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Evaluation of Regional Cerebral Blood Flow Abnormalities Using Radionuclide Brain SPECT Imaging and Their Correlation with Symptoms in Childhood Autism Spectrum Disorder

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ABSTRACT

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition that emerges early in life and remains challenging to diagnose accurately. This study evaluated regional cerebral blood flow abnormalities in 24 children with ASD, aged 3–12 years, using ^{99m}Tc ECD brain SPECT at the National Institute of Nuclear Medicine & Allied Sciences (NINMAS), Dhaka. Imaging data were analyzed with the Easy Z-Score Imaging System (eZIS) and correlated with Autism Diagnostic Checklist (ADCL) severity scores. Distinct hypoperfusion patterns were observed across severity levels. In mild ASD, hypoperfusion was consistently detected in the frontal lobe (100%), and in 70% of temporal and parietal regions. Low-moderate ASD cases exhibited widespread hypoperfusion across all brain regions, with universal involvement of the frontal and temporal lobes (100%). In high-moderate ASD, marked hypoperfusion was most pronounced in the parietal (100%) and frontal (83.3%) regions. Clinically, delayed speech was the most frequent symptom, followed by hyperactivity and cognitive impairment. Statistical analysis revealed a significant positive correlation between ADCL scores and Z-scores, indicating that greater perfusion deficits were associated with higher ASD severity. These findings demonstrate that brain SPECT not only identifies specific lobar perfusion deficits but also reflects symptom burden, underscoring its potential as a functional biomarker for diagnosis, monitoring, and guiding interventions in ASD.

1. Introduction

Autism Spectrum Disorder (ASD) is a group of complex neurodevelopmental disorders that manifest within the first three years of life, characterized by repetitive behaviors and challenges in social communication and interaction. Initially associated with self-withdrawal in schizophrenia, the term "autism" was redefined in the 1940s by Dr. Leo Kanner and Dr. Hans Asperger [1] to describe children with difficulties in social interaction, communication, and restrictive interests. Today, ASD encompasses a range of disorders with shared behavioral characteristics, including restrictive and repetitive behaviors.

Epidemiological studies reveal a rising prevalence of ASD, affecting 1 in 150 children worldwide. In Bangladesh, its prevalence ranges from 0.15–0.8%, with autism constituting 19% of recorded neurological disabilities in a 2016 study [2-3]. Diagnoses are based on DSM-5-TR criteria, focusing on social communication challenges and repetitive behaviors [4].

Nuclear neuroimaging, particularly Single Photon Emission Computed Tomography (SPECT), is a valuable tool for assessing ASD [5]. SPECT detects hypoperfusion in brain regions linked to ASD pathology, including the

frontal, temporal, and parietal cortices, thalami, and basal ganglia. Using Technetium-99m ethyl cysteinate dimer (Tc-99m ECD), SPECT can measure regional cerebral blood flow (rCBF), providing precise perfusion mapping. At NINMAS, SPECT is positioned to complement clinical tools, offering efficient, objective diagnostics and therapy monitoring for ASD.

2. Method and Patients

This 18-month cross-sectional observational study at NINMAS, Dhaka, involved 24 children aged 3–12 years with confirmed Autism Spectrum Disorder (ASD), selected through purposive sampling. Participants were diagnosed using DSM-IV/V criteria [4], and those with abnormal CT/MRI findings, persistent seizures, or known infectious, metabolic, or chromosomal diseases were excluded. Ethical approval was obtained, and informed consent was secured from guardians.

Cerebral imaging was performed using 99mTc ECD SPECT, following standard protocols. An intravenous dose of 1–3 mCi 99mTc ECD was administered with low-dose sedation, and blood oxygen levels and heart rate were monitored throughout the procedure. Imaging commenced 10 minutes post-injection to assess cerebral perfusion. Image 1 depicted the ongoing study with dual head gamma camera.

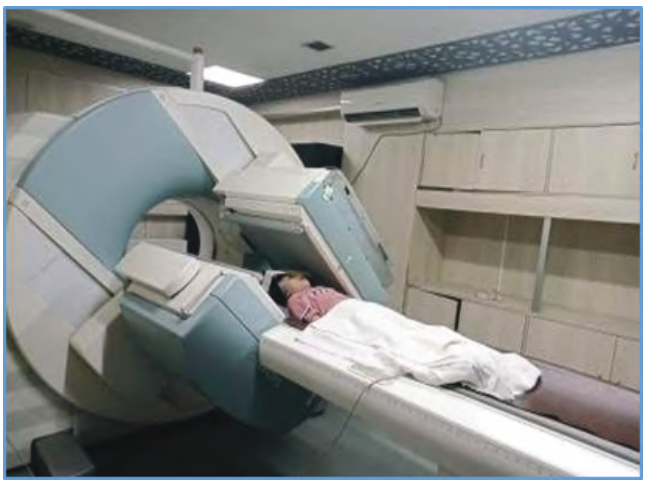

Image 1: Tc99m ECD brain perfusion is going on by dual head gamma camera at NINMAS

Data were analyzed using SPSS software, version 26 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. Statistical significance was defined as $p < 0.05$. The findings were summarized using appropriately formatted tables, figures, and graphs. Perfusion defects were quantified and correlated with autism spectrum disorder (ASD) severity using standardized Z-score analysis to ensure objective measurement of regional cerebral blood flow abnormalities. Image 2 depicted the brain perfusion composite image after eZIS software application in a case.

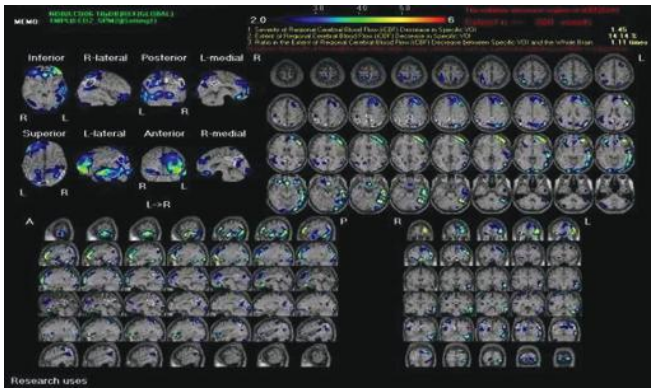

Image 2: A 6-year-old male child with a history of Autism Spectrum Disorder (ASD) presents with complaints of delayed speech, poor eye contact, and hyperactivity. His ADLC score was 215, indicating low to moderate functioning. Tc99m ECD SPECT brain perfusion imaging revealed hypoperfusion in both frontal lobes (more prominent on the left side), the left parietal lobe, left temporal lobe, and both occipital lobes. The Z-score for cognitive impairment severity was 1.45, indicating mild impairment.

3. Results and Discussion

The cross-sectional observational study was conducted in National Institute of Nuclear Medicine & Allied Sciences, BMU campus, Shahbagh, Dhaka; where 24 confirmed cases of childhood ASD of 3-12 years age range with mean age 7 years were enrolled at NINMAS for Brain-SPECT study. The severity of ASD in participants were categorized initially by ADCL score from history and clinical examination. Brain-SPECT was done in 24 cases. After performing SPECT imaging, Z-score for severity of cognitive function abnormality was calculated and areas of brain abnormality was also noted. The rCBF was also categorized based on Z-score. The study focused on 24 of these cases, utilizing Brain SPECT imaging to analyze ASD severity through the ADCL score, Z-score, and areas of brain abnormalities. The study also found that speech delay was the most common symptom associated with hypoperfusion across all brain regions, with

hyperactivity and poor cognitive function also linked to hypoperfusion, particularly in the frontal, temporal, and parietal regions. A significant positive correlation was found between ASD severity and rCBF status, with more severe cases showing greater reductions in rCBF. These findings underscore the relationship between brain hypoperfusion, symptom profile, and ASD severity, suggesting that more severe ASD is associated with greater abnormalities in brain perfusion and cognitive function. Appropriate statistical tests were applied for data analysis. P value ≤ 0.05 was considered as statistically significant.

The gender distribution of the study participants. Out of the total 24 children included in the study, the majority were boys (n = 18, 75%), while girls accounted for 6 cases (25%). This indicates a male predominance among the study population, with a 3:1 boy-to-girl ratio.

The most common symptom among the study cohort was speech delay, affecting 22 participants (91.6%), followed by hyperactivity in 16 participants (66.6%). Poor cognitive function and poor eye contact were observed in 9 participants each, corresponding to 37.5%. This highlights speech delay and hyperactivity as the predominant symptoms, with cognitive and social communication deficits being less frequent but still significant. Table I represent the distribution of study subjects with symptoms profile

Table 1: Distribution of study subjects with symptoms profile

Symptoms	Number (%)
Speech delay	22 (92.6%)
Hyperactivity	16 (66.6%)
Poor eye contact	09 (37.5%)
Poor cognitive function	09 (37.5%)

Table I summarizes the symptom profile of the study population. The most prevalent feature was speech delay (22 cases, 92.6%), followed by hyperactivity (16 cases, 67%). Poor eye contact and poor cognitive function were each observed in 9 cases (37.5%). This indicates that speech delay is the predominant presenting symptom in ASD, consistent with established clinical patterns, while hyperactivity and deficits in eye contact and cognition were also common but less frequent.

Analysis of regional cerebral perfusion patterns revealed that frontal lobe hypoperfusion was the most consistent abnormality, observed across all severity groups (100% in mild and low-moderate, and 83.3% in high-moderate ASD). Temporal and parietal hypoperfusion were also highly prevalent, detected in 70–100% of cases, highlighting their strong association with ASD severity. In contrast, precuneus hypoperfusion showed a variable distribution, ranging from 37.5% in low-moderate to 66.7% in high-moderate cases, suggesting greater involvement with increasing severity. Cingulate gyrus hypoperfusion was least frequent overall, present in 40% of mild, 12.5% of low-moderate, and 50% of high-moderate ASD cases.

These findings indicate that frontal, temporal, and parietal regions are the core areas of hypoperfusion in ASD, which correlate with key symptom domains such as speech delay (frontal/temporal dysfunction) and hyperactivity and poor cognitive function (parietal and cingulate involvement). The precuneus and cingulate regions appear to contribute more selectively, particularly in higher-severity ASD, aligning with their known roles in self-referential processing and executive control. Table II depicted the result of brain perfusion result.

Table 2: Distribution of study subjects with respect to areas of hypoperfusion and ASD severity

ASD severity	Frontal (n=23)	Temporal (n=20)	Parietal (n=20)	Precuneus (n=12)	Cingulate Gyri (n=8)
Mild (n=10)	10 (100%)	7 (70%)	7 (70%)	5 (50%)	4 (40%)
Low moderate (n=8)	8 (100%)	8 (100%)	7 (87.5%)	3 (37.5%)	1 (12.5%)
High moderate (n=6)	5 (83.3%)	5 (83.3%)	6 (100%)	4 (66.7%)	3 (50%)

Table II shows the distribution of brain hypoperfusion across different ASD severity levels. Mild ASD cases predominantly exhibit hypoperfusion in the frontal (100%), temporal (70%), and parietal (70%) regions. As ASD severity increases, hypoperfusion becomes more widespread, particularly in the parietal (100%) and frontal (83.3%) regions. Analysis of symptom-specific perfusion abnormalities demonstrated distinct regional patterns of involvement. Speech delay, the most frequent clinical manifestation, was strongly associated with frontal hypoperfusion (95.5%), along with high involvement of the temporal (81.8%) and parietal lobes (81.8%), and nearly half of cases also showed precuneus changes (50%). Hyperactivity displayed a universal link to frontal hypoperfusion (100%), with additional involvement of the temporal and parietal cortices (75% each), and less frequent precuneus deficits (43.8%). Similarly, poor cognitive function correlated with widespread abnormalities, with frontal hypoperfusion present in all cases (100%), and substantial contributions from the temporal (88.9%) and parietal (88.9%) regions; precuneus hypoperfusion was noted in 44.4%. In children with poor eye contact, hypoperfusion was observed most prominently in the frontal lobe (88.9%), followed by the temporal (77.8%) and parietal (77.8%) cortices, again with less frequent precuneus involvement (44.4%). Table III shown this outcome.

These findings suggest that frontal, temporal, and parietal lobes form the core regions of dysfunction underlying the predominant symptom domains of ASD, with frontal involvement particularly critical for speech delay, hyperactivity, and cognitive impairment. The precuneus, although less consistently affected, appears to play a supportive role across multiple symptom clusters, likely reflecting its contribution to self-referential processing and social cognition.

Table 3: Distribution of study subjects with respect to areas of hypoperfusion & symptom profile

Symptom profile	Frontal (n=23)	Temporal (n=20)	Parietal (n=20)	Precuneus (n=12)
Speech Delay(n=22)	21 (95.5%)	18 (81.8%)	18 (81.8%)	11 (50%)
Hyperactivity (n=16)	16 (100%)	12 (75%)	12 (75%)	7 (43.8%)
Cognitive function poor (n=9)	9 (100%)	8 (88.9%)	8 (88.9%)	4 (44.4%)
Poor Eye Contact (n=9)	8 (88.9%)	7 (77.8%)	7 (77.8%)	4 (44.4%)

Table III reveals that speech delay is most strongly associated with hypoperfusion in the frontal (95.5%) and temporal (81.8%) regions. Hyperactivity is linked to hypoperfusion in the frontal (100%) and temporal (75%) regions. Poor cognitive function and eye contact are less common but still associated with hypoperfusion, especially in the frontal region.

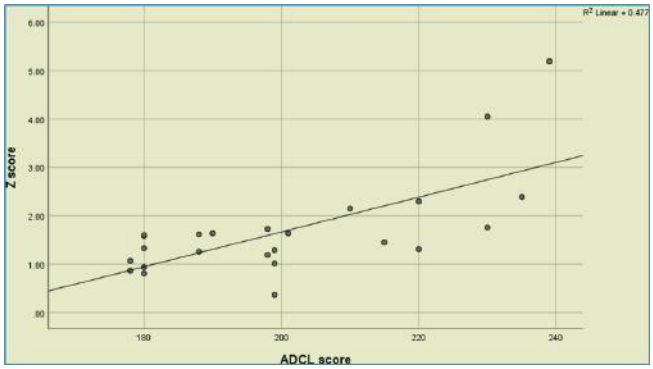

Fig. 1: Scatter diagram of correlation of ADCL score with Z score in total study subjects (n=24) (R^2 = Coefficient of determination) shows significant positive correlation between ADCL score and Z score. 48% of the increase in ADCL score is attributed to increase in Z score.

Analysis of Z-scores across different ASD severity groups demonstrated a clear gradient of perfusion abnormalities. The Kruskal–Wallis test confirmed a statistically significant difference among severity levels (p = 0.012). Children with high-moderate ASD exhibited the highest mean rank Z-score (19.83), which was substantially greater than that of the low-moderate group (11.06) and the mild group (9.25). This pattern indicates that increasing severity of ASD is strongly correlated with greater deviations in regional cerebral perfusion, as reflected by higher Z-scores. The findings suggest that Z-score analysis not only detects perfusion abnormalities but also provides an objective biomarker of disease severity. Higher Z-scores in the high-moderate group reflect more extensive or pronounced hypoperfusion,

which is consistent with the observed clustering of severe symptoms such as poor cognitive function and reduced social interaction. Thus, Z-score mapping may serve as a valuable quantitative tool for stratifying ASD severity and monitoring disease progression.

Table 4: Comparison of Z score among different ASD severity in total study subjects (n=24)

ASD severity	Mean Rank	p value
Mild (n=10)	9.25	**0.012**
Low moderate (n=8)	11.06	
High moderate (n=6)	19.83	

Kruskal-Wallis test was done to find out the p value.

Table IV shows a significant difference in Z-scores among ASD severity levels. The Kruskal-Wallis test revealed that high moderate ASD cases had the highest mean Z- score (19.83), significantly higher than mild (9.25) and low moderate (11.06) cases, with a p-value of 0.012 indicating statistical significance.

Table V presents the results of pairwise comparisons of Z-scores between ASD severity groups using the Dunn–Bonferroni post hoc test. The analysis demonstrated that children with high-moderate ASD had significantly higher Z-scores compared to both the mild group (p = 0.004) and the low-moderate group (p = 0.009). However, there was no statistically significant difference between mild and low-moderate ASD cases (p > 0.05). These findings indicate that Z-scores are particularly effective in differentiating high-moderate ASD from less severe forms, supporting their role as a quantitative marker of severity. The absence of significant differences between mild and low-moderate groups suggests that perfusion abnormalities may be less distinct in early or moderate stages but become more pronounced as severity increases.

Table 5: Pairwise comparison of Z score between different ASD severity (n=24)

ASD severity	p value
Mild (9.25) vs Low moderate (11.06)	>.05
Mild (9.25) vs High moderate (19.83)	**0.004**
Low moderate (11.06) vs High moderate (19.83)	**0.009**

Dunn-Bonferroni pairwise comparison was done to find out the p value.

Among the different ASD severity, Z score was significantly elevated in High moderate compared to Mild and Low moderate cases. Table V shows significant differences in Z-scores between ASD severity levels. Pairwise comparisons revealed that high moderate ASD cases had significantly higher Z-scores compared to mild (p=0.004) and low moderate (p=0.009) cases. No significant difference was found between mild and low moderate cases (p>0.05).

The distribution of regional cerebral blood flow (rCBF) abnormalities, expressed as Z-scores, across different ASD severity groups shown in Bar chart Figure 2. In the mild group, most children exhibited a slight decrease in rCBF (n = 7), with 3 cases showing normal perfusion. The low-moderate group was similarly dominated by slight decreases (n = 6), with one case each of normal and moderate decrease. In contrast, the high-moderate group demonstrated a more heterogeneous and severe pattern, with no normal cases; 2 cases each showed slight, moderate, and significant decreases. The findings indicate a progressive worsening of rCBF abnormalities with increasing ASD severity.

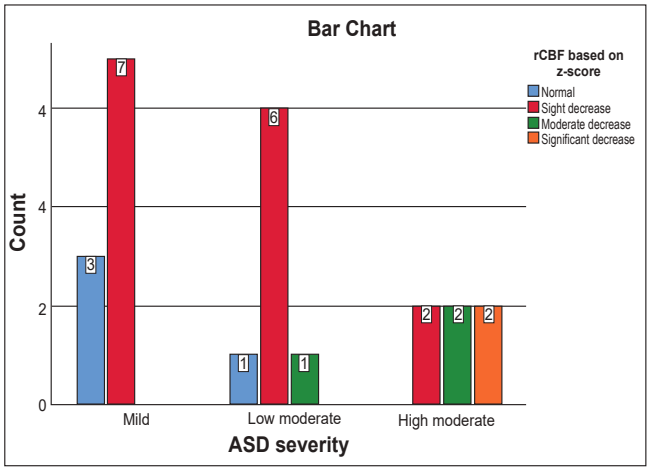

Fig. 2.: Bar chart of distribution of study subjects based on rCBF status among different ASD severity (n=24)

Correlation analysis demonstrated a significant association between ASD severity and regional cerebral blood flow (rCBF) abnormalities. Spearman's rho test revealed a moderately strong positive correlation (**ρ** = 0.609, p = 0.002), indicating that as ASD severity increased, the extent of perfusion deficits also became more pronounced. This finding supports the quantitative

results from Z-score analysis, where higher mean ranks were observed in the high-moderate ASD group, and aligns with the distribution patterns shown in the bar chart, where moderate to significant decreases in rCBF predominated among more severe cases. Table VI represent correlation between ASD severity and rCBF status in total study subjects (n=24)

Taken together, these results suggest that rCBF impairment progresses in parallel with clinical severity, reinforcing the potential role of perfusion imaging as a functional biomarker for disease stratification. By objectively linking hypoperfusion patterns to symptom burden, these findings strengthen the evidence that cerebral perfusion abnormalities may underlie the neurobiological basis of ASD severity.

Table 6: Correlation between ASD severity and rCBF status in total study subjects (n=24)

Parameter		Correlation Coefficientrho value (ρ)	p value
ASD severity	rCBF status	0.609	0.002

Spearman's rho correlation coefficient test was done.

Table VI indicates a significant positive correlation between ASD severity and rCBF status, with a Spearman's rho coefficient of 0.609 and a p-value of 0.002. This suggests that increased ASD severity is associated with more pronounced decreases in regional cerebral blood flow.

The current study provides valuable insights into the neurobiological and cognitive aspects of childhood autism spectrum disorder (ASD) through the use of Tc99m ECD Brain SPECT imaging. A sample of 24 confirmed ASD cases, primarily boy (75%), aligns with existing literature that highlights the higher prevalence of ASD among boys. This gender preponderance is consistent with findings by Baron-Cohen *et al*. [6], who suggest that genetic, hormonal, and neurobiological factors may account for this disparity. Yang Wen-Han *et al.* [7] similarly observed a male predominance (86.9%) in their study on brain perfusion in ASD children, reinforcing the biological basis for gender differences in ASD prevalence.

Among the participants, common symptoms included speech delay, poor eye contact, and significant cognitive impairments, findings echoed by Baron-Cohen *et al.* [8], in their study of 15 ASD children. Our study revealed that mild ASD cases exhibited hypoperfusion predominantly in the frontal (100%), temporal (70%), and parietal (70%) regions, while low-moderate and high-moderate ASD cases showed hypoperfusion across multiple brain regions, with the most significant involvement in the frontal, temporal, and parietal regions. These findings are comparable to those of Starkstein et al., (9) who also reported cerebral hypoperfusion in ASD patients, especially in the temporal, occipital, and basal ganglia regions. Wilcox et al., (10) further support our findings, noting significant hypoperfusion in the prefrontal regions of individuals with ASD. The broad areas of hypoperfusion observed in our study population align with findings from Sasaki *et al.* [11], who reported a mixed pattern of hypoperfusion, particularly in the prefrontal cortex, medial frontal cortex, and anterior temporal cortex of ASD children. Similarly, Gupta and Ratnam [12] found generalized hypoperfusion in their study of 10 children with ASD, predominantly in the frontal and prefrontal regions. The involvement of the frontal lobes in ASD-related hypoperfusion is also supported by Ito *et al.* [13], who found hypoperfusion in the left temporal region, and Degrirmencvi *et al.* [14], who noted involvement of both frontal and parietal regions.

Our study also found that speech delay was the most common symptom associated with hypoperfusion across all brain regions, particularly in the frontal, temporal, and parietal areas, further corroborated by Yang *et al.* [15], and Kaya *et al.* [16], who noted similar patterns of hypoperfusion in the frontal lobes and basal ganglia.

The study revealed a strong positive correlation between ADCL and Z scores, indicating that 48% of the increase in ADCL score could be attributed to increases in Z score. This finding underscores the relationship between cognitive function abnormalities and ASD severity. These results are consistent with studies by Lange *et al.* [17], which highlight the importance of cognitive assessments in ASD management. Furthermore, the significant elevation of Z scores in high-moderate ASD cases compared to mild and low-moderate cases aligns with previous research, such as that of Lai et al. [18], which suggests that more severe ASD symptoms are associated with greater cognitive impairments.

Recent advances in neuroimaging techniques, including functional MRI (fMRI) and diffusion tensor imaging (DTI), have further elucidated the neurobiological basis of ASD severity. Studies by Ecker *et al.* [19] and Vasa *et al.* [20], have identified specific brain regions and connectivity patterns linked to ASD severity, offering potential biomarkers for monitoring the condition. Understanding the relationship between ASD severity, cognitive function, and behavioral symptoms can guide the development of personalized intervention strategies, which are crucial for improving outcomes for individuals across the ASD spectrum (Dawson *et al.* [21] and Kasari *et al.* [22]. However, limitations such as the small sample size and potential confounding variables should be acknowledged. Future research should focus on longitudinal studies to examine changes in cognitive function over time and incorporate multimodal neuroimaging approaches. Additionally, exploring the effectiveness of tailored interventions based on individualized assessments will be key to advancing ASD management.

4. Conclusions

This study highlights a clear link between the severity of Autism Spectrum Disorder (ASD) and brain hypoperfusion, demonstrated through Brain SPECT imaging. The results show that as ASD severity increases, Z-scores rise, indicating more pronounced abnormalities in brain perfusion. Hypoperfusion was most prominent in the frontal, temporal, and parietal regions, with more severe cases exhibiting widespread reductions in regional cerebral blood flow (rCBF). A strong correlation between hypoperfusion and symptoms such as speech delay, hyperactivity, and poor cognitive function emphasizes Brain SPECT's value in understanding the neurobiological aspects of ASD. These findings underscore the importance of early detection and intervention, suggesting that addressing brain perfusion abnormalities may be crucial in managing ASD symptoms and improving outcomes for affected individuals.

Limitations

The study's small sample size may not adequately represent Bangladesh's diverse population of children with Autism Spectrum Disorder (ASD). Additionally, limited access to advanced imaging techniques like Brain SPECT, especially in rural and underserved areas, restricts the scope of similar studies. Cultural stigma around mental health may result in underreporting or delayed ASD diagnosis, affecting the findings' generalizability. Financial constraints and scarce healthcare resources further impede the broader application of study results and the implementation of early detection and intervention strategies throughout the country.

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Reference:

1. Kanner L; Autistic disturbances of affective contact, Nerv Child., 2: 217-50 (1943).
2. Akhter S, Hussain AHME, Shefa J, Kundu GK, Rahman F, Biswas A; Prevalence of Autism Spectrum Disorder (ASD) among the children aged 18-36 months in a rural community of Bangladesh: A cross-sectional study, 7: 424 (2018).
3. Christensen DL, Baio J, Van Naarden Braun K, Bilder D, Charles J, Constantino JN *et al.*; Centers for Disease Control and Prevention (CDC). Prevalence and characteristics of autism spectrum disorder among children aged 8 years, Autism and Developmental Disabilities Monitoring Network, 11 sites, United States, 2012. MMWR Surveill. Summ., 65(3):1-23 (2016).
4. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5. 5th ed. Washington, DC: American Psychiatric Association; 2013.
5. Zürcher NR, Bhanot A, McDougle CJ, Hooker JM. A systematic review of molecular imaging (PET and SPECT) in autism spectrum disorder: Current state and future research opportunities, Neurosci. Biobehav. Rev., 52: 56-73 (2015).
6. Baron-Cohen S, Lombardo MV, Auyeung B, Ashwin E, Chakrabarti B, Knickmeyer R; Why are autism spectrum conditions more prevalent in males? PLoS Biol., 9(6):e1001081 (2011).
7. Wen-han Y, Jin J, Li-juan X, Mu-hua C, Xin W, Peng B *et al.*; Regional cerebral blood flow in children with autism spectrum disorders: A quantitative 99mTc-ECD brain SPECT study with statistical parametric mapping evaluation. Chin Med J., 124(9):1362 (2011).
8. Baron-Cohen S. Theory of mind and autism: A review, Int Rev Res Ment Retard., 23:169-84 (2000).
9. Starkstein SE, Vazquez S, Vrancic D, Nanclares V, Manes F, Piven J *et al.*; SPECT findings in mentally retarded autistic individuals. J Neuropsychiatry Clin Neurosci., 12(3):370-75 (2000).
10. Wilcox J, Tsuang MT, Ledger E, Algeo J, Schnurr T; Brain perfusion in autism varies with age, Neuropsychobiology, 46(1):13-6 (2002).

11. Sasaki M, Nakagawa E, Sugai K, Shimizu Y, Hattori A, Nonoda Y *et al.*; Brain perfusion SPECT and EEG findings in children with autism spectrum disorders and medically intractable epilepsy, Brain Dev., 32(9):776-82 (2010).

12. Gupta SK, Ratnam BV. Cerebral perfusion abnormalities in children with autism and mental retardation: A segmental quantitative SPECT study, Indian Pediatr., 46(2):161-4 (2009).

13. Ito H, Mori K, Hashimoto T, Miyazaki M, Hori A, Kagami S, et al. Findings of brain 99mTc-ECD SPECT in high-functioning autism--3-dimensional stereotactic ROI template analysis of brain SPECT, J. Med. Invest., 52(1-2): 49-56 (2005).

14. Degirmenci B, Miral S, Kaya GC, İyilikçi L, Arslan G, Baykara A *et al.*; Technetium-99m HMPAO brain SPECT in autistic children and their families. Psychiatry Res Neuroimaging,162(3): 236-43 (2008).

15. Wen-han Y, Jin J, Li-juan X, Mu-hua C, Xin W, Peng B *et al.*; Regional cerebral blood flow in children with autism spectrum disorders: A quantitative 99mTc-ECD brain SPECT study with statistical parametric mapping evaluation. Chin Med J., 124(9):1362 (2011).

16. Kaya M, Karasalihoğlu S, Üstün F, Gültekin A, Çermik TF, Fazlıoğlu Y *et al.*; The relationship between 99mTc-HMPAO brain SPECT and the scores of real-life rating scale in autistic children, Brain Dev., 24(2):77-81 (2002).

17. Lange N, Travers BG, Bigler ED, Prigge MB, Froehlich AL, Nielsen JA *et al.*: Longitudinal volumetric brain changes in autism spectrum disorder ages 6-35 years, Autism Res., 7(6): 716-26 (2014).

18. Lai MC, Lombardo MV, Baron-Cohen S. Autism. Lancet., 383(9920): 896-910 (2014).

19. Ecker C, Bookheimer SY, Murphy DG; Neuroimaging in autism spectrum disorder: Brain structure and function across the lifespan, Lancet Neurol.,14(11):1121-34 (2015).

20. Vasa RA, Mostofsky SH, Ewen JB, Trujillo J; Progress and promise in autism spectrum disorder research: From bench to bedside. World Psychiatry,15(3): 242-3 (2016).

21. Dawson G, Rogers S, Munson J, Smith M, Winter J, Greenson J *et al.*; Randomized, controlled trial of an intervention for toddlers with autism, The Early Start Denver Model. Pediatrics,125(1): e17-23 (2010).

22. Kasari C, Gulsrud A, Freeman S, Paparella T, Hellemann G; Longitudinal follow-up of children with autism receiving targeted interventions on joint attention and play, J. Am. Acad. Child. Adolesc. Psychiatry, 51(5): 487-95 (2012).