AUTISM SPECTRUM DISORDERS IN PRETERM INFANTS

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ABSTRACT **Background:** Autism spectrum disorders (ASD) are characterized by deficits in social interaction, communication, and unusual repetitive behavior. The latest estimate of autism prevalence in US is about 1 in 59 children which is up to 16 percent; more than double reported in year 2001; the trend being steeply upward since then. Early intervention and routine early screening are the need of the moment. Of late, evidence is emerging that prematurity may be associated with later development of ASD. However, there is scarcity of data from India even in term infants for the prevalence of this disability, not a single study dedicated to preterm infants is reported from our country.
Aims and Objective :
*   To estimate the prevalence of ASD by screening children between 16-30 months of corrected age, born preterm and term, using the M-CHAT score and to estimate the severity using ISAA score.
*   To determine the risk factors associated with ASD.
Materials and Methods: This study included 2200 children born preterm and term, aged between 16 to 30 month. M-CHAT(Modified Checklist for Autism in Toddlers) screening tool were applied in these children to assess for the risk of ASD. Those screened positive were then subjected to ISAA(Indian Scale for Assessment of Autism) score for screening. Data was recorded on a pre-designed proforma for comparison and analysis. **Results:** Out of total of 2200 children, it was observed that among the preterm born children; 13 children (1.2%) were found to be associated with ASD and among term born children, 6 children (0.5%) were found to be associated with ASD. This signifies that ASD is more prevalent in the preterm study population. Early gestational age, low birth weight, male sex, maternal complications(anaemia and pre-eclampsia) were found to associated with ASD. **Conclusion:** It can be concluded that prevalence of ASD is alarmingly very high in children born preterm which is detected between 16 to 30 months of age. Hence, early screening is essential to identify and provide intervention which will substantially improve the prognosis in these children.

KEYWORDS : Autism Spectrum Disorder, Prematurity, Gestational age, Prevalence, M-CHAT , ISAA

INTRODUCTION

Autism Spectrum Disorders(ASD) are mainly neurodevelopmental disorders characterized by impairment in social/communication skills, repetitive and stereotyped behaviour. The term "spectrum" refers to the wide range of symptoms, skills and levels of disability in functioning that can occur in individuals with ASD.[1]ASD occurs in every racial and ethnic group, and across all socioeconomic levels. Preterm infants carry a high risk of long-term neurodevelopmental morbidities. Of late, evidence is emerging that prematurity may be a risk factor for later development of ASD. However, boys are significantly more likely to develop ASD than girls. [.]

The World Health Organization (WHO) has estimated the international prevalence of ASD at 0.76% accounting to approximately 16% of the global child population.[]The prevalence of autism in the United States has risen steadily since researchers first began tracking it in 2000 and presently is 1 in 59 children (approximately 1.7%).[]In another study in UK, the annual prevalence rates for each year were steady at approximately 3.8 per 1000 boys and 0.8/1000 girls.[] There is scarcity of data and very less studies regarding prevalence of ASD in India. However prevalence in our country is reported to be around 1 in 500 or 0.20% of the population.[] Standardized screening for ASD at 18 and 24 months of age with ongoing developmental surveillance continues to be recommended in primary care, because ASD is common and can be diagnosed in as young as 18 months of age.[4]Now, the most commonly used screening tool is M-CHAT (Modified Checklist for Autism in Toddlers.[]The M-CHAT is a psychological questionnaire that mainly evaluates the risk for autism spectrum disorder in children aged between 16–30 months. Because of scarcity of availability on prevalence in India, this study was undertaken to see the prevalence and its association with gestational age. The purpose of this study is early identification of symptoms, diagnosing at the right time and regular follow-up so that child can be managed as early as possible.

MATERIALS AND METHODS

This analytical study was conducted at SNCU Follow-up clinic and Out-Patient Department (OPD) of Pediatrics at Kamla Raja Hospital, G.R Medical college, Gwalior. Written informed consent from the parents were obtained before enrolling subjects in the study.

Setting: Kamla Raja Hospital, G.R Medical college, Gwalior
Study Design: Analytical study
Duration of Study Two years
Sample Size: 2200 children
i. Considering the prevalence of ASD in preterm infants as 1% and term babies as 0.1% the required sample size will be:

$$n_1 = n_2 = n = \frac{\left[Z_{\alpha 2}\sqrt{2PQ} + Z_{1-\beta}\sqrt{P_1 Q_1 + P_2 Q_2}\right]}{(P_1 - P_2)^2}$$

Where,
 P1=1, P2=0.1, P=3.9
 $Z_{\alpha/2}$ = 1.96, $Z_{1-\beta}$= 1.64
 n=1058 in each group Total Sample = 2116 ~ 2200

Inclusion Criteria
i. Study group- preterm born children at corrected age of 16-30 months of age who were born <37 weeks of gestation.
ii. Comparison group: term born children between 16-30 months of age who were born 37-42 weeks of gestation

Exclusion Criteria
i. Children with major congenital anomalies
ii. Children with progressive neurological disorder
iii. Severe neurological sequelae post HIE

METHODOLOGY

This is an analytical study in which children born preterm with corrected age of 16 to 30 months, attending SNCU Follow-up Clinic and Out-Patient Department of Pediatrics , Kamla Raja Hospital, G.R Medical college, Gwalior. A comparison group of children between 16-30 months of age, born between 37- 42 weeks gestation were also enrolled. Informed consent were obtained from parents of all the children under study. All children were evaluated using M-CHAT score.M-CHAT R/F is a 23-item scoring system for the identification of early behaviours associated with ASD in children aged 16-30 months.

Children who screened positive were further assessed using ISAA Scoring system (Indian scale for assessment of autism) which is also a screening test for diagnosis of ASD.

Study Flowchart
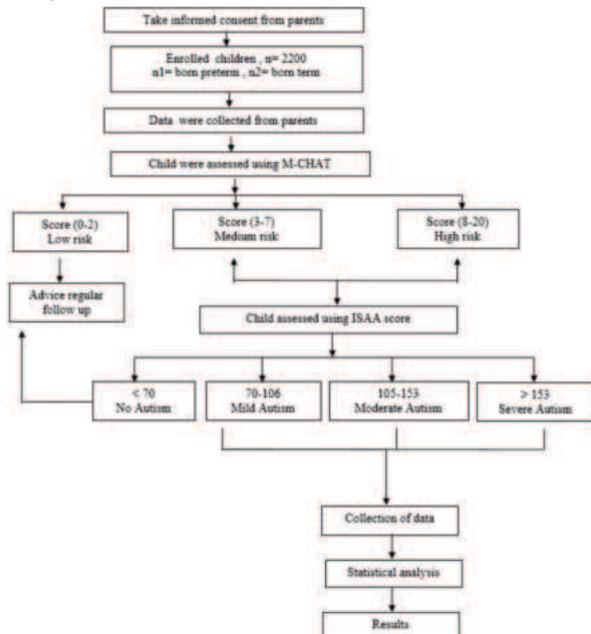
1. Statistics:
Table 1: Descriptive Variables Of The Study Group

Parameters	Range	Frequency	Percentages
Gestational Age	< 28 weeks	9	0.4
	29 to 31+ 6 weeks	94	4.3
	32 to 36+ 6 weeks	997	45.3
	> 37 weeks	1100	50.0
Sex	Female	966	43.9
	Male	1234	56.1
Birth Weight	< 1 kg	9	0.4
	1 to 1.49kgs	29	1.3
	1.5 to 2.49 kgs	1061	48.3
	> 2.5 kgs	1101	50.0
Mode of delivery	Lower segment C-section	586	26.6
	Normal Vaginal Delivery	1614	73.4

Table 2: Prevalence Of Autism Spectrum Disorders In The Study Population

Prevalence		
Preterm	Frequency	Percent
ASD	13	1.2
NORMAL	1087	98.8
Term	Frequency	Percent
ASD	6	0.5
NORMAL	1094	99.5

Table 3 : Comparison Of Mean And Median Values Of Gestational Age, Corrected Age And Birth Weight Among ASD Group And Normal Group

Unpaired t test	Group	N	Mean	S D	Median	Q1	Q2	Q3	P value
Gestational age	ASD	19	33.42	3.469	32.000	31.00	32.00	38.00	<0.001
	Normal	2181	36.55	2.662	38.000	34.00	38.00	39.00	
Corrected Age	ASD	19	23.11	3.914	32.000	31.00	32.00	1.700	0.010
	Normal	2181	21.80	3.070	38.000	34.00	38.00	39.00	
Birth weight in kg	ASD	19	1.76	0.444	1.700	1.600	1.70	1.800	<0.001
	Normal	2181	2.45	0.534	2.700	1.900	2.700	3.00	

Table 4 : Frequency Of Subjects With Different M-Chat Score

M-CHAT score			
		Frequency	Percent
Preterm	Low Risk	1087	98.8
	Medium Risk	9	0.8
	High Risk	4	0.4
Term	Low Risk	1094	99.5
	Medium Risk	4	0.4
	High Risk	2	0.2

Frequency of subjects with different ISAA score		
ISAA score		
	Frequency	Percent
No Autism	2181	99.1
Moderate Autism	13	0.6
Severe Autism	6	0.3

DISCUSSION
The study was intended to estimate the prevalence of Autism Spectrum Disorders (ASD) in both preterm and term population and the risk factors associated with ASD. By early screening and intervention, prevalence of ASD's can be reduced leading to better neuro-developmental outcomes in children particularly between age 16-30 months of age.

The present study shows that prevalence of ASD was more in the preterm population than the term population. Prevalence in the preterm population was 1.2% and in the term population was 0.5 % Moore T et al observed in their study population of 1031 children that prevalence of ASD in the preterm population was 1.4%.[] Another study conducted by Iva Dudova et and Joseph RM et al observed that the prevalence of ASD in preterm population was 12.9%.[] and 7.1 % respectively.[20]

In this study, it was observed that the mean birth weight of subjects in ASD group was 1.762 ± 0.411; which is significantly less compared to normal group – 2.448 ± 0.527 with p value <0.001. Thus, implying that ASD is more associated with decrease in birth weight. Lampi KM et al in her study observed that very low (<1500 g) and moderately low (<2500 g) birth weight showed increased risk of childhood autism .[] Also, another study by Maureen Hack et al and Mann JR et al observed that extremely low birth weight children were associated with high risk of ASD than normal birth weight children.[,18] A population-based case-control study conducted in Finland found out that very low and moderately low birth weight showed increased risk of ASD .[]

In this study, it was observed that mean gestational age of subjects in ASD group was 33.42 ± 3.469; which is significantly less compared to normal group – 36.55 ± 2.662 with p value <0.001, thus implying that ASD is significantly associated with decrease in gestational age. Allen L et al observed that there was a significant correlation between birth week and the risk of ASD.[] Saied Bashirian et al from his study found out that there was significant association between SGA and ASD establishing a strong connection between ASD and early gestational age.[11,19] Another study done in Norway, Sweden and Finland observed that other than early gestational age, even late gestational age (>42 weeks) were more associated with ASD.[]

In this study, it was observed that M-CHAT and ISAA are standard screening tools for the diagnosis of risk of ASD. In the preterm subjects, 1087(98.8%) were low risk and were not associated with ASD, 9(0.8%) were medium risk and were associated with ASD and 4(0.4%) were high risk and were associated with ASD. These study subjects who were M-CHAT positive were again screened using ISAA score. It was found out that 13(0.6%) had moderate Autism and 6(0.3%) had severe Autism.

In another study by Ozgur Oner et al it was observed that 89.7% of screen-positive children had 3–7 total score (moderate- risk), and 10.3% had 8–20 total score(high-risk).[] Another study by Raina SK et al in which ISAA score was used observed that 43 children out of a total of 28,070 children were diagnosed as cases of ASD yielding a prevalence of 0.15% (95% confidence interval [CI] =0.15–0.25).[13] Deepa C. Metgud et al in her study used Kannada version of M-CHAT-revised questionnaire to record their responses based on their child's behavior, and the total score was calculated. It was observed that among the 510 children screened for the risk of ASD, the prevalence was found to be 0.19%. The mean age of the participants was 24.5 ± 5.04 months.[] In a cross-sectional study done in

Kerala it was observed that a total of 6,237 toddlers were surveyed of whom 3,139 (50.3%) were males. The mean age of the sample was 20.13 (±2.72) months. Of the 341 toddlers (5.5%) who had a total score of 3 or above on the M-CHAT-R, 259 toddlers (4.2%) scored between 3-7 and were considered to have a medium risk and 82 toddlers (1.3%) scored between 8-20 and were considered to be at high risk for ASD. Thus, it was evident that M-CHAT R was a useful screening tool for the assessment of ASD.[]

LIMITATION

This study reports very high prevalence of ASD and since it was a prospective cohort study, follow up of these patients would have given a better picture of the existing burden.
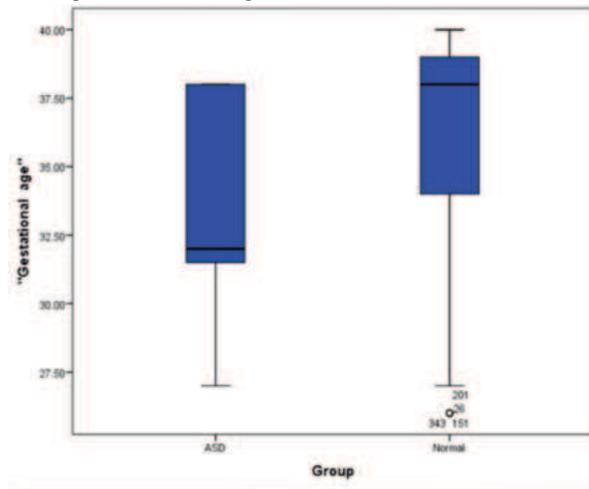

Figure 1: Box And Whisker Plot Showing Mean And Median Gestational Age Among ASD Group And Normal Group

CONCLUSION

The present study " To estimate the prevalence of autism spectrum disorders in pre term infants between 16 to 30 months of corrected age: an analytical study " was intended to estimate the prevalence of Autism Spectrum Disorders (ASD) in both preterm and term population and the risk factors associated with ASD. This study concluded that prevalence of Autism spectrum disorders in study population was 0.86%.Also, it was observed that early gestational age and low birth weight were associated with risk of developing ASD.

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