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ORIGINAL RESEARCH

Usage of 2nd to 4th digit (2d:4d) ratio as a potential screening tool in boys with autism: Case control study

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ABSTRACT

Introduction: Autism spectrum disorders (ASD) is a group of heterogeneous neurodevelopmental disorder characterised by deficits in social communication and the presence of restricted interest and repeated behaviours.The prevalence across the world is 16%. It is more common in males. Despite the global increase in the prevalence of ASD relevant research studies are lacking in India. Hence the study aims at early detection of autism by using 2D:4D ratio as a potential screening tool.

Methods: The study included 23 (cases) male children in the age group of 3 to 9 years diagnosedwith ASD using Indian Scale for Assessment of Autism (ISAA) and 20 controls. The length of both second digit and fourth digit fingers in both cases and control wereobtained and compared.

Results: Analysis of the grades of Autism showed that most of the children had moderate autism 47.8%. On Comparison of 2D:4D ratio with grade of autism showed that mild, moderate and severe autism had SD score of 0.013, 0.017, 0.18 respectively with a p value of 0.57. On comparing the mean 2D:4D ratio between the cases and control group showed a statistically significant association with the cases with p value of <0.001.

Key words: Autism spectrum disorders, Indian scale for assessment of autism

INTRODUCTION

Autism spectrum disorders (ASD) is a group of heterogeneous neurodevelopmental disorder characterized by deficits in social communication and the presence of restricted interest and repeated behaviors. The disease is influenced by both genetic and environmental factors affecting the developing brain.

The international prevalence of ASD is 0.76% which accounts for 16% of global child population with increasing prevalence in the recent years[1].

Autism spectrum disorders is more common in males, true male to female ratio is 3:1.One theory concerning the sex ratio is the extreme male brain theory (EMB) of autism, an extension of the empathizing systemising theory (E-S). Many studies have revealed that Autism may arise as a result of exposure to high concentration of prenatal testosterone. There is also evidence that ratio of lengths of second and fourth digit (2D:4D) may be negatively correlated to prenatal testosterone[2].

Studies have shown a significant association between a lowered 2D:4D ratio and ASD making it one of the potential phenotypic biomarkers for early detection of autism, which important for early intervention and management to improve the quality of life of individuals with ASD.

OBJECTIVES

To determine the association between 2D: 4D ratio and ASD male children between the age group 3 to 9 years.

METHODOLOGY

STUDY DESIGN: Case control.

STUDY PERIOD: January 2023 to March 2023.

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PLACE OF STUDY: Vanivilas hospital, Dept of Pediatrics (DEIC).

INCLUSION CRITERIA

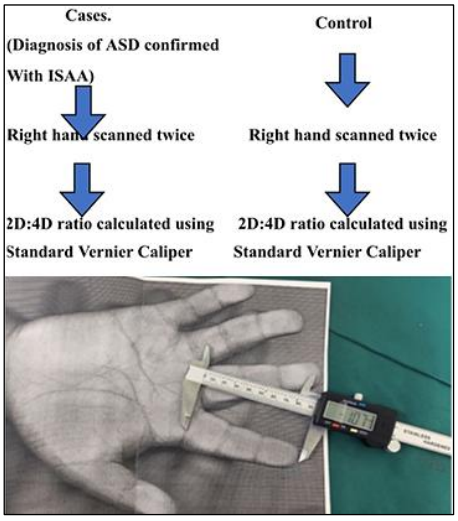
1. **Cases:**Male children between 3 to 9 years diagnosed with ASD attending OPD at Vani Vilas Hospital.
2. **Controls:** Male children between 3 to 9 years not diagnosed with ASD attending OPD at Vani Vilas Hospital.
3. Parents of children of cases and control who are willing to give written informed consent.

EXCLUSION CRITERIA

1. Children associated with other neuro developmental disorders and/or children with vision and hearing impairment.
2. Children with Syndactyly and polydactyly.
3. Parents of children who are not willing to give written informed consent.

Our study included 23 (cases)male children in the age group of 3 to 9 years diagnosed with ASD using Indian Scale for Assesment of Autism (ISAA) and 20 controls-Age and sex matched healthy children attending OPD Vani Vilas Hospital. The length of both index (second digit-2D)and ring (fourth digit-4D) fingers in both cases and control were obtained by placing their right hand on the surface of scanner machine. The scanned copy printout was taken. The length of 2-D and 4D was measured from basal Palmar crease of the finger to the tip using a standard Verniercalliper. The lengths were measured twice and average calculated and recorded. Demographic details and 2D:4D ratios of cases and control was recorded and statistically analysed.

Fig 1: STUDY WORKFLOW CHART



RESULTS

STATISTICAL ANALYSIS: Statistical Package for Social Sciences [SPSS] for Windows, Version 22.0. Released in 2013. Armonk, NY: IBM Corp., was used to perform statistical analyses.

DESCRIPTIVE STATISTICS: Descriptive analysis includes expression of all the explanatory and outcome variables in terms of frequency and proportions for categorical variables, whereas in terms of Mean & SD for continuous variables.

INFERENTIAL STATISTICS: The following tests were used for statistical analysis-Mann Whitney Test, Chi Square Test, Independent Student t Test, One-way ANOVA Test, ROC Curve analysis.

AGE DISTRIBUTION AMONG TWO GROUPS

The study comprised of 43 male children-23 cases and 20 Control in the age group of 3 to 9 years. The mean age group among the case group was 5.48 years and in the control group was 5.97 years.

Comparison of demographic profile between 2 groups using Chi square test.

Statistically significant positive correlation seen with consanginous marriage and lscs delivered babies with risk of autism with a p value of less than 0.005.

Analysis on Indian Scale for Assessment of Autism showed a mean value of 104.52 with a SD score of 28.93 with scores ranges between 71 and 167.

Analysis of the grades of Autism showed that most of the children had moderate autism 47.8% followed by mild Autism 34.8% and severe Autism 17.4%.

On Comparison analysis of 2D:4D ratio with grade of autism showed that mild, moderate and severe autism had SD score of 0.013, 0.017, 0.18 respectively with a p value of 0.57.

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On comparing the mean 2D:4D ratio between the cases and control group showed a statistically significant association with the cases with p value of <0.001.

Statistically significant ROC curve analysis was seen with Area under the curve 0.935.

Fig 2. AGE DISTRIBUTION AMONG TWO GROUPS

Variable	Category	Case		Control		p-value
		Mean	SD	Mean	SD	
Age	Mean	5.48	1.85	5.97	1.95	0.39[a]
	Range	03 - 09		03 - 09		

Fig 3. COMPARISON OF MEAN BIRTH WEIGHT

Comparison of mean Birth Weight (in kgs) between 2 groups using Independent Student t Test						
Parameter	Groups	N	Mean	SD	Mean Diff	p-value
Birth wt	Case	23	3.00	0.55	0.09	0.56
	Control	20	2.91	0.38		

Fig 4. DESCRIPTIVE TABLE FOR INDIAN SCALE FOR ASSESSMENT OF AUTISM

Descriptive table for Indian Scale for Assessment of Autism among study cases					
Parameter	N	Mean	SD	Min	Max
ISAA	23	104.52	28.93	71	167

Fig 5. DISTRIBUTION OF GRADES OF AUTISM

Distribution of grades of Autism among study cases			
Variable	Category	n	%
Grades of Autism	Mild	8	34.8%
	Moderate	11	47.8%
	Severe	4	17.4%

Fig 6. COMPARISON OF 2D/4D RATIO WITH GRADES OF AUTISM

Comparison of mean 2D/4D Ratio based on the Grade of Autism using One-way ANOVA Test						
Grades	N	Mean	SD	Min	Max	p-value
Mild	8	0.930	0.013	0.92	0.95	0.57
Moderate	11	0.937	0.017	0.91	0.97	
Severe	4	0.930	0.018	0.91	0.95	

Fig 7. COMPARISON OF MEAN 2D/4D RATIO BETWEEN CASES AND CONTROL GROUP

Comparison of mean 2D/4D ratio between Case & Control group using Independent Student t Test						
Parameter	Groups	N	Mean	SD	Mean Diff	p-value
2D/4D Ratio	Case	23	0.934	0.016	-0.045	<0.001*
	Control	20	0.978	0.024		

***-Statistically Significant**

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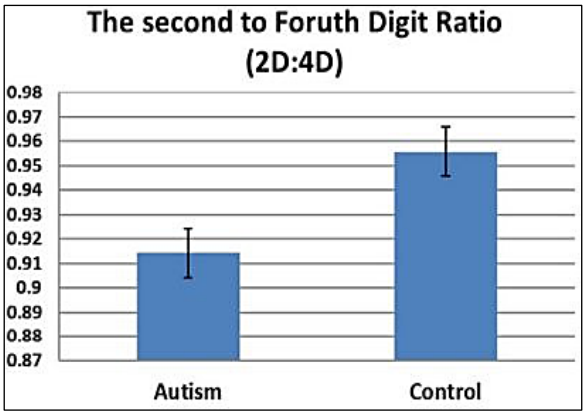
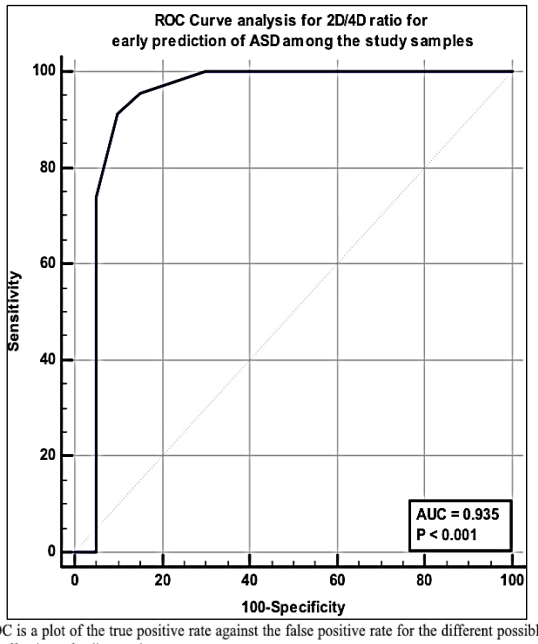


FIGURE8: Bar Chart Representing the Second to Fourth Ratio (2D:4D) in the Autism and Control Group

Fig 9. ROC CURVE ANALYSIS FOR 2D/4 RATIO IN EARLY PREDICTION OF ASD



ROC is a plot of the true positive rate against the false positive rate for the different possible cutoff points of a diagnostic test.
Accuracy is measured by the area under the ROC curve i.e AUC. An area of 1 represents a perfect test; an area of .5 represents a worthless test. A rough guide for classifying the accuracy of a diagnostic test as follows:
.90-1 = excellent (A)
.80-.90 = good (B)
.70-.80 = fair (C)
.60-.70 = poor (D)
.50-.60 = fail (F)

DISCUSSION

A case control study conducted in Brunei Darussalam comprised of 28 ASD and 62 controls showed median 2D:4D ratio of left hand in ASD males is significantly lower than those in controls (odds ratio-0.57 p=0.044 95% CI= 0.31-0.96) which was similar to the present study[3].

A case control study conducted in Saudi boys comprised of 31 children with autism and 29 controls showed significant lower 2D:4D ratio in boys with autism with p value <0.001 which was similar to the present study[4].

Mackus *et al*. conducted a study in Utrecht University,Netherlands to determine the usefulness of the 2D : 4D digit ratio as biomarker for autistic traits. A total of 401 healthy young volunteers participated in the study. For men, a significant positive correlation was found between the left 2D : 4D digit ratio and the total AQ score (r = 0.157; p = 0.042) and AQ sub scale "attention switching" (Rx = 0.182; p = 0.017). In conclusion, gender specific associations between the 2D : 4D digit ratio and specific autism traits were observed, which were stronger in men than in women[5].

CONCLUSION

The study shows a significant association between a lowered 2D:4D ratio and ASD making it one of the potential screening tool for early detection of autism, which important for early intervention and management to improve the quality of life of individuals with ASD.

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