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Clinico Demographic Profile and Short-term Outcome of Pediatric Idiopathic Intracranial Hypertension in a Tertiary Care Hospital of Bangladesh

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Abstract:

Background: Diagnosis of IIH (idiopathic intracranial hypertension) in children is challenging. The pathogenesis of IIH is still largely unknown. The aim of this study to evaluate the clinico-demographic profile and short-term outcome of IIH among Bangladeshi children.

Methodology: This observational cohort study was done in pediatric Neurology Department, National Institute of Neurosciences and Hospital Bangladesh from January 2018 to July 2019. Total 19 cases were enrolled who were clinically suspected and/or had normal CSF with opening pressure (OP) above 250 mmH_2O. They were further categorized as "definite IIH", definite IIH without papilledema, and "probable IIH". Clinical, radiological profile and short-term outcome were analyzed by SPSS version 22.

Result: Among them most were probable IIH (74%). Episodic (57.9%), moderate, diffuse headache was the predominant symptom along with vomiting, double vision, unilateral VI nerve palsy and papilledema. Obesity was found in 21% cases. Mean CSF pressure was 21.84+7.62cm H_2O and found high in definite IIH. All the cases were treated with acetazolamide and serial LP was done in 4(15.8%) cases. Definite IIH requires longer hospital stay (6.42 ± 2.87days). Recurrence was observed in 10.5% cases and visual impairment was found in 15.8% cases.

Conclusion: This study found wide range of diversity between clinical feature and CSF opening pressure in Pediatric IIH and diagnostic confirmation was challenging. Initial treatment response was satisfactory with a low recurrence rate.

Key Words: Pediatric Idiopathic intracranial hypertension (IIH), CSF pressure, Definite IIH, Definite IIH without papilledema, probable IIH.

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Introduction:

Idiopathic intracranial hypertension (IIH) is a rare pediatric neurological disorder affecting 1 in 100,000 to 150,000 children.[1 2 3] It is characterized by elevated intracranial pressure (ICP) without brain parenchymal lesions, vascular malformations, hydrocephalus or central nervous system infection.[4] The diagnosis is usually confirmed by high cerebrospinal fluid (CSF) opening pressure (OP) in the absence of secondary causes of intracranial hypertension. In 2013, the opening

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pressure (OP) for children aged 1-18 years was redefined, and the upper limit of normal OP in children is actually 28 cm H_2O.[5 66] Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology (2013) 81:1159–65.

The revised diagnostic criterion for the diagnosis uses a lumbar puncture (LP) opening pressure of more than 28 cm H_2O or more than 25 cm H_2O if the child is not obese and not sedated.[6] According to these revised criteria, IIH can be classified as "definite" (increased OP and either papilledema or abducens nerve palsy), "probable" (normal CSF pressure in presence of papilledema), or "suggestive of" (raised CSF pressure plus at least three valid neuroimaging markers of raised ICP, in the absence of papilledema and abducens nerve palsy).[6]

Idiopathic intracranial hypertension is a diagnosis of exclusion.[7] The pathogenesis of IIH is still largely unknown. Diagnosis of IIH in children is challenging due to its diverse presentation, limited examination compliance and investigation. Despite these difficulties, accurate diagnosis is essential to limit long-term morbidity.

In this study, we are looking forward to evaluate the clinic-demographic profile and outcome of management of IIH in pediatrics and adolescent patients.

Methodology:

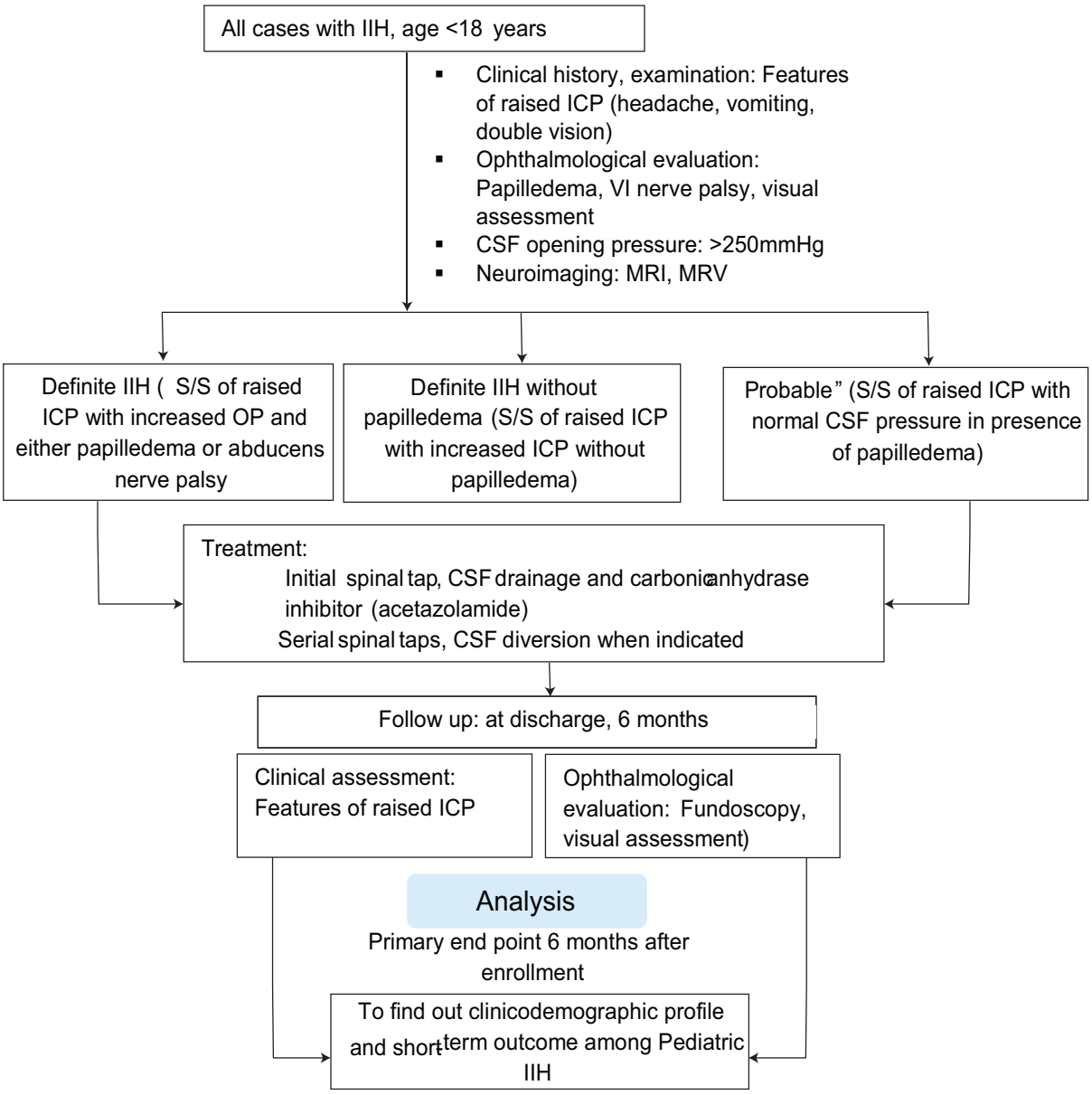
This observational study was done in Pediatric Neurology Department, National Institute of Neurosciences and Hospital Bangladesh from January 2018 to July 2019. All the cases with IIH who were diagnosed and treated in the Department of Pediatric Neurology with age less than 18 years were included. The diagnostic criteria of IIH were symptoms and signs of increase intracranial pressure (headache, vomiting, double vision), normal brain magnetic resonance image (MRI) without a space-occupying lesion or hydrocephalus, and/or normal CSF analysis with CSF opening pressure (OP) above 250 mmH_2O. In this study IIH cases were categorized as "definite IIH" (S/S of raised ICP with increased OP and either papilledema or abducens nerve palsy), definite IIH without papilledema (S/S of raised ICP with increased ICP without papilledema) and "probable" (S/S of raised ICP with normal CSF pressure in presence of papilledema).

All patients were evaluated thoroughly by taking comprehensive history regarding the symptoms and general medical, neurological, and ophthalmological examination. Radiological assessment included magnetic resonance imaging (MRI) and magnetic resonance venography (MRV). With all aseptic precaution lumbar puncture was carried out for all patients. The opening pressure was measured by central venous catheter, and CSF sample was taken for cytological, biochemical (protein level, glucose level) and microbiological analysis. Other laboratory investigations (complete blood picture, liver function test, kidney function test, serum electrolyte, and thyroid-stimulating hormone) were done to exclude secondary causes of IIH.

Initial spinal tap, CSF drainage and carbonic anhydrase inhibitor (acetazolamide) was used for 2 weeks in all patients. Serial spinal taps were performed in patients who did not improve, whereas CSF diversion was considered for patients with refractory symptoms or visual deterioration after three spinal taps. After discharge, weekly follow-up with neurological and ophthalmologic examinations was performed initially, then monthly for 3 months, and every 3 months thereafter to confirm clinical improvement and recurrence. At 6 month follow up thorough clinical and ophthalmological evaluation was done to find out recurrence rate, visual function and resistant cases. Recurrence is considered when reappearance of symptoms and signs occur after complete recovery; Resistant cases requiring repeated lumbar puncture or even CSF diversion procedures were considered. Recurrence was diagnosed after MRI ruled out new intracranial findings, but fundus photography confirmed papilledema and lumbar puncture confirmed elevated CSF opening pressure.

Analysis was performed with SPSS software, versions 22.0. Continuous data that were normally distributed was summarized in mean, standard deviation, median, minimum and maximum. Categorical or discrete data was summarized in frequency counts and percentages. For end points analysis, chi square test was used for categorical variables and an analysis of variance (one-way ANOVA Test) for continuous outcomes. Pearson correlation was done to see the correlation between two continuous variables. CONSORT flow chart was used for summarization the number of patients screened. A two-sided P value of less than 0.05 was considered to indicate statistical significance.

Flow Chart:



Ethical Clearance:

The institutional/ Ethical review committee of National Institute of Neurosciences and Hospital approved the study prior to launching and IRB number was IRB/NINS/279. Before enrolling parents were explained about the purpose of the study and written informed consent was sought from the participant's guardian

Result:

Among 19 cases, majority (74%) had probable IIH, 16% had definite IIH while 10% had definite IIH without papilledema (Figure 1). Mean age were 9.84 ± 2.40 years, male were predominant in definite IIH group while male female ratio was equal in other two groups which was not significant. Mean duration of illness were 24.52 ± 24.55 days. Cases in definite IIH without papilledema group presented earlier (7.50 ± 4.94) years then definite and probable IIH. Most the cases had episodic (52.6%); moderate intensity (73.7%) diffuse (63.2%) headache while 14% had severe headache. Double vision (78.9%), VI nerve palsy (73.6%), vomiting (68.4%) was common clinical presentation. Episodic headache was common

in definite IIH (52.6%) and probable IIH (57.1%) but constant headache was prominently found in definite IIH without papilledema groups which was not statistically significant. Vomiting, double vision were prominent presentation in all 3 groups. Majority of them had papilledema (89.5%), all the cases of definite and probable IIH cases had papilledema. Headache, double vision, and VI nerve palsy were present in all cases (100%) in definite IIH without papilledema group, while none of them had papilledema. Among the cases obesity (21.1%), post puberty (15.8%), recent weight gain (5.3%) and H/O recent infection (5.3%) were found. All these factors were found in probable IIH groups, none of these found in definite IIH and definite IIH without papilledema groups which was not statistically significant (Table 1). Mean CSF pressure among the study cases were 21.84 ± 7.62 cmH2O. CSF pressure were found high among definite IIH with or without papilledema groups then Probable IIH groups, which was found statistically

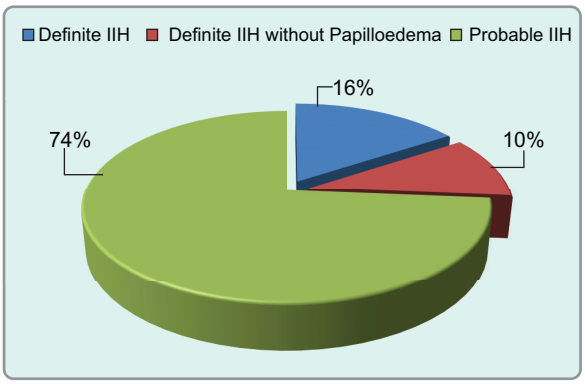


Figure 1: *Pattern of IIH among the study cases (N=19)*

Table-I

Clinico-demographic profile among the study cases (N = 19)

Variable	Total Frequency (%)	Definite IIH (3)	Definite IIH without papilloedema (2)	Probable IIH (14)	P Value
Age (Mean ± SD) years	9.84 ± 2.40	10.00 ± 2.00	7.50 ± 4.94	10.14 ± 2.14	0.367*
SexMale	11 (57.9%)	3 (100%)	1 (50%)	7 (50%)	0.274
Female	8 (42.1%)	0	1 (50%)	7 (50%)	
Weight (Mean± SD) kg	35.00 ± 16.61 (21-56)				
Duration of illness (days ± SD)	24.52 ± 24.55 (2-90)	22.00 ± 7.54	11.00 ± 9.89	27.00 ± 7.96	0.701
Headache	17 (89.5%)	3 (100%)	2 (100%)	12 (85.71%)	0.671
Episodic	10 (52.6%)	2 (66.67%)	0	8 (57.14%)	0.358
Constant	7 (36.8%)	1 (33.33%)	2 (100%)	4 (28.57%)	
Intensity					
Moderate	14 (73.7%)	2 (66.67%)	1 (50%)	11 (78.57%)	0.454
Severe	3 (15.8%)	1 (33.33%)	1 (50%)	1 (7.14%)	
Localization					
Focal	5 (26.3%)	1 (33.33%)	0	4 (28.57%)	
Diffuse	12 (63.2%)	2 (66.67%)	2 (100%)	8 (57.14%)	0.765
Neck pain	4 (21.1%)	1 (33.33%)	1 (50%)	2 (14.28%)	0.435
Vomiting	13 (68.4%)	3 (100%)	1 (50%)	9 (64.28%)	0.405
Visual impairment	6 (31.6%)	2 (66.67%)	0	4 (28.57%)	0.260
Double Vision	15 (78.9%)	3 (100%)	2 (100%)	10 (71.42%)	0.405
VI nerve palsy	14 (73.6%)				
Unilateral (right)	10 (52.6%)	1 (33.33%)	2 (100%)	7 (50%)	
Unilateral (Left)	2 (10.5%)	1 (33.33%)	0	1 (7.14%)	0.643
Bilateral	2 (10.5%)	0	0	2 (14.28%)	
Papilledema	17 (89.5%)	3 (100%)	0	14 (100%)	0.000
Obesity	4 (21.1%)	0	0	4(28.57%)	0.405*
Recent weight gain	1 (5.3%)	0	0	1 (7.14%)	0.828*
Post pubertal	3 (15.8%)	0	0	3 (21.42%)	0.529*
H/O recent infection	1 (5.3%)	0	0	1 (7.14 %)	0.8282*

*One-way Anova test, chi square test

significant (p= 0.000). Most of them had normal MRV (94.73%) while transverse sinus stenosis was found in 1 (5.26%) case which was in definite IIH without papilledema which was statistically significant (Table 2). All the study cases initially treated with acetazolamide while 1(5.3%) case received topiramate and serial lumber were done among 4(15.8%) cases and most of them were in probable IIH group. Mean age of hospital stay were 6.42 ± 2.87 days, definite IIH with or without IIH group required longer hospital stay than probable IIH. Majority of the cases were improved on discharge while 10.5% had recurrence on 1st 6 months and 15.8% had visual impairment (Table 3).

Table-II

Investigation profile of IIH among the study cases (N=19)

Investigation profile	Total Frequency (%)	Definite IIH (3)	Definite IIH without papilledema(2)	Probable IIH (14)	P Value
CSF study					
CSF Pressure (cmH_2O)	21.84±7.62	33.33±5.68	30.00 ± 7.07	18.28 ± 4.15	0.00**
Cell count	3 ± 1	2 ± 1	2 ± 1	3 ± 1	0.09**
Protein	28.33 ± 13.77	28.16 ± 11.72	17.50 ± 3.53	29.91 ± 14.82	0.518**
Normal MRI of Brain	19 (100%)	3 (100%)	2 (100%)	14 (100%)	
MRV	18 (94.73%)	3 (100%)	1(50%)	14 (100%)	
Normal					0.011*
Transverse sinus stenosis	1 (5.26%)	0	1 (50%)	0	

*Chi square test ** One-way Anova test

Table-III

Management and short-term outcome of IIH (n=19)

	Total Frequency (%)	Definite IIH (3)	Definite IIH without papilledema (2)	Probable IIH (14)	P Value
Management					
Acetazolamide	19 (100%)	3 (100%)	2 (100%)	14 (100%)	
Topiramate	1 (5.3%)	0	1 (50%)	0	0.011*
Serial lumber puncture	4 (15.8%)	0	1 (50%)	3(21.42%)	
Outcome					
Hospital stays	6.42 ± 2.87	7.33 ± 2.51	8.50 ± 6.36	5.92 ± 2.49	0.439
Improvement on discharge	16 (84.2%)	2 (66.67%)	2 (100%)	12 (85.71%)	0.579
At 6 months	2 (10.5%)	0	2 (100%)	0	0.000
Recurrence	3 (15.8%)	1 (33.33%)	0	2 (14.28%)	0.579
Vision loss					

Chi Square test

Discussion:

Pediatric IIH have been reported long time ago but there are no definite diagnostic criteria. The modified Dandy criteria is used in adult cases which is not applicable for most of the pediatric patients as children are not able to expresses their symptoms effectively in addition to the controversies about the diagnostic value of CSF opening pressure. We studied 19 cases over the period of 1 year. Among 19 cases, majority (74%) had probable IIH, 16% had definite IIH while 10% had definite IIH without papilledema. Hamedani et al [8] found 48.03% had definite IIH, 7.87% had probable IIH and 24.40% had IIH without papilledema, the median age was 13.6 years and 64.6% were female, which differ the present study. In our study mean age of the cases were 9.84 ± 2.40 years, male were predominant (57.9%). D Agraz et[9] al found similar to present study, males composed the majority in the ages 12 and under group at 61.5%, but females made up the majority of the ages 13 and older group at 84.6%. A meta-analysis of the epidemiological characteristics of pediatric IIH was reported by Genizi et al. showed 44% of those affected under 12 years of age were female. This increased to 79% in the 12–17 age groups. This increased to 79% in the 12–17 age group[10].

Although the clinical presentation of IIH is variable[11] headache and papilledema are the most important clinical presentations in adults with or without additional symptoms or signs of increased ICP[11 12]. However, typical IIH was diagnosed without headache[6] or papilledema[13]. The previous study showed, adolescent IIH group have quite similar clinical findings and diagnostic criteria to adult IIH as headache is the most common symptom while non-specific symptoms of increased ICP as deterioration of the school performance, irregular sleeping and irritability, and loss of appetite were significant in pediatric age group[11]. In this study, Most the cases had episodic (52.6%); moderate intensity (73.7%) diffuse (63.2%) headache while 14% had severe headache. Episodic headache was common in definite IIH (52.6%) and probable IIH (57.1%) but constant headache was prominently found in definite IIH without papilledema groups.

In pediatric IIH, strabismus, due to the sixth nerve palsy, is the most common presenting symptom in the prepubertal patients[14], and another study reported 44.4% in pediatric IIH group but not reported in adolescent group[15] ; also, the sixth nerve palsy was reported in the series of Mosquera Gorostidi and his colleagues.[16] The present study showed, double vision (78.9%), VI nerve palsy (73.6%), vomiting (68.4%) were common clinical presentation in all 3 groups of IIH. Majority of them had papilledema (89.5%), all the cases of definite and probable IIH cases had papilledema. 100% cases of definite IIH without papilledema had headache, double vision, VI nerve palsy but none of them had papilledema.

Multiple potential risks for the development of IIH in adult as female sex and obesity were reported[11 16 17] while in pediatric patients, infection, malnutrition, and pharmacological causes may be significant risk factors[17] and S Abouhashem[18] found anemia and infection which involved pharyngitis, otitis media, and bronchitis were the potential risk factors in pediatric IIH while obesity was not the prominent risk factor, Mosquera Gorostidi and his colleagues[17] did not report obesity as associated risk factor in patient less than 15 years old. In this study, most the cases had no identifiable risk factor but obesity (21.1%), Post puberty (15.8%), recent weight gain (5.3%) and H/O recent infection (5.3%) were found common risk factor.

At a systemic level, a recent paper by Westgate et al. elegantly investigated the underlying metabolic state of adult IIH patients. In this paper, it was shown that the elevated insulin and leptin-resistance seen in adult IIH patients was in excess of what would be expected from the obesity. The metabolic and transcriptional behavior of adipose cells was investigated and found to be predisposed to liposynthesis indicating obesity may be a feature of the metabolic syndrome of IIH, and not a casual factor.[15]

In this study, mean CSF Pressure were 21.84 ± 7.62 cmH_2O, CSF protein were 28.33 ± 13.77mg/dl. CSF pressure was found high among definite IIH with or without papilledema groups then Probable IIH groups. Another study[18] found the mean opening pressure was 29.1 ± 7.95 cmH2O and the minimum value for opening pressure in pediatric group was 18.0 cmH2O, while the minimum value in adolescent group was 25.0 cmH20; however, the diagnostic limit of the CSF opening pressure is considered a matter of debate in the diagnosis of pediatric IIH, but in the presence of typical IIH, symptoms and signs with papilledema low opening

pressure could not exclude the diagnosis as the lumbar puncture may be done during the nadir of a pressure wave.Error! Bookmark not defined. [19] In another retrospective observational study, the highest opening pressure in pediatric IIH was between 20 and 24 cmH2O in 11% of the patients while it was between 25 and 39 cmH2O in 48% and more than 40 cmH2O in 42% of the patients[20]. In a newer study, opening pressure eŠ 28 cmH2O is mandatory for diagnosis of intracranial hypertension for obese patients and 25 cmH2O if the patient is not obese[2121] Avery RA. Reference range of cerebrospinal fluid opening pressure in children: historical overview and current data. Neuropediatrics. 2014; 45:206–11.

All the cases had normal MRI of brain and most of them had normal MRV (94.73%) while transverse sinus stenosis was found in 1 (5.26%) case which was in definite IIH without papilledema of this study. Similar finding was found in another study[18].

IIH in pediatric patients usually respond to pharmacological treatment with early clinical improvement after the initial lumbar puncture[17 20]. All the study cases of the present study initially treated with acetazolamide while 1(5.3%) case received topiramate and serial lumber were done among 4(15.8%) cases and most of them were in probable IIH group. Mean age of hospital stay were 6.42 ± 2.87 days, definite IIH with or without IIH group required longer hospital stay then probable IIH. Majority of the cases were improved on discharge while 10.5% had recurrence on 1st 6 months and 15.8% had visual impairment. The treatment and outcome results in this this study are similar to the results of Abouhashem[18], Mosquera Gorostidi and his colleagues[17]. The recurrence rate of symptomatic IIH in pediatrics is between 6 and 24%[17 22].

Conclusion

This study found that, there were wide range of diversity between clinical feature and CSF opening pressure in Pediatric IIH and diagnostic confirmation was challenging. Initial treatment response was satisfactory with a low recurrence rate.

Conflict of interest: None

Limitation

The Sample size was small and Single center study. This study recommended large scale multi-center study with big sample size are needed to make a recommendation for modification of diagnostic criteria for pediatric IIH among Bangladeshi children.

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Conflict of Interest

There is no conflict of interest regarding the research, authorship and publication of this article.

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