

## Original Research Article

# A study on prevalence of minor physical anomalies in mentally retarded children in a tertiary care centre of India

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## ABSTRACT

**Background:** Paucity of studies in world literature and lack of any Indian study assessing the frequency, prevalence and severity of minor physical anomalies (MPAs) in children with mental retardation (MR) as well as their importance for prediction and timely recognition of mental insufficiency, if any.

**Methods:** A cross-sectional observational study involving 273 mentally retarded children aged 5-18 years was conducted over a period of one year and were compared with their age and sex matched controls. Waldrop and Halverson (1971) physical anomaly scale was used to assess those MPAs.

**Results:** In the study group, higher percentage (79.85% vs. 40.29%) of children had MPAs with a predominance of multiple MPAs in comparison to healthy children (40.29% and 0%, respectively). Higher average frequency of MPAs per child was noted in the study group (1.42) than control group (0.40). Mean Waldrop weighting score was significantly higher among mentally retarded children than their controls ( $3.7 \pm 0.8$  versus  $0.8 \pm 0.2$ ,  $P < 0.0001$ ). Authors noticed a gradual and significant decrease in Waldrop score with increase in intelligence quotient (IQ) [ $F = 175.72$ ,  $P < 0.001$ ]. A significant strong negative correlation between Waldrop score and IQ level ( $r = -0.89$ ,  $P < 0.001$ ) was also observed. Out of eighteen variables of Waldrop score, seven were found as significant in binary logistic regression model for MR. Our model can explain 37.6% to 50.1% variability of the MR.

**Conclusions:** MPAs are more prevalent in mentally retarded children than healthy children. A clear-cut demarcation between these two groups is possible by the frequency of anomalies and the increased strength of their expression (i.e. their weighting scores).

**Keywords:** Intelligence quotient, Mental retardation, Minor physical anomalies, Waldrop weighting score

## INTRODUCTION

Mental retardation (MR) refers to a group of disorders that is characterized by significantly sub-average intellectual functioning, existing concurrently with related limitations in two or more of the following applicable adaptive skills: communication, self-care, home living, social skills, community use, self-direction, health and safety, functional academics, leisure, and work; and manifests before 18 years of age.<sup>1,2</sup> Though the

more appropriate term “intellectual disability” is increasingly being used in its place, it has not been adopted universally. As per statistical data, 2.5% of the population should have intellectual disability, and 75% of these individuals should fall into the mild to moderate range.<sup>3</sup> The global prevalence of intellectual disability has been estimated to be approximately 16.41/1,000 persons in low income countries, approximately 15.94/1,000 for middle-income countries, and approximately 9.21/1,000 in high-income countries.<sup>3</sup> The minor physical anomalies

(MPAs) are defined as a slight physical defect, a deviation in appearance from essential physical characteristics resulting from abnormal development during the first and second fetal trimester, that are found in less than 4% of the general population.<sup>4</sup> It is assumed that these anomalies are indicators of central nervous system (CNS) abnormalities that developed during the same period from the same causes. They are noted to arise more commonly in children with minimal cerebral dysfunction, behavioral disorder and MR, especially in boys.<sup>5,6</sup> Recently, the term “informative morphogenetic variants” has been preferred intended to denote mild morphogenetic errors that are prenatal in origin.<sup>7,8</sup> But some researcher preferred this term for those anomalies which arise after organogenesis.<sup>9</sup> Although they are clinically and cosmetically insignificant, it is possible to use them effectively for diagnostic, prognostic and epidemiological purposes and their presence in children makes the existence of major malformations more likely.<sup>4,5,8</sup>

When several specific MPAs are seen together in an individual, they can serve as external markers for underlying genetic disorders.<sup>10</sup> As because 71% of anomalies are present in the craniofacial area and the hands, careful attention to these areas can be helpful in diagnosing occult major anomalies.<sup>11</sup>

Early diagnosis of intellectual disability facilitates earlier intervention, identification of abilities, realistic goal setting, easing of parental anxiety, and greater acceptance of the child in the community. Most children with intellectual disability first come to the attention of the pediatricians in infancy because of dysmorphisms, associated developmental disabilities, or failure to meet age appropriate developmental milestones. So, it is very much important to identify those MPAs. There is insufficient data of prevalence of MPAs in mentally retarded children in our country as well as in the universe. Some of the early studies focused on the incidence of major as well as MPAs in normal and deviant children.<sup>12</sup> They found that compared with normal children, children with cleft lip and/or palate had 10% more anomalies and an 18% increase in children with a septal defect and 92% in a group of retarded children. Various literature published in the past has concentrated on the prevalence, association and/or correlation of the MPAs in various psychiatric disorders like schizophrenia, attention-deficit hyperkinetic disorder (ADHD), first episode psychosis etc.<sup>6,13-18</sup> There are only few studies in world literature where prevalence of MPAs has been assessed in children with mental impairment.<sup>8,16,17</sup> To our knowledge this is the first Indian study where prevalence of MPAs is being assessed in mentally retarded children. The present study has, therefore, been conducted to gain knowledge about the frequency, prevalence and severity of MPAs in MR. Specifically to assess their importance for prediction and timely recognition of mentally insufficiently developed children.

## METHODS

A cross-sectional observational study was conducted among 273 mentally retarded children and adolescents aged between 5-18 years of age in the out-patient clinic of Department of Psychiatry and Pediatrics of Burdwan Medical College and Hospital, Burdwan, West Bengal, India; over a period of one year (between March 2015 to February 2016). Cases were selected by simple random sampling, and age and sex matched controls were selected for each case. Taking confidence level as 99%, precision as 2% and prevalence of mental retardation as 1.6%, necessary minimum sample size was approximately 262. Appropriate written consent was taken from the guardian of the children and adolescent who were involved in the study. Ethical clearance was obtained from the institutional ethical committee [vide memo no. BMC/PG/122/1(1) dated 9th January 2015].

### Inclusion criteria

Study population was selected depending upon the following inclusion criteria:

- Significantly sub-average intellectual function: an intelligence quotient (IQ) score of below 70
- Significant impairments in adaptive function
- Onset before 18 years of age.

### Exclusion criteria

- Mentally retarded children with identifiable etiology like those who suffered and/or suffering from meningitis, meningoencephalitis, head trauma, hypothyroidism etc. were excluded from present study.
- Significantly ill, uncooperative children and whose parents did not give consent to participate in the study were also excluded from the study.

### Assessment of MPAs

Both cases and controls were checked for MPAs. For assessment of MPAs, the Waldrop and Halverson (1971) physical anomaly scale was used.<sup>18</sup> It includes 18 morphological abnormalities from six body regions: head, eyes, ears, mouth, hands, and feet. Abnormalities either scored qualitatively as present (1) or absent (0). All the anomalies were scored according to their weight. Average number of minor anomalies per child was regarded as Waldrop score one (W1) and total weighting scores of anomalies as Waldrop score two (W2). The W2 gave an indication as to the number and severity of MPAs present in a subject. Waldrop's scoring system was applied to both groups of children analysing number of anomalies per child. The comparison also comprised weighting scores (W2) between the groups. Authors added scoring weights to minor anomalies in both subject groups, expressing their weight as Waldrop's weighting scores. Each finding was double-checked by two

investigators. The investigators and the participants were not aware of the purpose of the study.

**Statistical analysis**

Collected data were entered into Microsoft Excel worksheet. Categorical variables were coded while mean and standard deviation were calculated for continuous variables. Shapiro-Wilk test was used for testing skewness of data. The proportion of each variable with 95% confidence interval was calculated for cases and controls. Chi-square test was used to find the significance of difference among categorical variables, whereas one-way ANOVA was used for continuous variables. Pearson’s product moment correlation was used to compute the strength and direction of association between Waldrop score and IQ, i.e. the degree of MR. A binary logistic regression model was also created taking mental retardation as a dependent variable. The adjusted odds ratio was calculated with 95 % confidence interval. All analysis was done in SPSS software, version 19.0. A P value of <0.01 was taken as statistically significant

**RESULTS**

Total 273 mentally retarded patients studied, 161 (58.97%) were male and 112 (41.03%) were female

patients. Among 273 patients 207 (75.82%) patients were between the age group of 5 to 12 years and rest 66 (24.17%) were in 13 to 18 years age group. There was no statistically significant difference (P>0.05) in the mean age of the children between study (10.4±3.4 years) and control group (10.5±3.6 years). Both the groups were also comparable (P>0.05) in sex distributions (58.97% male versus 58.24% male). Among 273 patients 218 (79.85%) patients had at least one MPA present. Among 273 controls only 110 (40.29%) had MPAs (Table 1).

**Table 1: Distribution of age, sex, and number of MPAs# in case and control group.**

	Cases with MPAs (n=218)	Controls with MPAs (n=110)
<b>Age distribution</b>		
5-12 years	159 (72.93%)	77 (70%)
13-18 years	59 (27.06%)	33 (30%)
<b>Sex distribution</b>		
Male	133 (61%)	67 (60.9%)
Female	85 (38.99%)	43 (39.09%)
<b>Number of MPA</b>		
Single	108 (49.54%)	110 (100%)
Multiple	110 (50.45%)	0 (0%)

# MPAs = minor physical anomalies

**Table 2: Distribution of minor physical anomalies in case and control group.**

Minor physical anomalies	Case (N=273)	Control (N=273)	P value
Fine electric hair	21 (7.7,5.1-11.5)	2 (0.7)	<0.001
Two or more hair whorls	22 (0.3, 0.07 -2.05)	15 (5.5)	0.2333
Head circumference outside normal range	45 (19.4, 15.2-24.5)	37 (13.5)	0.3379
Epicanthus	15 (6.7, 4.5-10.6)	2 (0.7)	0.001
Hypertelorism	23 (12.1, 8.7-16.5)	4 (1.4)	<0.001
Low seated ears	31 (16.2, 12.2-21.0)	9 (3.3)	<0.001
Adherent ear lobes	13 (8.4, 5.7-12.3)	0 (0.0)	<0.001
Malformed ears	21 (9.2, 6.3-13.2)	3 (1.1)	<0.001
Asymmetrical ears	18 (9.2, 6.3-13.2)	2 (0.7)	<0.001
Soft and pliable ears	13 (3.7,2.0-6.6)	12 (4.4)	0.2752
High steepled palate	29 (11.4, 8.1-15.8)	9 (3.3)	<0.001
Furrowed tongue	18 (8.8,5.9-12.8)	2 (0.7)	0.0036
Tongue with smooth rough spots	7 (2.6,1.2-5.2)	6 (2.2)	0.7790
Curved fifth finger	14 (5.1,3.1-8.4)	0 (0.0)	<0.001
Single transverse palmar crease	28 (13.2,9.7-17.7)	2 (0.7)	<0.001
Third toe longer than second	15 (12.4, 9.0-16.9)	2 (0.7)	<0.001
Partial syndactylia of two middle toes	12 (1.5,0.6-3.7)	0 (0.0)	0.001
Big gap between first and second toes	36 (16.9,12.9-21.7)	3 (1.1)	<0.001

Among all MPAs, two or more hair whorls (P=0.2333), head circumference out of normal range (P =0.3379), soft and pliable ears (P=0.2752), high-steepled palate (P=0.185), tongue with smooth-rough spots (P=0.7790) were the only variables that were comparable in both case and control group. All the other MPAs were seen in a

statistically significant number of cases (P>0.05) in the study group. The MPAs that were not found even in single children were adherent ear lobes, curved fifth finger, and partial syndactylia of two middle toes (Table 2). In mentally retarded children two or more anomalies predominated (seen in 110 cases i.e. 40.29%), but in

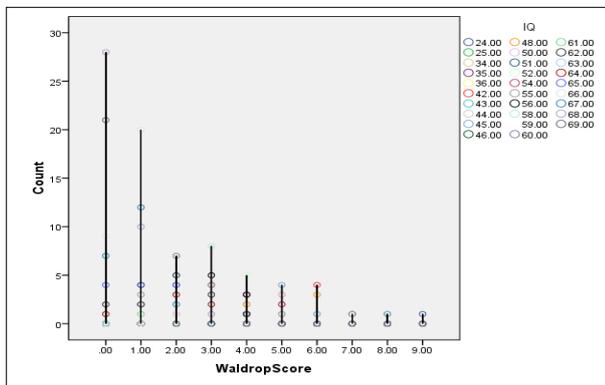
healthy children, no one had multiple MPAs. Among mentally retarded children the percentages of MPAs were as follows, single MPA 39.56% (108), two MPAs 27.1% (74), three MPAs 5.86% (16), four MPA 5.12% (14) and five MPA 2.19% (6). Single anomaly comprised only 40.29% in well children group. It was noticed that there was a gradual and significant decrease in Waldrop score with the increase in IQ ( $F=175.72, P<0.001$ ). Post-hoc analysis (Tukey) also revealed that differences between every group were significant. There was a significant strong negative correlation between Waldrop score and IQ level ( $r=-0.89, P<0.001$ ) (Table 3 and Figure 1).

**Table 3: Correlation between Waldrop score and IQ level in mentally retarded children group.**

IQ level	No of cases in MR group, N=273 (%)	Waldrop score (Mean±SD*)
<35	4 (1.5)	7.75±0.96
36-50	34 (12.4)	5.38±1.04
51-70	235 (86.1)	1.43±1.34

§ IQ = intelligence quotient, \* SD = standard deviation

In comparison of minor anomaly, weighting scores between the two children’s groups displayed a clear-cut difference. There was a definite shift toward higher weighting scores (from 2 to 5) among mentally retarded children.



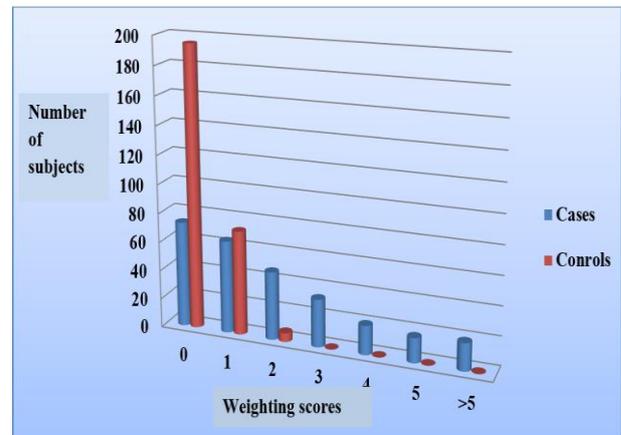
§ IQ = intelligence quotient

**Figure 1: Relationship between Waldrop score and IQ level in mentally retarded children group.**

In well children, however, lower weighting scores (from 0 to 1) predominated. 42.4 % of mentally retarded children had a total Waldrop weighting score (W2) of 2-5, whereas more than 5 scores comprised 10.3% of children. All the children of the control group had a total Waldrop weighting score (W2) of either 2 or below (Figure 2).

Out of eighteen variables of Waldrop score, seven were found as significant in the binary logistic regression model for mental retardation. Our model can explain 37.6% to 50.1% variability of the mental retardation.

Among MR children the average frequency of minor anomalies per child (W1) was 1.42, this being 0.40 in healthy children. Mean waldrop weighting score was significantly higher among MR children group than controls ( $3.7±0.8$  versus  $0.8±0.2, P<0.0001$ ).



# MPAs = minor physical anomalies

**Figure 2: Distribution of weighting score of MPAs# in case and control group.**

**DISCUSSION**

Early prenatal ectodermal insult is a common inciting event for both MPAs and the associated brain disorders.<sup>5,6,19</sup> A high number of MPAs are thought to arise primarily from a disruption that occurs during the first trimester of development when the ectodermal germ layer of the fetus is developing which is also responsible for the creation of the CNS.<sup>5,19</sup> Therefore, the presence of MPAs may indicate underlying CNS dysfunctions. MPAs do not directly cause behavioral deviance but can serve as a marker for some fetal disturbance of development in the first trimester.<sup>4,19</sup> In addition to the teratogenic cause, neurological damage resulting from either prenatal or perinatal factors is also a frequently cited cause for the development of MPAs.<sup>5,20</sup> Occurrence of increased number of MPAs in families or its association with chromosomal abnormalities, or with obstetric complications, suggests that the role of variety of intrauterine processes in their pathogenesis.<sup>6,21</sup> MPAs may also reflect early, largely extra-genetic, stressful events.<sup>22</sup>

The wide distribution (from 0 to 5) of the number of minor anomalies in mentally retarded children per individual was noticed in present study. Most healthy children exhibited no anomaly or just a single one. In present study, mentally retarded children exhibited thrice as many minor anomalies than well children did as evidenced by the number of detected minor anomalies per child in healthy children which was less than one-third the children with MR (1.42 vs. 0.40). So, authors can easily justify our set hypothesis (i.e. the frequency of MPAs in the mentally retarded children group is higher

than in the healthy children group) with the obtained results. More severe forms of individual minor anomalies (i.e. anomalies with higher weighting scores like fine electric hair, epicanthus, clinodactyly of fifth finger, and third toe longer than second) were either not found or seen in an insignificant number of cases in the control group. Along with these, hypertelorism, adherent ear lobes, asymmetrical ears, furrowed tongue, single transverse palmar crease, partial syndactylia of two middle toes were also recorded in negligible number of cases in the control group. Two or more hair whorls, soft and pliable ears and tongue with smooth rough spots were seen in significant number of children in the control group when compared with the study group. Other studies have also stated that certain minor anomalies are even more common in a healthy child group than in children with MR.<sup>23,24</sup> The control group of present study showed a greater number of subjects with smaller weighting score values per child if we analyze the distribution of MPAs through their weighting scores. Even authors noted that children and adolescents with few minor anomalies usually had lack of weight (i.e. they had a zero value) in the control group. In present study, mentally retarded subjects had a greater number of detected physical anomalies and were affected by their severer forms (anomalies with higher weighting score) and greater number of subjects had higher weighting scores per child ( $3.7 \pm 0.8$  versus  $0.8 \pm 0.2$ ) in comparison to the control group. Previous studies also found that significantly greater average frequency of total physical anomalies in the mentally retarded children group than healthy children supporting our findings<sup>25</sup>. Regardless of the fact that minor anomalies also occur in the healthy population, it has been proved that significantly larger proportions of these anomalies occur in individuals who have undergone developmental disorders during morphogenesis, regardless of the factors involved in their pathogenesis.<sup>2,16</sup> The fact that children with some major anomaly also have a greater number of minor anomalies is of great practical significance.<sup>15</sup> The reverse is also true. In the absence of an identifiable syndrome, an increase in MPAs has also been reported in several groups including newborns, school-aged children, schizophrenic and autistic individuals, mentally retarded children, psychoneurotic children learning-disabled children speech, language and hearing-impaired children, hyperactive children and inhibited children.<sup>6,8,9,11,13,16,16-19,21-25,28-33</sup> The previous literature described wide differences in the average frequency of MPAs per child among healthy school children. Steg et al, found an average value of 2.88, while Firestone et al, found 1.4 minor anomalies per child, for boys.<sup>31,33</sup> In girls, Waldrop et al, found this value to be 3.54, against 2.61 minor anomalies per child found by Rosenberg et al.<sup>18,34</sup> In present study, authors have found the frequency of 0.40 in the healthy group. The application of different criteria while assessing minor anomalies might be a cause of these variations. Authors can explain these differences by the different characteristics of the populations studied.<sup>25</sup> Authors could not find any universal models for

investigating MPAs till the present date. Further research is needed in designing a uniform concept of minor anomalies. Although it is very difficult to achieve a universally accepted model as authors cannot exclude researcher's subjectivity in making their assessment. In present study, authors found male: female ratio of 1.56:1 among study population having MPAs. Elizarraras-Rivas et al, have also found that male: female ratio is 1.5:1.<sup>35</sup> The only study by Lal and Sharma<sup>30</sup> showed that the females had higher MPAs score compared to males; however, only thirty females were included in the study which probably had influenced the outcome. Authors found a significant difference in the prevalence of minor anomalies, in relation to sex. Males were having more MPAs than females. Various deviations from normal morphogenesis are most striking in the head, hands, and feet. Green et al found more mouth abnormalities and an increased head circumference in female schizophrenic patients compared to male schizophrenic patients and female controls.<sup>22,30</sup> In present study, authors could not find higher occurrences of MPAs in the craniofacial region compared to the other body areas. During embryogenesis, there are overlapping critical periods of sequential development that could result in multiple malformations in different areas of the body. Each organ has a critical period of development where vulnerability to teratogens can result in the disruption of proper development.<sup>36</sup> For example, critical hand and feet development occurs during the eight weeks of gestation while palate development occurs during the ninth week. It is therefore plausible that disruptions during a critical stage of development of a physical feature can cause MPAs that can lead to a change in brain development causing other behavioral problems. Because of the overlapping developmental sequences in embryogenesis, an insult would need to occur early on in development, particularly before the eighth week, in order to find anomalies, present in more than one region of the body. Authors usually underscore the importance of MPAs because of the fact that 3% of children with one minor anomaly also have a major malformation. Children with three or more minor anomalies usually have an associated major malformation in as many as 90% of cases.<sup>8,12</sup> Consequently, early recognition of MR is possible by knowing the number and severity of minor anomalies, especially in children. In order to detect the underlying developmental disorder in a child, the finding of a greater number of minor anomalies in him or her, can be used as an indication to perform complex examinations and tests. The finding of MPAs in a disorder could suggest a genetic origin of the condition as because of the fact that multiple minor anomalies are strictly determined genetically.<sup>8,33</sup> As authors found that high percentage of subjects with MR had two or more minor anomalies (40.29%), it can be explained by the presence of dominant genetic etiology in examined children. This suggests that each apparently healthy child having a greater number of minor anomalies, as well as a higher sum of their weighting scores must undergo detailed medical examination and analysis which could increase

the possibility of timely recognition of individuals with MR.<sup>8,31</sup> Where manifestation of MR comes later, minor anomalies can be recorded (if looked for) much earlier. In this way, early rehabilitation is possible by early recognition of MR and by starting early interventions.

To improve the quality of life, such rehabilitation will be very much effective as it will help children in completing a higher degree of training. Present study also supports the finding of the other study that authors can differentiate the healthy children group and mentally retarded children in an easier way, depending on the frequency of anomalies and the strength of their expression (i.e. according to their weighting scores).<sup>8</sup> Some of the earlier literature suggested that MPAs may have a correlation with the IQ, and school achievement.<sup>37</sup>

Dimambro et al, found that in a sample of people with schizophrenia, MPA count was associated with lower intelligence.<sup>38</sup> This correlation between MPAs and IQ in mentally retarded children has definitely been proved in our article.

## CONCLUSION

Our findings of the occurrence of significantly higher number of minor anomalies per child and their higher Waldrop weighting score in a group of children with MR than in healthy children further reinforces the interplay of a common genetic factor or factors during early developmental phase leading to the simultaneous occurrence of underlying developmental disorders (i.e. MR) and of MPAs. It should always be kept in mind that while assessing the general population, particularly children, for predictors of behavioral variation other possible explanations such as dysmorphology assessment should also be considered.

Children having high number of anomalies who present with learning problems and behavioral variations, a single gene mutation or a rearrangement within and among the chromosomes may be the cause rather than prenatal brain injury. Further research to enlighten the gray areas regarding the biological origin of the MPAs and to develop a more reliable scale for their assessment may prove beneficial.

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