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Clinical and Etiological Profile of Children with Developmental Delay: An Observational Cross - Sectional Study from Eastern India

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Abstract: ***Children who do not meet developmental milestones in at least one of the key streams-including motor, perceptual, speech, cognition, and behavior-are said to have developmental delay (DD). The following observational cross - sectional study was undertaken to assess the clinical profile and etiology of children with developmental delay in Eastern India. Children with developmental delay, developmental concerns or intellectual disability up to 15 years of age were included. The study included 70 children with Global Developmental Delay. Majority of children were males (72.9%). The mean age of the children was 4.1 years. The prevalence of gross motor, fine motor, socio - adaptive, hearing, speech and vision delays were 65.7%, 70%, 92.9%, 25.7%, 92.9% and 8.6%, respectively. Autism Spectrum Disorder (ASD) was the most common factor (26.2%), followed by perinatal (18.5%) and structural (15.4%). In the present study, 11.4% of the children with developmental delays were preterm babies and 4.6% of the children had metabolic etiology. Genetic factors accounted for 13.8% of the cases included in our study. Karyotype - 47XY+21 was the most common genetic finding (44.4%) Microcephaly was the most common clinical feature among the children (18.6%). Neuroimaging yielded structural changes in 47.1% of the children***

Keywords: developmental delay, child, etiology, Autism Spectrum Disorder, India

1. Introduction

Children who do not meet developmental milestones in at least one of the key streams-including motor, perceptual, speech, cognition, and behavior-are said to have developmental delay (DD). [2] Global developmental delay (GDD) prevalence estimates vary from 1-3 percent worldwide. [1] Recent data indicate a substantially higher frequency of 6.4 percent among Turkish youngsters and 8 percent among UAE children. [3, 4] According to several research, the incidence in India ranges from 3-13 percent, depending on the age group tested, the methods used, and the regions questioned. [5]

There are both controllable (like birth asphyxia) and non - modifiable (like hereditary factors) reasons of developmental delay. Understanding the causes of developmental delays might aid policy makers in creating more effective public health initiatives that focus on the most prevalent risk factors and aim to reduce the number of such children who have developmental delays. The primary care physician is most equipped to identify and refer these kids, even if early diagnosis might be difficult. [6] To be able to identify kids who are suspected of having DD at an early age and then keep track of how they are developing, it is crucial to evaluate the risk factors. A full service system for early intervention could then be provided by clinicians if it could be established early on whether children suspected of having DD really do have developmental issues and to define the breadth of related deficiencies. [7, 8]Thus, for the physicians to quickly recognise and handle the case, it is critical that they be aware of the presenting characteristics and any relevant predisposing variables.

Clinical issues in children with developmental delays range from dental decay, anaemia, and more severe malnutrition, etc. When these kids are seen at a tertiary level hospital, particularly with congested OPDs, data on the most prevalent clinical diseases linked with them will provide better insight into their health.

2. Literature Survey

The intricate process of child development starts in the womb and lasts until maturity. It is impacted by biology and the environment, which may have a favourable or negative impact on it. The level of development a person had as a youngster has a significant impact on their mental health. The child develops and grows after the neonatal stage. Gross motor, fine motor, language, cognition, and social - emotional behaviour are the primary developmental domains. [9] When a child does not meet developmental milestones in comparison to others from the same group, a developmental delay is often identified. The degree of delay is sometimes categorised using statistical terminology as mild (functional age [FA] 33 percent below chronological

age [CA]), moderate [FA] 34 percent to 66 percent of CA], and severe [FA] 66 percent of CA]. [10, 11]

Based on the number of domains affected, there are three different kinds of developmental delays: Three types of developmental delays exist: (1) Isolated (involving a single domain); (2) Multiple (affecting two or more domains or developmental lines); and (3) Global (involving considerable delay in the majority of developmental domains). [11, 12]

Studies have been undertaken in the past to understand and evaluate the developmental delays in children. Tsai et al reported cognitive delay as the most typical subtype of DD and that it was more frequent in men. [13] Aggarwal et al. in their study from north India identified aetiology of mental retardation (MR) /developmental delay (DD) in 196 individuals (58 percent) was a hereditary disease. In a sizable majority of individuals, the aetiology of MR/DD was variable and difficult to determine. They recommended genetic workup is necessary for all such individuals since many MR/DD cases are caused by chromosomal and different monogenic diseases. [5] Occurrence of birth asphyxia, sepsis, convulsions, aberrant neurological findings, and dysmorphism were found to be the significant aetiology for the DD in another study. [14] Stunting and maternal illiteracy appeared as important biological predictors, but preterm and a history of seizures emerged as micro- environmental factors for the DD in a study by Sachdeva et al. [15]Chen et al. found that the majority of children with global delay had either neuromuscular conditions or mental/psychological disorders and were associated with genetic risks or congenital anomalies, while most children with motor delay had neuromuscular or brain conditions and were at risk of being born prematurely or with low birth weight. [7] Other factors such as small - for - gestational - age (SGA), multiple pregnancies and previous maternal obesity were also linked with the DD. [16] Male sex have also been linked with significantly higher prevalence of the DD. [17, 18] Socioeconomic risk factors such as low household income, low household education levels for both parents, and having fewer than three children per family were all significantly linked with developmental achievements in the children. [19]

Based on the literature review, studies on the clinical features and etiology of developmental delays are limited in India. The data on clinical profile would vary across region and socio - economic status and such data is lacking for children in Eastern India. Hence, the following study was undertaken to study the clinical profile and etiology of children with developmental delay in Eastern India.

3. Methodology

The present study was conducted as an observational cross - sectional study at the pediatrics department of the Command hospital, Kolkata between March 2021 and September 2022. The study population included the children with developmental delay, Developmental concerns (both global developmental delay as well as isolated developmental delays, not achieving milestones as per age) or intellectual disability (poor in academics as reported both by parents and teachers, school drop outs) up to 15 years of age. Children with developmental stagnation due to acute illness and refractory epilepsy were excluded from the study. Previous studies have shown that etiology of developmental delays can be identified in 60 - 80 % of cases. Based on these reported, taking the prevalence of etiology as 80% and an absolute error of 10%, at 95% confidence levels and including 10% missing data, a sample size of 70 children was estimated for the study.

A pre designed set of questionnaires and proforma was used to collect the data for the study. After taking written consent from the parents, detailed history and examination were done. Family history including three generation pedigree was charted. Relevant investigations like Ophthalmology/ ENT consultation & EEG if required were carried out. Neuroimaging in all cases of GDD/ID/Isolated language delay was done. EMG/NCV was conducted in cases of isolated motor delay. Metabolic & Genetic evaluation was done where applicable. In case of presence of dysmorphic features or signs suggestive of metabolic disorders specific tests were performed. Etiological diagnosis was considered established only if clinical features was supported by investigations. Data was entered in MS Excel and analysed by SPSS v26.0. Categorical variables were expressed in frequency and percentages. Age and anthropometry were expressed in Mean (Standard deviation) &Median (Interquartile range). Appropriate graphs were included.

4. Results and Discussion

The study included 70 children with Global Developmental Delay, in which majority were males (72.9%). This is in line with findings of the most of the previous similar studies. [5, 7, 13, 14, 18]Male gender has been attributed as a potential cause for the developmental delays from the previous studies. [20]The mean age of the children was 4.1 years. (Table 1) This was slightly younger than age group included in Aggarwal et al (Mean=4.8 years). [5] This is older in comparison to Tikaria et al (mean=23.6 months) and Chun - Chen et al (mean=37.8 months). [7, 14] This might be due to the fact that Tikaria et al included children under 5 years of age only. [14] Kim et al reported a similar age as the children in our study. [18]

Table 1: Demographic & anthropometric profile of the children in the study

	Frequency	Percentage
Sex		
Male	51	72.9
Female	19	27.1
Period of gestation		
Early term	1	1.4
Late pre term	7	10.0
Term	62	88.6
	Mean	SD
Age	4.1	2.5
Height	100.4	18.5
Weight	17.4	8
OFC	48.8	4

The prevalence of gross motor, fine motor, socio - adaptive, hearing, speech and vision delays were 65.7%, 70%, 92.9%, 25.7%, 92.9% and 8.6%, respectively. (Table 2) Chun - Chen et al reported lower prevalence of speech (21.9%) and motor (13.9%) delays in their study children from Taipei. [7]

Kim et al found a 3.8% prevalence of motor delay, which was lower than ours. [18] Tsai et al reported motor delay among 47.9% of DD children. [13]

The mean (SD) DQ/IQ was 45.9 (10.7) in the current study, was higher than the IQ reported by Aggarwal et al (mean=39.8). [5] The difference might be because Aggarwal et al included mentally retarded children as well. Chun - Chen et al reported 2% prevalence of cognitive delay in their study. [7]

Table 2: Distribution of the developmental delay among the children

Developmental delay	Frequency	Percentage
Gross motor	46	65.7
Fine motor	49	70.0
Socio - adaptive	65	92.9
Hearing	18	25.7
Speech	65	92.9
Vision	6	8.6

Table 3: Etiology of developmental delay

	Frequency	Percentage
ADHD	3	4.6
ASD	17	26.2
Genetic	9	13.8
Idiopathic	5	7.7
Metabolic	3	4.6
Perinatal	12	18.5
Postnatal	5	7.7
Prenatal	1	1.5
Structural	10	15.4

Etiology and clinical features are enumerated in Table 3 & 4. Autism Spectrum Disorder (ASD) was the most common factor (26.2%), followed by perinatal (18.5%) and structural (15.4%). Hypoxic ischemic encephalopathy was reported as the most common aetiology by Kim et al. [18] Aggarwal et al reported a lower percentage of CNS structural defects (7.4%). [5]Genetic factors accounted for 13.8% of the cases included in our study. Tikaria et al reported a slightly higher percentage of chromosomal cause (17%). [14] Similar to Tikaria et al, Chun - Chen et al and Kim et al also reported higher genetic defects (20% & 22.6%). [7, 18]

In the present study, 4.6% of the children had metabolic etiology, which was in line with the findings of Tikaria et al (4%). [14] Aggarwal et al found that 10.1% had neurometabolic syndromes. [5]Idiopathic was reported as 7.7% in our study. In contrast, Tikaria et al study had 27% as idiopathic, which was the most common one as well in their study. [14] Aggarwal et al also reported high proportion of idiopathic cause (25.2%). [5] The difference might be due to the better diagnostic work - up in our study, owing to advancement that had happened during the period that elapsed between.

Prematurity has been a significant risk factor for the DD. [19, 21] In the present study, 11.4% of the children with developmental delays were preterm babies, which is in line with Tikaria et al who reported 13% preterm deliveries among the children with global developmental delay. [14]Ozkan et al reported a lower prevalence of preterm deliveries (8.2%). [19] Kim et al in their study found that preterm babies were there between 12.5 and 29.2%, among the DD children. [18]

Among the perinatal factors, we found that perinatal asphyxia was reported in 18.6% of the studied children, while Tikaria et al found birth asphyxia among 20% of the GDD children. Our study had a IUGR among 8.6% of the children. [14]Kerstjens et al in their study reported that IUGR as a significant risk for developing the DD among small for gestational age babies, among the pre - term deliveries. [17] Among the postnatal factors assessed in our study, neonatal sepsis was found in 8.6% of children, which is higher than the proportion reported by Tikaria et al (5%) and Savioli et al (5.5%). [14, 22]

Microcephaly was the most common clinical feature among the children (18.6%). Tikaria et al reported higher microcephaly prevalence of 34%, while 2% had macrocephaly. [14]

Neuroimaging was done among 34 children, which yielded structural changes in 47.1%, HIE related changes in 26.5% and infective in 2.9%.14.7% showed no MRI abnormality. (Table 4) Fundus abnormalities were reported in 9.9% of cases, among which brushfield spots were common (4.3%). SNHL was the most common ENT finding (5.7%). Prevalence of seizures was 34.3%

Table 4: Distribution of etiology& clinical features of the developmental delay

	Frequency	Percentage
Antenatal		
Pre - eclampsia	2	2.9
Perinatal		
Perinatal asphyxia	13	18.6
IUGR	6	8.6
Postnatal		
Neonatal sepsis	6	8.6
Kernicterus	1	1.4
Neonatal hypoglycemia	4	5.7
Neonatal meningitis	3	4.3
Clinical Features		
Microcephaly	13	18.6
Facial dysmorphism	10	14.3
Undernourishment	9	12.9
Hypertonia	13	18.6
Hypotonia	5	7.1
Abnormal fundus	7	10
ENT abnormalities	8	11.4
Seizures	24	34.3
Neurocutaneous markers	2	2.8
Neuroimaging findings		
Structural changes	16	47.1
HIE related changes	9	26.5
Infective changes	1	2.9
Others	4	11.8
NAD	5	14.7

Metabolic screening was done for 18 patients, among which 12.5% turned out to be positive, 2 were indeterminate. Tikaria et al found higher proportion of abnormalities among the metabolic tests (17%). [14]

Genetic screening was done among 20% (14) of cases, among which 64.3% (9) turned out to be positive. In the

current study, karyotype - 47XY+21 was the most common genetic finding (44.4%) (Table 5) Tikaria et al found lower proportion of children with karyotyping abnormality. [14] 33.1% had chromosomal syndromes as aetiology as per Aggarwal et al. [5] KARYOTYPE - 47XY+21 was the most common genetic finding (44.4%) in our study, while 92.4% were shown to have Trisomy 21 by Aggarwal et al. [5]

Table 5: Genetic markers among the children tested positive for genetic screening

Genetic markers	2	2.8
CLN3 gene mutation	2	22.2
Inconclusive	1	11.1
Karyotype - 47XY+21	4	44.4
Mutation in COL5A1	1	11.1
Mutation in TSC1	1	11.1

5. Conclusion

The prevalence of gross motor, fine motor, socio - adaptive, hearing, speech and vision delays among the children in the present study were 64.7%, 69.1%, 92.6%, 22.1%, 94.1% and 7.4%, respectively. ASD has been found to be most common aetiological factor. Genetic aetiology was found among 12.9% of the cases. Karyotype - 47XY+21 was the most common genetic finding. Microcephaly followed by facial dysmorphism were the common clinical features of the DD children.

6. Future Scope

The index study was not devoid of limitations. Since the study was a single centric study, the findings cannot be applied to other settings or regions in India. Owing to the cross sectional and descriptive nature of the study, association of the potential risk factors and aetiologies with the development delays could not be established. Socio - economic risk factors of the children were not assessed. Hence, in the future multi - centric, prospective analytical studies must be conducted to establish the causal association between the risk factors and the DD. The studies must also include socio - economic risk factors also, to bring out the risk profile of the developmental delay among the children in a holistic manner.

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