bijoy Kumer Paul



Department of Public Health and Informatics, Bangabandhu Sheikh Mujib Medical University (currently, Bangladesh Medical University), Dhaka, Bangladesh

Correspondence

Bijoy Kumer Paul
bijoykumerpaul@bsmmu.edu.bd

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M Mostafa Zaman
0000-0002-1736-1342

Reviewers

Najnin Akhter
0000-0002-5560-849X

Md Rasel Ahmad
0009-0009-2936-0169

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Doctors need to learn how to teach, and residents can start developing this skill during their medical education. Teaching enhances communication with patients, junior residents, faculty, and peers. Medical residents who understand teaching and learning principles can become better learners. Medical residents should learn teaching skills, including professional values. Teaching skill is a crucial component of the medical education curriculum in Western countries. Literature suggests that residents allocate nearly 25% of their residency programmes to teaching, despite being inadequately trained for this role [1].

Universities across the globe strive to improve the teaching skills of residents, thereby enriching their educational journey and preparing them for the future. This initiative is not confined to developed nations; even developing countries such as Nigeria are incorporating medical residents into teaching positions to overcome resource limitations [2]. The duration, structure, and subject matter of these teaching programmes, nevertheless, exhibit significant variation [3]. There is unequal distribution of resources and expertise for instruction among residency programmes.

Bangabandhu Sheikh Mujib Medical University, the premier institution in Bangladesh for nurturing skilled healthcare professionals, is dedicated to providing quality medical education, research, and healthcare services. In 2009, the University introduced competency-based medical education for

postgraduate residents, featuring a 5-year training programme in clinical faculties (3-4 years for the Basic and Para-clinical Sciences) leads to the degrees MD/MS. This comprehensive programme is divided into two phases, namely Phase-A and Phase-B. Phase-A involves broad-based specialty training, while Phase-B focuses on in-depth, specialty-specific training, ensuring residents' competence and preparing them for specialty qualifications. As part of their Phase-B training, residents of Phase-B participated in a mandatory short course on the 'basics of medical education' that focused on pedagogical skill training of residents. The Division of Medical Education is responsible for this formal pedagogy skill training for the residents.

Structure of the programme

Postgraduate residents undergo a comprehensive one-month training in pedagogical skills, featuring interactive lectures conducted by qualified (MMEd degree holders) internal and external faculty members. The course covers various topics of medical education, including the introduction to medical education, formulation of educational objectives, effective teaching and learning facilitation, curriculum planning and development, basics of communication, construction of lesson plans, small and large group teaching, bedside teaching, ambulatory care teaching preparation of instructional materials, principles of assessment, and the planning and execution of assessment tools such as written, structured oral examinations, and clinical

Key messages

Bangabandhu Sheikh Mujib Medical University incorporate training on teaching methods and assessment for residents to improve ethical, technical, and scientific knowledge. Including teaching training during residency can enhance clinical skills and patient care. It's important to accurately identify teaching abilities in medical residents and help them understand effective teaching methods. Existing efforts are not enough, and with more medical residency programmes, there's a need for qualified teachers.

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Table 1 Percents of resident's feedback regarding the short course on basics of medical education (n=102)

Statements	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
The course enhanced my knowledge of the subject matter	27	65	6	0	2
The course contents, modules and structure were relevant and beneficial	26	68	3	2	1
Instructors were engaging, supportive, easy to understand, and provide a clear instruction	46	46	15	0	3
I feel competent and confident on the on the subject matter at the end of the course	15	50	27	6	2
I would recommend this course to others	47	49	3	1	0

competency assessments like objective structured practical/clinical examinations, long cases, short cases, and portfolio assessments. Faculty members deliver 2-hour-long interactive lectures on these topics, and a formative assessment (objective types of written assessments) is conducted at the end of the placement.

The residents provided feedback on the course through a semi-structured questionnaire using a 5-point Likert scale. Approximately 84% expressed overall satisfaction. Moreover, around 92% of the residents agreed that the course enhanced their knowledge, making them competent and confident in the subject matter. They found the course content relevant and beneficial, and the instructors were noted as engaging, supportive, and providing clear instructions. Ninety six percent stated their intention to recommend this course to others (Table 1). Studies showed that the evaluation of the most programmes was very positive in terms of curriculum appreciation, learning outcomes and teaching behaviour [4, 5].

Although residents gave positive feedback, there were challenges—such as lack of time (added to their workload) and a shortage of skilled trainers. The institution should prioritize teaching skill training to develop competent doctors who can also train future doctors well.

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METHODS ARTICLE

Multi-dimensional research impact assessment through bibliometrics, altmetrics, semantometrics, and webometrics



Ahmed Al Marouf¹  | Tanvir C Turin²  

¹Department of Computer Science, University of Calgary, Calgary, AB, Canada

²Department of Family Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

Abstract

Research impact assessment (RIA) has emerged as a critical approach for evaluating the societal, academic, and policy-related influence of scholarly work, particularly within the evolving landscape of Open Science. This paper provides a synthesis of quantitative RIA metrics, which offer standardised, data-driven insights into the reach and significance of research outputs. It outlines four principal methodologies: (i) bibliometrics (analyse citation patterns through indicators such as citation counts, co-citation, and bibliographic coupling); (ii) altmetrics (track online engagement and dissemination); (iii) semantometrics (assess textual contributions using semantic similarity measures); and (iv) webometrics (evaluate digital presence through web interactions and backlink analysis). While these quantitative approaches are valuable for benchmarking and strategic decision-making, they often fail to capture the nuanced societal and intellectual impacts of research. To address this limitation, the paper advocates for a hybrid assessment model that integrates quantitative metrics with qualitative methods, such as case studies and narrative analyses, to provide both scalability and contextual depth. Ultimately, the work underscores the importance of critically and judiciously interpreting RIA metrics to fully reflect the multifaceted nature of research impact across disciplines and stakeholder domains.

Correspondence

Tanvir C Turin
turin.chowdhury@ucalgary.ca

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Key messages

Employing diverse metrics—such as bibliometrics, altmetrics, semantometrics, and webometrics—allows for multifaceted and comprehensive evaluation of research impact. Each of these metrics offers unique insights into different dimensions of scholarly influence: bibliometrics primarily measure academic citation impact, altmetrics capture broader online engagement, semantometrics focus on the semantic and content-based relationships between works, and webometrics assess the online presence and visibility of research outputs.

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Research impact assessment

Research impact assessment (RIA) has become an increasingly important topic in academia and scientific communities, further underscored by the rise of Open Science practices that promote greater accessibility and transparency of research outputs [1]. RIA refers to the process of evaluating the influence and effects of research outputs on various actors, including other researchers, policymakers, and society at large [2]. The importance of measuring research impact lies in its ability to demonstrate the value of scientific endeavours, inform funding decisions, and guide future research directions.

RIA employs two main approaches

a) **The Qualitative** approach involves collecting and analysing rich, narrative-based information to understand how research findings shape behaviours, practices, and policies in nuanced ways. They provide in-depth, contextual insights into the broader societal and academic influence of research. Common methods include peer reviews, in-depth case studies, stakeholder interviews, and documentary or policy analysis. These methods capture context-specific impacts, like changes in public discourse or organisational culture, that are not reflected in numerical metrics, though they can be time-consuming and subjective. Although qualitative evaluations can be time-consuming and subjective, they offer deeper contextual understanding, revealing the breadth and complexity of research influence in real-world settings. In contrast, quantitative approaches use numerical data and statistical analyses, including bibliometric indicators and citation counts, to measure research impact. These include bibliometric indicators, citation counts, and various impact factors. This methods paper will primarily focus on quantitative RIA metrics, examining their types, applications, strengths, and limitations to provide an overview of data-driven tools for evaluating research influence.

b) **The quantitative** metrics play an integral role in assessing the reach, influence, and significance of scholarly outputs. Among the various approaches, bibliometrics focus on citation-based academic impact, altmetrics capture broader online engagement, semantometrics explore semantic and content-based relationships, and webometrics/cybermetrics gauge digital visibility and presence (Figure 1). In combination, these metrics offer a multifaceted lens through which to evaluate research influence.

Bibliometrics

Bibliometrics is indeed a common and widely used method for assessing research impact. It primarily emphasises on citation counts and publication patterns [3]. A highly cited paper in a scientific journal indicates its significant influence in that field. Bibliometrics can show how often this paper is referenced by other researchers (in terms of citation), highlighting its importance. Registering in bibliometric tools enhances the visibility and

discoverability of a researcher's work, facilitating broader academic recognition. Maintaining an up-to-date profile supports accurate attribution, fosters networking and collaboration, and is increasingly important for career advancement, funding, and institutional evaluations.

Tools/Websites

Scopus (<https://www.scopus.com/>): Scopus is one of the largest curated abstract and citation databases, covering a wide range of scientific journals, conference proceedings, and books. It includes over 76 million records, ensuring extensive coverage of global and regional scientific literature. It offers comprehensive citation data and analytics. Scopus data is widely used in research assessments, science policy evaluations, and university rankings. Its reliable and high-quality data supports large-scale analyses and benchmarking studies [4].

Web of science (<https://www.webofscience.com/>): Web of Science includes millions of records from high-quality, peer-reviewed journals, conference proceedings, and books. It covers a wide range of disciplines, including natural sciences, social sciences, arts, and humanities. It provides citation reports and impact factors for journals.

Google scholar (<https://scholar.google.com/>): Tracks citations and provides metrics like the year-wise citation counts, total citation count, h-index, i-10 index, i-100 index, article-wise citation counts, article-wise cited papers list etc. The h-index (Hirsch index) was proposed in 2005 by Jorge E. Hirsch, a physicist at UC San Diego, as a metric to measure both the productivity and citation impact of a researcher's publications [5]. It represents the number of papers (h) that have received at least h citations each [6]. For example, if a researcher has published five papers with citation counts of 250, 170, 120, 15, and 8, their h-index would be 4, as they have four papers each cited at least four times. Related metrics include the i10-index (number of papers with at least 10 citations) and i100-index (number of papers with at least 100 citations). In our example, the researcher would have an i10-index of 4 and an i100-index of 3. These indices help evaluate research quality and impact more dynamically than simple publication or citation counts alone, as they consider both productivity and influence of a researcher's work. The h-index varies between bibliometric tools because of differences in database coverage, citation-tracking methods, and the accuracy of author disambiguation. Variations in indexing criteria and update frequency also contribute to these discrepancies.

Bibliometric analysis

The analysis approach is to collect the citation data and conduct in-depth analysis using the citation counts. Some of the widely used methods in bibliometrics are citation analysis [7], co-citation analysis [8], bibliographic coupling [9] etc. Citation happens when one research paper mentions another in its references. Citation analysis [7] looks at how often a paper is cited, which can indicate its influence in a field. For example, if article "A" cites article "B", it

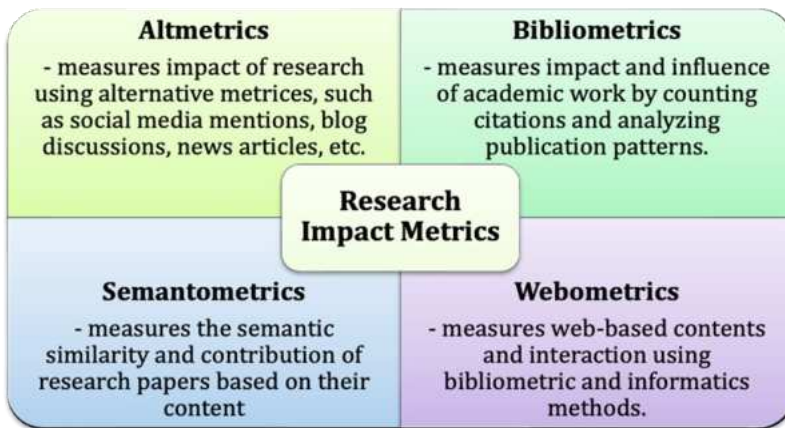


Figure 1 Research impact matrices

means that article "A" is using information from article "B". If article "B" is cited by many other papers, it is likely an important study. Co-citation occurs when two papers are cited together by a third paper. This suggests that both papers are related in content. The more often two papers are cited together, the stronger their connection. The process of finding these from various research articles is known as co-citation analysis [8]. For example, if article "C" cites both article "A" and article "B", we say that article "A" and article "B" are co-cited. If many other papers also cite them together, it suggests that they belong to the same research area. Bibliographic coupling [9] happens when two papers cite the same earlier paper. This indicates that these two papers are working with similar background research and are related. For example, if both article "A" and article "B" cite article "C", then article "A" and article "B" are bibliographically coupled. This means they are likely studying similar topics.

Altmetrics

Altmetrics, abridgement of "alternative metrics," measure the impact of scholarly work based on online interactions and mentions [10]. This includes social media shares, blog posts, news articles, and other online platforms. Unlike the bibliometrics, which focuses on academic citations and publication trends, altmetrics analyses quantitative values of online presence.

Imagine a research paper on diabetes epidemiology that gets shared widely on Twitter, Facebook, discussed in blog posts, and covered in news articles. Altmetrics would track these interactions, showing how the paper is influencing public discourse and reaching a broader audience.

Tools/Websites

Altmetric (<https://www.altmetric.com/>): Altmetric captures where and how often a research output is mentioned online over the news portals, policy documents, social media platforms (Facebook, X, Twitter etc.), Wikipedia, or any blogs. For example, as of 22 May 2025, a paper titled "Lifetime risk of diabetes among First Nations and non-First Nations people" published in Canadian Medical Association Journal had an "altmetric attention score" of 640, which places the paper in the top 5% of all research

outputs scored by Altmetric (<https://cmaj.altmetric.com/details/12089307>). This paper was mentioned in 80 news outlets, 1 policy source, 1 Facebook page, 24 X posts, etc. The overall score represents the summation of weighted counts all over online presence. This paper is in the top 5% of all research outputs scored by Altmetric and has High Attention Score compared to outputs of the same age (99th percentile).

PlumX (<https://www.elsevier.com/insights/metrics/plumx>): This is a product of Elsevier which offers insights into how research is being used and discussed across various platforms.

Semantometrics

Semantometrics evaluates research by analysing the full text of publications, rather than just counting citations [11]. It measures the semantic similarity and contribution of research papers based on their content.

By comparing the text of a new research paper with existing literature, semantometrics can assess how much new knowledge the paper contributes to its field. For instance, it can identify novel concepts or methodologies introduced by the paper. Grounded on the idea of semantic similarity-based method, Petr Knuth *et al.* developed a formula assessing the publication's contribution [11],

which is based on quantifying the semantic distance

$$\text{Contribution}(p) = \frac{\bar{B}}{A} \cdot \frac{1}{|B| \cdot |A|} \sum_{a \in A, b \in B, a \neq b} \text{dist}(a, b)$$

between publications cited by p to the publications citing p . In the above shown formulation, "B" is the set of publications citing publication 'p' and "A" is the set cited by 'p'. The sum in the equation is used to calculate the total distance between all combinations of publications in the sets "A" and "B". It is expected that the distance is calculated using semantic similarity measures on the full-text of the publications, such as with cosine similarity on TF-IDF [12] document vectors.

Tools/Websites

As of now, there is no mainstream, publicly available app or web platform where we can simply upload a publication and receive a semantometric score in the same way that one might check an Altmetric score or bibliometric citation count.

Semantometrics-python Package: The Digital Humanities Lab of Utrecht University, Netherlands developed the "semantometrics-python" package [13], which is open source. This tool analyzes the semantic content of research papers to evaluate their contribution. For example [11], the paper "The Triple Helix of university-industry-government relations" by Loet Leydesdorff (2012) had a contribution score of 0.4026, while "Search engine user behaviour: How can users be guided to quality content?" by Dirk Lewandowski (2008) had a contribution score of 0.5117. Although these two papers had similar citation counts 27 and 30, respectively- their



Figure 2 Tools used for bibliometrics, altmetrics, semantometrics, and webometrics

contribution scores differed noticeably. This highlights the value of considering contribution score in addition to citation count, as publications with similar citation numbers can vary significantly in their actual contribution.

Webometrics/Cybermetrics

Webometrics studies the quantitative aspects of the web, such as the structure and usage of websites [14]. It applies informetric methods to analyze web-based content and interactions. Analysing the number of backlinks to a university's website can indicate its online visibility and influence. Webometrics can also measure the impact of online publications and the reach of digital content.

Tools/Webites

Webometric Analyst (<http://lexiurl.wlv.ac.uk/>): Webometric Analyst is a free Windows-based program for analysis of webometrics, including link analysis, network diagrams of the links between a collection of web sites. Users can find where a specific digital object and digital collections are being connected to.

Webometrics (<https://www.webometrics.info/>) *Ranking of World Universities*: Ranks universities based on their web presence, visibility, and open access to knowledge. For Example, Harvard University has been ranked as number one university in 2024 based on its strong digital footprint for scholarly activities [15]. This approach for RIA considers factors such as the volume of scholarly content published on the web, the number of external networks linking to the institution's web domain, and overall, how accessible and influential a university's research outputs are on the internet.

The evolving role of university libraries in research impact assessment

As research impact measurement becomes increasingly complex, university libraries are well-positioned to play a more strategic role — but many require additional support, training, and resources to do so effectively. Building institutional capacity within libraries to engage with bibliometrics, altmetrics, webometrics, and scientometrics is essential. This includes investing in tools and infrastructure, developing staff expertise on digitalization and computing, and fostering cross-campus, national, and global collaborations. By equipping librarians with the knowledge and systems needed to support impact analysis, universities can ensure more meaningful, responsible, and inclusive research evaluation that reflects both academic and societal contributions. Strengthening libraries in this way also reinforces their evolving identity as active partners in research development and strategic decision-making.

Conclusions

Quantitative RIA metrics provide valuable, standardised insights into scholarly influence and reach, offering a bird's-eye view of research performance that enables comparisons across domains, institutions, and time periods. These metrics are essential for academic decision-making and strategic planning. However, while they offer comparability, they may not fully capture the complexity or broader significance of research impact, which often goes beyond numerical measures. Qualitative methods such as study quality assessments, narratives, and case studies complement quantitative metrics by adding depth and context. Therefore, the most effective research assessment combines both approaches, providing a holistic view that better reflects the multifaceted nature of research impact on academia and society.

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METHODS ARTICLE

Research ethics: Overcoming the exploitative dynamic through ethical research



Tanvir C Turin¹ | Mohammad M H Raihan² | Meriem Aroua² | Nashit A Chowdhury²

¹Department of Family Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

²Department of Community Health Science, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

Correspondence

Tanvir C Turin
turin.chowdhury@ucalgary.ca

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Abstract

Research ethics is a framework of principles and guidelines designed to ensure that scientific inquiry protects participants' rights and welfare while upholding integrity. Core principles includes respect for persons, beneficence, and justice which govern all research stages. Respect for persons requires informed consent, confidentiality, and additional safeguards for individuals with diminished autonomy. Beneficence involves maximizing benefits and minimizing harm. Justice demands equitable distribution of both research burdens and benefits. Despite these safeguards, exploitative dynamics persist when power imbalances enable researchers to pursue agendas at the expense of marginalized communities. Such dynamics manifest as tokenistic participation, extractive "helicopter" research, lack of reciprocity, disregard for local context, and unaddressed harms, all of which erode trust and compromise research validity. Mitigating these issues for ensuring ethical research requires proactive strategies at both the investigator and institutional levels. Researchers should co-design studies with community partners, implement participant-centered informed consent, ensure fair recruitment, prioritize participant welfare, establish benefit-sharing agreements, and maintain transparency and accountability. Academic institutions must bolster ethics infrastructures — streamlining review processes, providing ongoing ethics training, facilitating genuine community engagement, and fostering a culture that rewards ethical conduct. By embedding these measures into research design and oversight, the research community can prevent exploitation, honour participants' dignity, and advance knowledge in an equitable manner. Upholding rigorous ethical standards not only safeguards scientific credibility but also builds public trust and contributes to a more just and inclusive society.

Key messages

Ethical research should transcend mere regulatory compliance, actively addressing and mitigating exploitative dynamics inherent in knowledge production. This commentary explores critical ethical concerns such as tokenism, extractive methodologies, and the absence of reciprocal engagement, while promoting the adoption of more equitable research paradigms. By emphasizing participant agency, fostering transparency, and ensuring mutual benefit, researchers can uphold principles of integrity and equity within their scholarly endeavors.

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Research ethics and principles

Research ethics is a framework of principles, standards, and guidelines that govern how research should be conducted [1]. It includes the rules and norms that researchers must follow to ensure their work is ethical. These guidelines are often established by professional organizations, institutions, and regulatory bodies [2]. Research ethics encompasses fundamental ethical principles such as respect for persons, beneficence, and justice, which apply throughout all stages of research activities—planning, conduct, and reporting. Research ethics ensures that scientific inquiry is conducted responsibly, protecting the rights and well-being of participants while upholding the integrity of the research process. It involves strategies and standards that ensure the responsible and ethical execution of scientific inquiry. The core principles [1,2] of research ethics, as described in several sources, include:

Respect for persons: Respect for Persons is a fundamental principle in research ethics that acknowledges the inherent dignity and worth of all human beings [1]. This principle underscores the importance of treating individuals as autonomous agents who have the capability to make informed decisions when participating in research. It requires researchers to provide comprehensive information about the study, its potential risks and benefits, and to ensure that participation is truly voluntary. Respect for Persons also extends to protecting those with diminished autonomy, such as children, individuals with cognitive impairments, or those in vulnerable situations, including individuals marginalised by policy choices and narratives of racial inferiority. This protection involves additional safeguards and careful consideration of their ability to provide informed consent. The principle is typically implemented through processes like obtaining informed consent, maintaining confidentiality, and allowing participants to withdraw from studies without negative consequences [1,2].

Beneficence/ concern for welfare: This emphasizes maximizing benefits and minimizing harm to participants and society [1,2]. This concept goes beyond simply avoiding harm, actively promoting participants' well-being across physical, mental, and social dimensions. Researchers must carefully balance potential risks and benefits, ensure participant safety, and contribute positively to individual and collective welfare. This principle requires providing comprehensive information to participants, respecting their autonomy, and considering broader societal implications of the research. It serves as a crucial ethical safeguard, ensuring research is conducted with genuine concern for human dignity and welfare while advancing knowledge that serves human interests [1,2].

Justice: Justice in research ethics refers to the fair and equitable treatment of all individuals involved in or affected by research [1,2]. This principle ensures that the benefits and burdens of research are distributed fairly across different populations and that no group is unfairly targeted or excluded from potential

benefits. Justice requires careful consideration in the selection of research participants, ensuring that they are not chosen merely for convenience or due to their vulnerability [2]. It also demands that research questions and methodologies are relevant and beneficial to the communities involved in the studies. Furthermore, justice in research ethics extends to broader societal considerations, including how research might impact health equity and social justice at population or systems levels. Researchers must strive to conduct studies that not only advance scientific knowledge but also contribute to reducing disparities and promoting fairness in society.

Historical context

The evolution of contemporary research ethics frameworks developed in direct response to historical methodological transgressions. Many international standards of ethical conduct emerged as direct responses to egregious abuses in scientific studies. Examples include Nazi physicians' non-therapeutic experimentation on concentration camp prisoners (1940–1945) [3,4], involving hypothermia trials and forced sterilization procedures (Blacker). Similarly, the Tuskegee Syphilis Study (1932–1972) [3,4] by the U.S. Public Health Service withheld effective treatment from 399 African American men infected with syphilis, under the guise of providing free healthcare, to observe the natural progression of the disease. This unethical study emphasised the importance of beneficence and justice in research practices. Another egregious example is the Willowbrook Hepatitis Study (1956) [3,4], where researchers deliberately infected institutionalised children with hepatitis to study the disease. Parents were effectively coerced into consenting by being promised quicker access to institutional services, exposing vulnerabilities in voluntary participation safeguards. In a similar vein, the Jewish Chronic Disease Hospital Study (1963) [4] involved injecting live cancer cells into elderly patients without their informed consent. The primary investigator deliberately avoided using the word “cancer” when explaining the procedure, instead employing vague language to obscure the true nature of the experiment. These types of incidents spurred the creation and reinforcement of ethical research principles, which are reflected in seminal guidelines such as the Belmont Report [1] and the Declaration of Helsinki [5], which emphasize informed consent and right to withdraw from the study, respect for persons, beneficence, and justice in research involving human subjects.

Ethical research and exploitative dynamic

Ethical research: Ethical research is a practice that adheres to established ethical principles and guidelines, upholding participants' rights and welfare throughout the research process [6,7]. Ethical research, a crucial aspect of scientific inquiry, encompasses a commitment to integrity, transparency, and accountability in all aspects of the research endeavor. It involves obtaining informed consent from participants, respecting their autonomy, and ensuring fair treatment in participant selection and distribution of benefits [2]. Ethical research also

emphasizes justice, maintaining honesty in reporting data, avoiding fabrication or falsification, and upholding scientific integrity. It also protects participants' confidentiality and privacy and responds to potential harms. Adhering to ethical research standards is essential for building public trust in research, safeguarding participants' dignity and rights, and ensuring the credibility of scientific inquiry. A key aspect of ethical research is preventing the exploitation of participants by ensuring that their participation is informed, voluntary, and free from coercion or deception. It also emphasizes that participants' contributions are respected and valued throughout the research process. By upholding these standards, researchers ensure that their work not only advances knowledge but also benefits society as a whole.

Exploitative dynamic: In research, investigators traditionally hold significant power [8], influencing critical aspects of a study from designing questions to planning, recruitment, data collection, analysis, and dissemination. This imbalance can lead to disproportionate benefits for researchers or institutions while offering minimal or no reciprocal advantages to marginalised, vulnerable, or underrepresented groups. As a result, community/patient needs, priorities, and contributions are often overlooked, compromising both the integrity of the research process and participants' well-being. Moreover, social inequality perpetuates exploitation by reinforcing oppressive power imbalances through cultural, economic, and institutional norms—often bolstered by economic exploitation, systemic oppression, and entrenched hierarchies. In this perspective article, “exploitative dynamics” in research refer to actions that unfairly advantage investigators—for instance, neglecting proper consent, imposing unreasonable risks or burdens, or providing inequitable benefits. These dynamics can significantly hinder research involving patients or marginalised populations, particularly at the design stage, where a lack of standardised engagement practices may result in tokenistic participation, extractive methods, disproportionality, context stripping, and unaddressed harms [9]. In ethical research, such exploitative dynamics may manifest in several ways:

- a) **Tokenism:** Communities/ patients are involved superficially, often to meet diversity requirements, without genuine integration into decision-making or research processes. Top-down decision making and resource disparity occurs.
- b) **Extractive practices:** Researchers collect data or knowledge from communities without adequately sharing findings, credit, or benefits with those communities. This one-sided or one-off research approach can strip communities of their agency and insights. This is known as ‘helicopter research’, or “parasitic research” or ‘parachute in and out research’ [10].
- c) **Lack of reciprocity:** Despite their contributions to the research, communities may be left without meaningful benefits, such as improved resources, knowledge, or outcomes. This

absence of reciprocity can foster resentment and distrust.

- d) **Disregard for context:** Researchers may impose their own frameworks, goals, or methods without considering the cultural, social, or historical context of the communities involved. Such disregard can lead to misinterpretations and reinforce existing inequalities.
- e) **Unaddressed or hidden harms:** The research process may inadvertently perpetuate stereotypes, stigmatize communities, or fail to mitigate potential risks or harms to participants. Ethical oversight is essential to prevent such negative outcomes.

Addressing these above dynamics is crucial to fostering ethical, equitable, and community-centered research practices that genuinely respect and uplift the voices of those involved.

Addressing exploitative dynamics

Addressing these exploitative dynamics is crucial for fostering ethical research practices that genuinely respect and benefit all participants involved. While other stakeholders—such as funding agencies, community members, and regulatory bodies—play important roles in overcoming these exploitative dynamics and ensure ethical research practices, researchers and academic institutions are the primary actors central to this effort.

Researchers' action: To overcome exploitative dynamics in research, researchers can take several proactive actions. Here are key strategies based on the context of ethical research practices:

- i. **Inclusive and empowered community engagement and involvement:** Actively involve community members at every stage of the research process—planning, design, implementation, and dissemination [9,10]. This ensures the research aligns with community priorities and fosters shared ownership.
- ii. **Create and apply participant-centered informed consent:** Create clear, comprehensive information about the study's purpose, risks, benefits, and participants' rights to empower individuals to make informed decisions about their involvement.
- iii. **Implement fair and equitable participant selection:** Use unbiased and inclusive criteria for participant recruitment, avoiding discrimination based on gender, race, socioeconomic status, or other factors.
- iv. **Prioritize participant welfare:** Conduct thorough risk assessments and implement strategies to minimize harm and maximize benefits, always prioritizing the well-being of participants.
- v. **Establish benefit-sharing agreements:** Clearly identify how research benefits will be shared with participants and their communities, ensuring recognition and reciprocity for their contributions.
- vi. **Ensure transparency and accountability:** Maintain openness about research goals, methods, and potential impacts, and remain accountable to participants and stakeholders throughout the process.

- vii. *Commit to ongoing ethical education:* Continuously pursue ethical education to uphold high standards.
- viii. *Monitor and evaluate impact:* Implement systems to track the research's impact on communities, identifying and addressing any unintended consequences or exploitative dynamics.
- ix. *Advocate for ethical research practices:* Promote awareness of ethical standards and equitable partnerships within institutions and among peers, emphasizing the importance of addressing exploitative dynamics.

Academic institutions' action: To overcome exploitative dynamics and ensure ethical research practices, academic institutions can take several proactive actions. Here are some key strategies:

- A. *Establish a strong ethics infrastructure:* Create and maintain a robust ethics infrastructure that includes Institutional Review Boards (IRBs) or Research Ethics Boards (REBs) to oversee research proposals and ensure compliance with ethical standards.
- B. *Develop comprehensive ethical guidelines:* Institutions should develop clear ethical guidelines and policies that outline expectations for researchers regarding the treatment of participants, informed consent, and data management. These guidelines should be easily accessible to all researchers.
- C. *Facilitate ethical review processes:* Streamline the IRB or REC review process to make it more efficient while maintaining rigorous ethical standards. This helps reduce delays in research approval while ensuring participant protection.
- D. *Provide resources, training, and support:* Ensure that adequate resources, including funding, staff, and training, are available to support ethical research practices. This includes providing support, training for IRB/Research Ethics Board members to help them effectively conduct ethical research practices. Also, offer regular training programs for researchers, faculty, and students on ethical research practices, emphasizing the importance of avoiding exploitative dynamics and fostering a culture of integrity.
- E. *Encourage and facilitate community/ patient engagement:* Promote inclusive and meaningful engagement with communities/patients involved in research [9,10,11]. Also, institutions can facilitate partnerships with community organizations to ensure that research addresses local needs and priorities.
- F. *Monitor research practices:* Establish mechanisms for monitoring ongoing research projects to ensure compliance with ethical standards and address any emerging issues related to exploitative dynamics.
- G. *Promote transparency and accountability:* Encourage transparency in research processes by requiring researchers to disclose potential conflicts of interest and ensuring that findings are reported honestly and accurately.
- H. *Foster a culture of ethical research:* Cultivate an institutional culture that prioritizes ethical research by recognizing and rewarding ethical conduct among researchers. This can include highlighting projects that demonstrate innovative approaches to ethical accommodations, implementing ethics mentorship programs, and celebrate researchers who have made significant contributions to advancing ethical practices in their fields.
- I. *Engage in advocacy for ethical standards:* Academic institutions can advocate for ensuring broader ethical standards within the research community, influencing policies at national or international levels to promote ethical practices across various disciplines.

By implementing these strategies, scholars and academic institutions can play a crucial role in overcoming exploitative dynamics in research, ensuring that all participants are treated ethically and that the research conducted is of high integrity and quality.

Conclusions

As research continues to evolve in complexity and scope, it is imperative that ethical considerations remain at the forefront. By prioritizing ethical practices and addressing exploitative dynamics head-on, researchers can contribute to a more just and equitable society where the benefits of research are shared by all participants involved. Ultimately, ensuring ethical research is a collective responsibility that requires collaboration among all stakeholders involved. By fostering a culture of respect, transparency, and accountability, the research community can work towards overcoming exploitative dynamics and enhancing the overall quality of research.

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4. Main body: Introduction (clearly mention the objective/s), Methods, Results (only text referring to tables/figures), and Discussion (conclusion should be the subheading).
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6. References: should be in Vancouver style. DOIs for journals and URLs for websites to be given.
7. Table(s) or figure(s) page (separate page for each table or figure).



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