Section: Pediatrics

Original Research Article

CLINICAL PROFILE AND ETIOLOGICAL RISK FACTORS IN CHILDREN LESS THAN SIX YEARS WITH AUTISM SPECTRUM DISORDER AND SHORT-TERM OUTCOME OF BEHAVIOUR THERAPY

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Abstract

Background: Autism spectrum disorder (ASD) is a neurobiological disorder of early childhood characterised by impaired social communication and interaction, as well as restricted and repetitive behaviours. This study aimed to evaluate the clinical profile of autism spectrum disorder (ASD) in children less than six years old and the short-term outcome of behaviour therapy in these children. **Material and Methods:** Autism spectrum disorder (ASD) is a neurobiological disorder of early childhood characterised by impaired social communication and interaction, as well as restricted and repetitive behaviours. This study aimed to evaluate the clinical profile of autism spectrum disorder (ASD) in children less than six years old and the short-term outcome of behaviour therapy in these children. **Results:** The most common symptom of ASD was loss of eye contact. Behavioural therapy (88%, n = 44) improved symptoms in children with ASD. The most common comorbidity associated with ASD was seizure disorder (62%, n = 31). Antenatal risk factors such as non-routine maternal medicine during pregnancy, dysthyroid status, maternal infection, PIH, and maternal stress during pregnancy predispose children to ASD worldwide. Postnatal risk factors such as preterm birth, LBW baby, non-exclusively breastfed baby, NICU graduate, preschool screen exposure, and screen time of more than an hour all predispose children to ASD worldwide. The correlation between these factors and ASD was statistically significant ($p < 0.05$). **Conclusion:** This study shows the clinical profile, comorbidities, and short-term outcome of behaviour therapy and establishes the etiological risk factors for ASD in children less than six years of age.

INTRODUCTION

Autism is a neurobiological disorder characterised by three cardinal features. It typically occurs during the early developmental periods. It usually manifests before three years of age and significantly affects the functioning of the child. The last 50 years have seen an amazing revolution in child and adolescent psychiatry, which has been reflected in the diagnosis, classification, and management of autism spectrum disorder. The nomenclature, diagnostic criteria, and classification of this condition have changed over time.

The first epidemiological study of autism showed a population prevalence of approximately 4 per 10,000, but the prevalence of autism has dramatically increased because of the evolution of child and adolescent psychiatry over the past 50 years. Autism spectrum disorder (ASD) is one of the most common neurodevelopmental disorders in the world. Most epidemiological studies have shown that male children are affected more than female children. The male-to-female ratio varied from 2:1 to 3:1. According to recent data, in the United States, the prevalence of ASD is 1 in 44 children. However, the incidence of ASD was diagnosed at 1:54 in males and 1:252 in females.

In India, a recent study by INCLEN on the prevalence of neurodevelopmental disorders in children showed a prevalence of autism spectrum disorder, which was estimated at 1.4%. In a study by INCLEN, Among the estimated prevalence of neurodevelopmental disorders in children, the prevalence of autism spectrum disorder in India was

estimated at 1.1% (range=0.7-1.7). The prevalence in rural areas was estimated at 1.1% (0.7-1.8). The prevalence in urban areas was estimated at 1.2% (0.5-2.7).

In the last decade, because of increased awareness among both families and professionals, leading to earlier and more accurate diagnoses of autism, its incidence seems to be on the rise. The prevalence of autism spectrum disorder has increased significantly over the past 25 years, primarily because of improved diagnosis and case findings, as well as the inclusion of less severe presentations within the autism spectrum. There was a 4:1 male predominance. The prevalence is increased in siblings (up to 10% recurrence rate), particularly in identical twins, and there are no racial or ethnic differences in the prevalence. Children from racial minorities and those with lower socioeconomic status are at risk of late diagnosis.

Autism spectrum disorder (ASD) is a genetic and environmental disorder with a high heritable contribution in childhood. Its genetic contribution is addressed by higher concordance rates in monozygotic twins. Sibling recurrence was 19%, which is higher for children immediately following the index case's birth. First-degree relatives have a 20-80-fold increased risk for autism. Modifiers, such as epigenetics, sex-linked modifiers, CNVs, double-hit mutations, and environmental factors, are unknown. Autism spectrum disorders are associated with numerous genes involved in brain development and synaptic function. Many improvements in diagnostic modalities help in the identification of genetic background in autism spectrum disorder.

Aim

This study aimed to evaluate the clinical profile, comorbidities, short-term outcomes of behaviour therapy, and etiological risk factors of ASD in children less than six years of age.

MATERIALS AND METHODS

This case-control study was conducted on 50 children with autism spectrum disorder at the Institute of Child Health and Research Centre, Government Rajaji Hospital & Madurai Medical College, Madurai, from June 2020 to June 2021. The study received institutional ethics committee approval before its initiation, and informed consent was obtained from the parents or guardians of all the children after fully explaining the study procedure.

Inclusion Criteria

Children of less than six years who were diagnosed to have autism spectrum disorder according to AIIMS MODIFIED INCLEN DIAGNOSTIC TOOL FOR AUTISM SPECTRUM DISORDER based on DSM 5 criteria were included in the study as cases. Age- and sex-matched healthy children were used as controls.

Exclusion Criteria

A standard questionnaire was developed to evaluate the clinical profile, comorbidities, short-term outcomes of behaviour therapy, and risk factors. The study population was interviewed using this questionnaire, and the data were documented in proforma.

Statistical Analysis

Descriptive variables were expressed as frequencies and percentages. The chi-square test (with/without Yates' correction) and Fisher's exact test were used for inferential statistical analysis, and multiple logistic regression/bivariate regression analysis was used for the risk factor assessment in our case-control study. Statistical significance was set at $p < 0.05$.

RESULTS

Autism spectrum disorder was diagnosed at 3-4 years of age in 38% of the children, 2-3 years of age in 34%, 1-2 years of age in 20%, and 4–5 years in 8%. In the autism spectrum disorder group, 74% (n=37) of the children were male and 26% (n=13) were female. In the autism spectrum disorder group, 66% (n=33) of children were 1st order by birth, 16% (n=16) of children were 2nd order by birth, and 2% of children were 3rd order by birth.

Loss of eye contact is the most common symptom and preferring to play alone is the 2nd most common symptom. The least common symptom was upset if there was any change in daily routine. Language difficulty was seen in 78% (n=39) of the children with autism spectrum disorder.

Among the comorbidities, 62% (n=31) had seizure disorder, 56% (n=26) had sleep disturbances, 52% (n=26) had intellectual disabilities, 34% (n=17) had obesity, and 20% (n=10) had GI disturbances. Seizure disorder were the most common, and GI disturbances were the least common. 88% (n=44) of the children underwent behaviour therapy, and 12% (n=6) of the patients did not undergo behaviour therapy. [Table 1]

We observed a statistically significant correlation between behavioural therapy and autism spectrum disorder ($p < 0.05$). Among the 31 children who underwent behaviour therapy for > 24 h/day, 29 children (93.5%) showed improvement, whereas only 5 children (38%) showed improvement among 13 children who underwent <24 h/day behaviour therapy. [Table 2]

There was a statistically significant correlation between maternal medication use, maternal hypothyroidism, maternal infection, PIH, and autism spectrum disorders ($p<0.05$). There was no significant correlation between maternal anaemia, GDM, overall mood of the mother, educational status, socioeconomic status, and family history of autism spectrum disorder ($p>0.05$).

There was a statistically significant correlation between gestational age, birth weight, NICU

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graduate, exclusive breastfeeding, screen time, and screen exposure and autism spectrum disorder ($p<0.05$). [Table 3]

Table 1: Demographic data of the study

		Frequency (%)
Age at the time of diagnosis (years)	1-2	10(20%)
	2-3	17(34%)
	3-4	19(38%)
	4-5	4(8%)
Gender	Male	37(74%)
	Female	13(26%)
Birth order	1	33(66%)
	2	16(32%)
	3	1(2%)
Symptoms	Loss of eye contact	50(100%)
	Prefer to play alone	46(92%)
	Doesn't enjoy the company of other	46(92%)
	Repeating any inappropriate movements	41(82%)
	Difficulty in using language	39(78%)
	Appropriate facial expressions	27(54%)
	Talk to you about things he/she likes	26(52%)
	Share his/her happiness	25(50%)
	Imaginative play	23(46%)
	Inappropriate fascination with movement	19(38%)
	Able to speak normally	8(16%)
	Upset if there is any change in the daily routine	4(8%)
Comorbidities	Seizure disorder	31(62%)
	Sleep disturbance	26(52%)
	Intellectual disability	26(52%)
	Obesity	17(34%)
	GI disturbance	10(20%)
Behaviour therapy	Taken	44(88%)
	Not Taken	6(12%)

Table 2: Outcome of behaviour therapy in the study

Behaviour therapy	Symptoms			P-value
	Improved	Static	Worsened	
Not Taken	0	4	2	<0.05
<24 hours/week	5	7	1	
>24 hours /week	29	2	0	

Table 3: Correlation of various parameters between the groups

		Case	Control	P-value
Maternal medication	Medication (other than routine) taken	18(36%)	4(8%)	0.008
	Medication (other than routine) not taken	32(64%)	46(42%)	
Maternal anaemia	Mothers with anaemia	15(30%)	10(20%)	0.355
	Mothers without anaemia	35(70%)	40(80%)	
Maternal dysthyroid	Mothers with dysthyroid	14(28%)	5(10%)	0.04
	Mothers without dysthyroid	36(72%)	45(90%)	
Maternal infection	Mothers with infection	13(26%)	4(8%)	0.03
	Mothers Without infection	37(74%)	46(92%)	
PIH	Mothers with PIH	15(30%)	35(70%)	0.04
	Mothers without PIH	6(12%)	44(88%)	
GDM	Mothers with GDM	9(18%)	6(12%)	0.575
	Mothers without GDM	41(82%)	44(88%)	
The overall mood of the mother during a period	Neutral	5(10%)	11(22%)	<0.001
	Happy	7(14%)	34(68%)	
	Sad	38(76%)	5(10%)	
Education status	Educated mother	46(92%)	44(88%)	0.739
	Uneducated mother	4(8%)	6(12%)	
Socioeconomic status	Lower SES	6(12%)	9(18%)	0.401
	Middle SES	44(88%)	41(82%)	
Gestational age	Preterm	14(28%)	4(8%)	0.01
	Term	36(72%)	46(92%)	
Birth weight	Low birth weight	16(32%)	6(12%)	0.02
	Normal birth weight	34(68%)	44(88%)	
NICU graduate	NICU graduate	16(32%)	34(68%)	0.01
	No NICU admission	5(10%)	45(90%)	
Exclusive breastfeed	Exclusive breastfeeding	10(20%)	36(72%)	0.01
	Not exclusive breastfeeding	40(80%)	14(28%)	
Family history	Family history of autism	5(10%)	1(2%)	0.09

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	No family history	45(90%)	49(98%)	
Screen time	Screen time >1 hour /day	48(46%)	41(82%)	0.02
	Screen time <1 hour /day	2(4%)	9(18%)	
Screen exposure	Screen exposure <2year of age	21(42%)	9(18%)	0.01
	Screen exposure > 2 years of age	29(58%)	41(82%)	

DISCUSSION

In our study, ASD was most commonly diagnosed between 3 and 4 years of age (n=19, 38%). This was based on previous studies of the average age at diagnosis of ASD at 3.1 years by Mandell et al.[1] In our study, male children (n = 37, 74%) were more common than female children. This was similar to previous studies on sex distribution, which showed that the male-to-female ratio of ASD patients was 3:1 by Loomes et al.[2]

In our study, we observed that ASD was most common in first-born children (n=33, 66%). This was based on previous studies related to birth order by Mandell et al.[1]

In our study, we observed that the most common symptom of ASD was the loss of eye contact (n=50, 100%). The least common symptom was upset if there was any change in the daily routine (n=4,8%). This was based on the results of a previous study by Lisa Jo Rudy.[3]

In our study, we observed that among the children, 62% (n = 31) had seizure disorder, 56% (n=26) had sleep disturbances, 52% (n=26) had intellectual disabilities, 34% (n=17) had obesity, and 20% (n=10) had GI disturbances. Among the comorbidities, seizure disorder was the most common and GI disturbance was the least common. This was based on previous studies related to ASD comorbidities by Mohammadi et al.[4]

In our study, we observed that among cases, 88% (n=44) of children underwent behaviour therapy, 12% (n=6) of those not undergoing behaviour therapy, and we observed a statistically significant correlation between behaviour therapy and symptomatic improvement, with a p-value <0.05. This is in accordance with previous studies on behavioural therapy for ASD by Mark Bertin.[5]

In our study, we observed a statistically significant correlation between maternal medication (other than routine medication) and autism spectrum (p <0.05). This was in accordance with previous studies by Clements et al.. and Boukhris et al., in which maternal medication during the antenatal period increased the risk of ASD.[6,7]

In our study, we observed a negative correlation between maternal anaemia and autism spectrum disorder. The p-value was >0.05 which was not statistically significant. However, this finding was not in accordance with previous studies by Wiegersma et al. which showed that anaemia diagnosed earlier in pregnancy was associated with an increased risk of the development of ASD, ADHD, and particularly ID in the offspring.[8]

In our study, we observed a statistically significant correlation between maternal dysthyroid status and maternal infection with autism spectrum disorder. The p-value was <0.05 which was statistically significant. This was in accordance with the results of a previous study by Getahun et al.[9]

In our study, we observed a statistically significant correlation between PIH and ASD ($p < 0.05$). This was in accordance with previous studies by Xu et al., which showed a possible link between PIH and the risk of ASD in the offspring.[10]

In our study, we observed no correlation between GDM and ASD; the p-value was >0.05, which was not statistically significant. This is not in accordance with the results of previous studies by Rowland and Wilson.[11]

In our study, we observed that 76% of mothers who had a sad mood during their antenatal period had children with autism. There was no statistically significant correlation between the educational status of the mother and the socioeconomic status of the family with ASD ($p > 0.05$).

In our study, we observed that there was a statistically significant correlation between preterm birth (77%), LBW (72%), and NICU graduation (76%) with ASD ($p < 0.05$). This was in accordance with the results of previous studies by Allen et al. and Chen et al.[12,13]

In our study, we observed that ASD was most common in children who had a screen time of more than an hour per day (46%, n=48) and who had screen exposure at less than 2 years of age (42%, n=21). The p-value was 0.02, which was statistically significant. This is in accordance with previous studies on screen timing and exposure by Chen et al.[14]

CONCLUSION

Our study showed that ASD was most commonly diagnosed between the ages of 3 and 4 years. This was dominated by male children, with first-born children being the most affected. Behavioural therapy improves symptoms in children with ASD, and the most common comorbidity associated with ASD is seizure disorder. Antenatal risk factors such as non-routine maternal medicine during pregnancy, dysthyroid status, maternal infection, PIH, and maternal stress during pregnancy predispose children to ASD worldwide. Postnatal risk factors such as preterm birth, LBW baby, not exclusively breastfed baby, NICU graduate, preschool screen exposure, and more than an hour of screen time all predispose children to ASD worldwide. Larger clinical studies are required to establish the therapeutic outcome of ASD and etiological risk factors associated with ASD

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Limitations

Single-centre study and small sample size.

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