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IMPACT OF PRENATAL, ANTENATAL AND PERINATAL RISK FACTORS IN SEVERITY OF AUTISM

Pediatrics

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ABSTRACT

One of the most important neurodevelopmental syndromes is Childhood Autism. This study has explored the Positive family history, Parental age, Antenatal, Perinatal risk factors, with Autism severity, adaptive functioning and Minor physical anomalies in children diagnosed with Childhood Autism. Sample consists of 47 children (34 males and 13 female children) who attended Psychiatry Department, Government Rajaji Hospital, Madurai, a tertiary care centre for a period of 8 months. Socio demographic data sheet, Kuppusamy socio economic status scale, CARS, MPA scale and VSMS were used. Statistical analysis was done by using SPSS version 14. The present study found that, Antenatal, Perinatal risk factors, positive family history, developmental regression, birth asphyxia, LSCS delivery, low birth weight significantly increase the severity of Autism, increases the Minor Physical Anomalies and decreases the adaptive functioning. As Paternal age and Maternal age increases the severity of Autism and Minor physical anomalies increases and adaptive functioning decreases. Developmental regression, AN risk factors, Birth asphyxia, and birth weight contribute much to the severity of autism than other factors. The study concluded that Presence of Antenatal and Perinatal risk factors are significantly increase the severity of Autism, increases the Minor Physical Anomalies and decreases the adaptive functioning.

KEYWORDS

Autism, adaptive functioning, Minor Physical Anomalies, antenatal and Peri-natal risk factors.

One of the most important Neurodevelopmental syndromes is Childhood Autism. This Pervasive Developmental Disorder is characterized by impairment in reciprocal social interaction, impairment in communication, restricted repetitive and stereotyped patterns of behavior, interests and activities (Sadock BJ et al. 2015)

GENETIC MECHANISMS IMPLICATED IN THE ETIOLOGY OF AUTISM

Family and twin studies show that Childhood Autism has a higher heritable contribution (Thapar.A et al. 2015). This genetic contribution is evidenced by higher concordance rates in monozygotic twins (~60–90%), when compared to dizygotic twins. Furthermore, about10% of sporadic cases occurs due to de novo copy number variations in either single genes or multiple genes. Increase in paternal age may act as a contributory factor for accumulation of these de novo mutations. Chromosomal abnormalities have been identified at different loci confirming the genetic heterogeneity of the disorder. Abnormalities at Chromosome 7q and 15q are commonly studied. Single gene or chromosomal abnormality has been found in about 5-15% of individuals. Complex genetic mechanisms operate together with environmental factors which modulate the epigenetic state resulting in aberrant brain development and function. (Tasman A, et. al 2015)

STUDIES ON PRENATAL, ANTENAL AND PERINATAL RISK FACTORS

Strong genetic involvement in Autism is supported by various family studies which confirm the higher concordance rate (70%), other factors may also play a role since the concordance rate is never 100% (Thapar. A et al. 2015). This suggests the role of non-heritable factors in the etiology of Autism. Pre and perinatal risk factors have been the focus of research for more than 40 years. Meta -analysis of various epidemiological studies conclude that the following factors – increased paternal age, increased maternal age, maternal immigration, gestational bleeding and gestational diabetes, medication use increase the risk of Autism (Gardener. et al 2009). Paternal age>35yrs carries higher risk for Autism. Risk has been found to be doubled up with each 10 year increase in age (Reichenberg A et al 2006). Sven Sandin, Hultmanet al. 2012 reviewed 16 large epidemiological studies confirm the evidence that advanced maternal age increases the risk of Autism independent of any other factors. Maternal use of psychiatric drugs (Gardener et al 2009; Maimburg RD et al 2006) has found to have significant association with Autism. Use of other drugs like thalidomide, valproicacid (VPA), ethanol, misoprostol, and chlorpyrifos (Thapar. A et al. 2015).) during pregnancy also increases the risk for autism.

Several researchers have hypothesized that peri natal conditions that precipitate hypoxia in the neonate increases the risk for major neuropsychological and neuropsychiatric disturbances (Naeye et al 1987, Robertson CM et al 1993). Gestational diabetes increases the risk of autism as supported by many studies (Cannon, Rosso et al 2000; Seidman et al., 2000; Hultman et al2002; Larsson 2005. Following studies support the view that Pre eclampsia could be identified as a risk factor -Larsson et al 2005;Hultman et al 2002; Seidman et al 2000. Bleeding during pregnancy (Hultman et al 2002; Eaton et al 2001 and smoking (Larsson et al2005) have significant association with Autism. Caesarean section (Hultman et al 2002; Glasson et al 2004(16), and LowApgar score <7 at 5minutes acts as a predictor for development of autism in early developmental period(Eaton2001; Hultman 2002;Larsson 2004). Congenital malformations have been identified as a risk factor (Hultman 2002). Low birth weight acts as a marker for development of later psychiatric and neurological conditions (Breslau et al 1995). Low birth weight <2500gm/Small forGestational Age has a significant association with Autism (Larsson et al 2002 and Hultman et al 2002).

MINOR PHYSICAL ANOMALIES IN AUTISM

Minor physical anomalies (MPA) are subtle morphological abnormalities of the cranio-facial region and limbs that does not cause any significant cosmetic or functional impact to the individual. (Manouilenko I et al. 2014) They act as markers for deviant morphogenesis during the first or early second trimester. Both MPAs and developing brain have ectodermal embryonic origin. Hence, analyzing MPAs would pave way for understanding deviance in the growth of developing brain in autistic children.

SCOPE OF THIS STUDY

Our study has been framed to explore clinical characteristics, severity, adaptive functioning and minor physical anomalies and it relationship with Antenatal and Perinatal risk factors identified in these children and analysis of these factors is done to identify which of these would influence the severity of autism.Thus, by understanding these factors, autism prevention can be aimed and early intervention based on the screening for autism in the children who present with these factors and thereby ultimately bringing improvement in their quality of life.

AIM OF THE STUDY

To study the relationship of Positive family history, Parental age, Antenatal, Perinatal risk factors, with Autism severity, adaptive

functioning and Minor physical anomalies in children diagnosed with Childhood Autism.

OBJECTIVES

1. To study the socio-demographic profile, Parental age, Antenatal Risk factor, Perinatal Risk factors and Positive Family History in children diagnosed with Childhood Autism.
2. To assess the severity of autism in these children.
3. To evaluate the adaptive functioning and presence of Minor Physical Anomalies in these children.
4. To study the relationship among perinatal risk factors, minor physical anomalies, social maturity and severity of autism.

MATERIALS AND METHODS

This is part of the Study where Gender differences in children with Autism were already published (Geethaanjali et al. 2018).The additional data collected regarding risk factors associated with autism is explored in this study. From the Psychiatry out Patient Unit, Government Rajaji Hospital, Madurai Consecutive Children fulfilling the criteria of Childhood Autism ICD-10 RDC (F 84.0) between 2-8 years of age, for whom informed consent is obtained from parents are included. Children with other Pervasive Developmental Disorders, with sensory deficits, with anyneurological deficits and for whom consent couldn't be obtained from parents were excluded from the study. So only 55 children met the inclusion criteria. For want of time parents of 3 children didn't consent for the study and 5 children had co-morbid neurological illness and they were excluded. Hence, the study was conducted in a sample of 47 children- which comprises of 34 males and 13 female children. The study was approved by institutional ethical committee, Government Rajaji Hospital. The study was done for a period of 8 months, Semi structured proforma is used to collect data regarding socio-demographic profile, and clinical variables like age of parents, prenatal risk factors, clinical characteristics etc. Complete physical examination including neurological evaluation was done in those children. Scales administered are-Modified Kuppusamy's Socio economic scale, ChildhoodAutism Rating Scale (for severity), Vineland Social Maturity Scale (for adaptive functioning)and Waldrop scale (for minor physical anomalies).

STATISTICAL DESIGN

Statistical analysis was done using SPSS (Statistical Package for Social Studies) version 14.0. In comparison of the data for categorical variables chi-square and for numerical variables student t test and multiple comparisons of more than two numerical variables and ANOVA tests were used. Correlation among variables was studied using Pearson's correlation coefficient.

TOOLS USED

SEMI STRUCTURED PROFORMA

Semi-structure proforma includes demographic details, Antenatal risk factors(nausea and vomiting, hypertension, Gestational Diabetes, Antepartum haemorrhage, drug intake)and Perinatal risk factors(duration of pregnancy, mode of delivery, birth weight, birth asphyxia) developmental milestones, family history, clinical characteristics , physical and neurological examination details.

1. KUPPUSAMY SOCIO ECONOMIC STATUS SCALE

Originally proposed in 1976. The scale was revised in 2012 and the monthly family income was modified based on current consumer price index. (BP Ravi Kumar et al, 2012). Based on the scale, socio-economic status is classified as Upper, Upper middle, Lower middle, Upper lower and lower.

2. CHILDHOOD AUTISM RATING SCALE

This scale is designed to diagnose autism as well as to assess the severity. CARS was developed by Eric Schopler, Robert J Reichier and Barbara Rochen Renner. CARS is also useful in differentiating autism from other neurodevelopmental disorders including Intellectual Disability. 15 domains are utilized in CARS for the assessment of severity. Total CARS score ranges from 15-60 with the minimum score of 30 is necessary to diagnose autism. Based on the total score, severity is categorized as mild, moderate and severely autistic. Internal Consistency of CARS is high, with co-efficient alpha of .94 and inter-rater reliability is also high.

3. VINELAND SOCIAL MATURITY SCALE – INDIAN ADAPTATION

VSMS was originally devised by E.A.Doll in 1935. This scale is useful in measuring the social maturity of children and young adults. Indian Adaptation of Vineland Social Maturity Scale (VSMS) was done by Dr.A.J.Malin while he was working at Nagpur Child Guidance Centre. It provides a measure of Social Age and Social Quotient., and through this social deficits as well assets can be evaluated. This scale uses following 8 domains for assessment- Self help general, Self help eating, Self help dressing, Self direction, Occupation, Communication, Locomotion and Socialization. The test is administered in a semi-structural informal atmosphere by having the mother along with the child or having the child alone depending upon the demands made by the items. S.Q= Social Age/Actual Age * 100. Recent studies have shown a consistent and higher co-variation between VSMS Social Age (S.A) and the Stanford Binet Mental Age(M.A) and the correlation is about 0.96 . This is a clear reflection of how social development and mental development are highly correlated.

4. MINOR PHYSICAL ANOMALIES SCALE

Waldrop Physical Anomaly Scale was designed by Waldrop and Halverson in the year 1971. It is widely used for the assessment of minor physical anomalies in an individual. It consists of six subscales that reflect anatomic body areas: head, eyes, ears, mouth, hands and feet. Total score ranges from 0-24.

RESULTS

THE PATERNAL AND MATERNAL AGE AT THE TIME OF CONCEPTION OF THESE CHILDREN

Paternal and Maternal Age

Study statistics reveal that around 3 (11%) had their paternal age of below 24 years,22(44.6%) of children had their paternal age between 25-29 years, 12 (26 %) had paternal age 35 years and above and 11(23%) had their paternal age between 30-34 years. Regarding maternal age, 16 (34%) of children had maternal age below 24 years, 15 (32%) had maternal age between 25-29 years, 12 (26%) of children had maternal age between 30-34 years and 4 (9%) had maternal age of above 35 years.

Antenatal Risk factor

Majority 36 (76.6%) of children were first born and around 11 (23%) were born later. AN risk factors were present in about 13(27.7%) of children. Of these risk factors- Nausea and Vomiting was present in about 3 (6.4%), Hypertension in about 4 (8.5%), Gestational DM in about 2 (4.3%), Antepartum Hemorrhage in about 3 (6.4%) followed by drug intake in 1 (2.1%) of children.

Perinatal Risk factors

Data collected show that 6 (12.8%) were born pre-term,term were 38 (81 %) and 3(6.4%) were post-term. Mode of delivery was by LSCS in about 15 (32%) and Vaginal 32 (68%) and low birth weight was present in about 8(17%), appropriate birth weight was 39 (83) of children. Birth asphyxia was present in about 9(19%) and developmental regression was identified in about 4 (8.5%) of children.

Positive Family History

Around 4 (8.5%) of children had positive family history of which 2 (4.3%) had positive family history of Mental Retardation and 2 (4.3%) had family history of Autism.

TABLE 1: TABLE SHOWING THE CARS, VSMS SCORE and MPA Scores OF THESE CHILDREN

CARS TOTAL SCORE		FREQUENCY	PERCENTAGE
MILD – MODERATE		27	57.4
SEVERE		20	42.6
VSMS Findings			
NORMAL		3	6.4
BORDERLINE		10	21.3
MILD		28	59.6
MODERATE			12.8
MPA	Score		
MPA HEAD	0	20	42.6
	1-2	26	55.3
	3	1	2.1
MPA EARS	0	19	40.4
	1-2	28	59.6
MPA MOUTH	0	41	87.2
	1	6	12.8

MPA FEET	0	27	57.4
	1-2	20	42.5
MPA EYES	0	47	100
MPA HANDS	0	47	100
MPA TOTAL SCORE	0	7	14.9
	1-2	21	44.6
	3-5	19	40.5

From the above table we infer that just more than half of children fell in Mild-Moderate category in CARS and just less than half of children were in severe category. In VSMS, one fourth of children fell in normal and borderline category and majority was in mild and 12.8% were in moderate category of social quotient. Most of the children in the study had Minor physical anomalies and it was commonly noted in head, ears, feet and to a lesser extent in mouth. MPAs of eyes and hands were not present in these children. 44.6% children scored between 1-2 and 40.5% scored between 3-5in MPA scale. 15% of children didn't have any minor physical anomalies.

Table 2 shows that there is a positive correlation between Paternal age and Maternal age with Severity of autism and Minor Physical Anomalies i.e., when Parental age and Maternal age increases CARS score and MPA score also increases. There is a negative correlation between Paternal age and Maternal age with adaptive functioning i.e., when Paternal age and Maternal age increases the adaptive functioning decreases as measured by VSMS. There is a positive correlation between CARS score and MPA score i.e., as Severity of Autism increases Minor Physical Anomalies also increases. There is a negative correlation between CARS score and MPA score with VSMS i.e., when severity of autism and Minor Physical Anomalies increases the social maturity decreases.

TABLE 2: RELATIONSHIP BETWEEN CARS, VSMS, MPA, AGE AT FIRST DIAGNOSIS, PATERNAL AND MATERNAL AGE.

*=P<0.05, ** = P<0.01

S.NO	VARIABLES	CARS TOTAL SCORE	VSMS SCORE	MPA SCORE
	PATERNAL AGE	.370*	-.323*	.368*
	MATERNAL AGE	.366*	-.350*	.376**
	VSMS	-.864**	-------	-.715**
	CARS	--------	-------	.795**

Table 3:SHOWING THE COMPARISON OF VARIOUS RISK FACTORS WITH RESPECT TO CARS SCORE

S. NO			N	CARS Mean Score	SD	t – score and F.Value
1	AN RISK FACTORS	PRESENT	13	39.23	4.085	T test
		ABSENT	34	36.23	4.424	2.118*
2	DURATION OF PREGNANCY	PRE TERM	6	39.16	4.535	Fvalue
		TERM	38	36.55	4.446	1.29
		POST TERM	3	39.33	4.725	
3	MODE OF DELIVERY	VAGINAL	32	36.06	4.406	T test
		LSCS	15	39.20	4.039	-2.334*
4	BIRTH WEIGHT	LOW	8	40.25	4.200	T test
		APPROPRIATE	39	36.41	4.320	2.299*
5	BIRTH ASPHYXIA	PRESENT	9	40.77	3.270	T test
		ABSENT	38	36.18	4.323	2.982**
6	DEVELOPMENTAL REGRESSION	PRESENT	4	44.75	.957	T test
		ABSENT	43	36.34	3.992	4.157**
7	FAMILY HISTORY	PRESENT	4	42.75	2.753	T test
		ABSENT	43	36.53	4.272	2.839**

*=P<0.05, ** = P<0.01

Table 3 shows that CARS score increases with presence of Antenatal risk factors, LSCS delivery, low birth weight, birth asphyxia, developmental regression, presence of family history and it is statistically significant. When the CARS score is compared among term born, preterm born, post term born the difference in the CARS score is not statistically significant.

Table 4:SHOWING THE COMPARISON OF VARIOUS RISK FACTORS WITH RESPECT TO VSMS (Social Quotient) SCORE

S.NO	RISK FACTORS		N	Social Quotient Mean score	SD	t-score and F-value
1	AN RISK FACTORS	PRESENT	13	56.30	10.225	T test
		ABSENT	34	63.85	13.482	-1.823*
2	DURATION OF PREGNANCY	PRE TERM	6	53.16	8.207	F value
		TERM	38	63.55	13.462	2.01
		POST TERM	3	56.33	6.806	
3	MODE OF DELIVERY	VAGINAL	32	65.37	13.904	T test
		LSCS	15	54.06	5.909	3.011**
4	BIRTH WEIGHT	LOW	8	50.75	7.304	T test
		APPROPRIATE	39	64.02	12.819	-2.820**
5	BIRTH ASPHYXIA	PRESENT	9	52.55	6.267	T test
		ABSENT	38	63.94	13.284	-2.492**
6	DEVELOPMENTAL REGRESSION	PRESENT	4	42.50	4.123	T test
		ABSENT	43	63.55	12.065	3.442**
7	FAMILY HISTORY	PRESENT	4	46.50	7.724	T test
		ABSENT	43	63.18	12.526	-2.603**

Table 4 shows that VSMS (Social quotient) score decreases with Presence of Antenatal risk factors, LSCS delivery, low birth weight, birth asphyxia, developmental regression, presence of family history and it is statistically significant. When the VSMS score is compared among term born, preterm born, post term born the difference in the VSMS score is not statistically significant

Table 5: SHOWING THE COMPARISON OF VARIOUS RISK FACTORS WITH RESPECT TO MPA SCORE

S.NO	RISK FACTORS		N	MEAN OF MPA SCORE	SD	t-score and F value
1	AN RISK FACTORS	PRESENT	13	3.30	1.315	T test
		ABSENT	34	1.70	1.360	3.64**
2	DURATION OF PREGNANCY	PRE TERM	6	2.50	1.760	F value
		TERM	38	2.60	1.506	1.27
		POST TERM	3	3.333	1.577	
3	MODE OF DELIVERY	VAGINAL	32	1.93	1.435	T test
		LSCS	15	2.60	1.638	-1.410
4	BIRTH WEIGHT	LOW	8	2.87	1.246	T test
		APPROPRIATE	39	2.00	1.538	1.506

5	BIRTH ASPHYXIA	PRESENT	9	3.11	1.452	T test 2.202*
		ABSENT	38	1.92	1.459	
6	DEVELOPMENTAL REGRESSION	PRESENT	4	4.25	0.500	T test 3.166**
		ABSENT	43	1.95	1.430	
7	FAMILY HISTORY	PRESENT	4	4.00	0.816	T test 2.722**
		ABSENT	43	1.97	1.455	

Table 5 shows that MPA score increases with Presence of Antenatal risk factors, birth asphyxia, developmental regression, presence of family history and it is statistically significant. When the MPA score is compared among term born, preterm born, post term born the difference in the MPA score is not statistically significant. The same when compared within modes of delivery and within birth weights.

TABLE 6: TABLE SHOWING MULTIPLE LINEAR REGRESSIONS ANALYSIS WITH CARS AS DEPENDENT VARIABLE

S.NO	INDEPENDENT VARIABLE	R	R2	R2 CHANGE	B	Beta	T	Sig
1.	DEVELOPMENTAL REGRESSION	.527	.277	.277	6.037	.379	3.31	P<.002
2.	AN RISKFACTORS	.612	.374	.097	3.342	.336	3.16	P<.003
3.	BIRTH ASPHYXIA	.684	.468	.094	4.019	.335	3.21	P<.003
4.	BIRTH WEIGHT	.727	.529	.061	3.069	.259	2.33	P<.025
5.	VSMS	0.864	0.747	0.747	-.209	-.606	6.46**	P<.000
6.	MPA	0.901	0.811	0.064	1.071	.361	3.85**	P<.000

For the dependent variable CARS, independent variables namely developmental regression, AN risk factors, birth asphyxia and birth weight have been considered. By using multiple linear regression analysis (Stepwise), it has been found out that all these independent variables are contributing for CARS. Developmental regression alone could contribute about 27.7% (R2= 0.277) and AN risk factors could contribute about 9.7 % of variance, and birth asphyxia could contribute about 9.4% of variance and birth weight contributes about 6.1% of variance. Put together 72.7% of variance. t value for the 'B' co-efficient and the F ratio are all significant at 0.00 level.

For the dependent variable CARS, two independent variables namely VSMS and MPA have been considered. By using multiple linear regression analysis (Stepwise), it has been found out that both the independent variables are contributing for CARS. VSMS alone could contribute about 74.7% (R2= 0.747) and MPA could contribute about 6.4% of variance, put together 81.1% of variance. Regression Equation: CARS= 47.701+(-0.209)VSMS+(1.071)MPA. This equation is said to be the best equation since the t value for the 'B' co-efficient and the F ratio are all significant at 0.00 level. Thus this analysis could predict the CARS score when VSMS and MPA scores are provided.

DISCUSSION

The present study identifies the factors which affect the Severity of Autism, by comparing the children with Autism who have environmental and genetic risk factors with children with autism who don't have these risk factors. Autism severity score in CARS is statistically significant for children who have Antenatal risk factors, Positive family history, developmental regression and birth asphyxia when compared with children those who don't have these. Significant difference is also obtained on comparing mode of delivery among children born by vaginal and LSCS delivery -with children bornby LSCS score high in CARS. Also low birth weight children score high in CARS when compared to children who had appropriate birth weight. The duration of pregnancy had no significant influence on CARS scores. Study findings of Severity of Autism being higher in children with Antenatal and perinatal risk factors are supported by previous Studies- (Gardener H et al 2009; Larsson et al 2009 and Hultman et al 2002).

Increase in paternal and maternal age also contributes to the severity of autism in this study. The present research compared various groups of paternal age and obtained significant difference in CARS score when paternal age is 35 and above. Also CARS score is higher when maternal age is 35 and above. The study findings are replicated in previous studies (Hannah Gardener et al 2009). Mechanism behind which increased paternal age is associated with Autism are- increased frequency of point mutation, de novo mutation CNVs, and gene imprinting defects and epigenetic changes (Shelton et al., 2010; Sandin et al.,2012). Mechanism behind which increased maternal age associated with autism increase in chromosomal abnormalities (Persico AM 2001 and Zhang 2002)

Adaptive functioning (VSMS), MPA, Developmental regression, AN risk factors, Birth asphyxia, and birth weight contribute much to the severity of autism than other factors. Thus,all these factors play a complex role in compromising the growth of foetus and make the brain vulnerable to the development of Autism. Developmental regression is found to have significant contribution for the severity of autism. Antenatal risk factors play a complex role in compromising the growth of foetus and make the brain vulnerable to the development of Autism (Hultman et al 2002). It has been hypothesized that perinatal conditions that precipitate hypoxia in the neonate increases the risk for major neuropsychological and neuropsychiatric disturbances (Naeye et al 1987,Robertson CM et al 1993) and also increases the risk for Autism. According to Bolton PF and Murphy 1997, there is a common genetic vulnerability to autism and adverse pregnancy outcome. Hence children with autism also have genetic predisposition for the presence of adverse pregnancy outcome and this might also be the reason for the prevalence of perinatal risk factors in these children. The increased severity of autism would itself interfere with Adaptive functioning. Hence, this might also be reason for the results of poor adaptive functioning among children in high CARS score. Also, the current didn't utilise any standardized instruments for testing IQ. Use of Performance based tests would have been better since Autistic children perform poorer with verbal tests. Children who fall in severe category in CARS have higher MPA when compared with children who fall in mild - moderate category. This finding is in par with previous studies- which state that higher numbers of MPAs are found in children with severe autism (Mc Grath et al 1995). Early in foetal morphogenesis, the development of structures in the craniofacial region occurs simultaneously with central structures of the brain implicated in the pathogenesis of Autism (Haznedar et al 2006). Thus, early Cerebrocraniofacial Dysmorphogenesis reflects an early stage of pathogenesis that occurs before behavioral manifestations in Autism (Helmset al 2005). MPAs are also related to adverse prenatal/perinatal environment. As the prenatal risk factors increase the vulnerability of developingbrain to Autism, it also modifies/deviates the development of facial and limbic structures. Thus children with increased prenatal and perinatal risk factors have higher rates of MPAs (TayJ S et al 1979).

CONCLUSION

The Present study concluded that presence of Antenatal risk factors, positive family history, developmental regression, birth asphyxia, LSCS delivery, low birth weight significantly increases the Severity of Autism and Minor Physical Anomalies and decreases the adaptive functioning. As Paternal age and Maternal age increases the Severity of Autism and Minor physical anomalies increases and adaptive functioning decreases. Developmental regression, Antenatal risk factors, Birth asphyxia, and birth weight contribute much to the severity of autism than other factors. When Severity of autism is high the Minor physical anomalies scores are high and adaptive functioning decreases significantly.

LIMITATIONS OF THE STUDY

1. Results would have been better if there were a larger sample size.
2. Standardized diagnostic instruments for Autism was not used and formal IQ testing for children was not done in our study.
3. Analysis of Antenatal and perinatal risk factors in these children would have been better if the prevalence of these was compared with general population which was not possible in our current study design.
4. Study being done at Government Hospital settings which caters

middle and low socio-economic class, these findings could not be extrapolated to general population.

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