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Developmental Disorders- Genetic View

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ABSTRACT

Objective: To review genetic cause of developmental disorders.
Methodology: A survey consisting of 70 children with developmental disorder was done for genetic evaluation of these disorders through case history and interview of the parents.
Results: The cause was found to be combination of genetic variation with environmental risks due to which epigenetic changes might have taken place in prenatal stages in 81% of the cases in the survey. Only 16% of cases showed mendelian inheritance.
Conclusion: The results indicate that developmental disorders are of epigenetical nature rather than mendelian inheritance.

INTRODUCTION

Developmental disorders are a group of psychiatric conditions that interrupt normal development in childhood. They may affect a single area of development (specific developmental disorders) or several pervasive developmental disorders.[1] These disorders comprise language disorders, learning disorders, motor disorders and autism spectrum disorders. Most notable among them are the ability to socialize with others, to communicate, and to use imagination. Children with these conditions often are confused in their thinking and generally have problems understanding the world around them.[2]

The scientific study of the causes of developmental disorders involves many different theories. Some of the major differences between these theories involves whether or not environment disrupts normal development, or if abnormalities are pre-determined. Normal development occurs with a combination of contributions from both the environment and genetics. The theories vary in the part each factor has to play in normal development, thus affecting how the abnormalities are caused.[3]

Early intervention is absolutely essential for pervasive developmental disorders, many of which will respond to an aggressive approach that may combine speech therapy, occupational therapy, physical therapy, behavior modification techniques, play therapy, music therapy, theory of mind therapy and in some cases medication to treat isolated symptoms of these disorders.[2,4-6]

METHODOLOGY

The study participants were a part of Dr. Shreepad Khedekar's Imperial Clinics in India. The study population size was 70. The number of males in the present study was 61 and number of females was 9. The age of the study population in India ranged from 2 years to 14 years. The case history was taken of all the participants. The genetic evaluation based on the case history and parent interview was also carried out.

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RESULTS

The study population size was 70. The number of males in the present study was 61 and females was 9 (Figure 1). The ratio of male to female in the study was 6-7:1 male to female. The age range was between 2 years to 20 years (Figure 2). The average age of the population was found to be 6.5 years when they came to clinic.

The developmental disorders seen in the study were Autism spectrum disorder (ASD), Delayed Global Development, Learning disability, Fragile X syndrome and other disorders like Ataxia Telangectasis, Cornelia de Lange Syndrome, Epilepsy, Morquio's syndrome Type IV B and Severe right carpal tunnel syndrome (Figure 3). The developmental delay in most of the study population was found to be from the age of 1.5 years.

During genetic evaluation of the cases it was observed that 75% of the cases were epigenetic, 16% were mendelian and 3% were de novo mutation (Figure 4). While 6% showed combination of epigenetic and mendelian inheritance. In the mendelian inheritance, 36% of cases were of autosomal recessive mutation, 18% were sex-linked and 46% were undetermined (Figure 5). Therefore, in the present study, the cause of the disorder has been found to be combination of genetic variation with environmental risks.

DISCUSSION

The study population size was 70. The number of males in the present study was 61 and female was 9. The ratio of male to female in the study was 6-7:1 male to female. Similar gender bias was seen worldwide in diagnosis of autism spectrum disorder[7,8] which may be due to better abilities of masking the symptoms of the disorder by the females which make diagnosis difficult. In recent years, the genetic aspect of this gender bias is being analyzed by many researchers which suggest sex-linked inheritance of neural developmental genes.[9,10]

The age range of India population was between 2 years to 20 years. The average age of the population was found to be 6.5 years when they came to clinic.Similar average age range was observed worldwide[4] and in Indian population.[11] These finding are similar to the observations made in European and American population.[12] This indicates that the diagnosis of the disorder made by the clinicians is between 3 to 6 years. Thus, a persistent delay between the initial suspicion of a difference in development and the diagnosis of these disorders was seen in the present population.

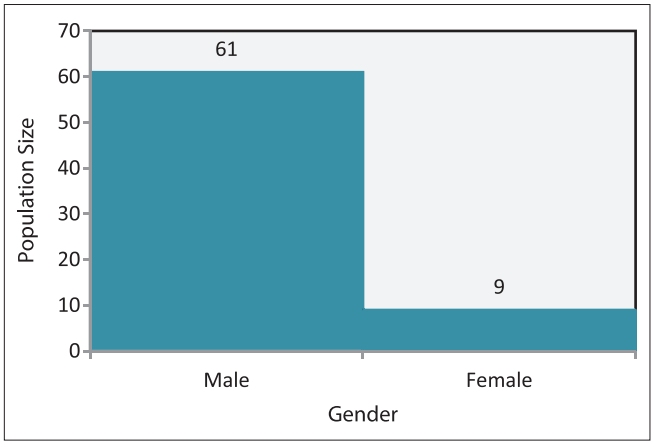

Figure 1: Gender of the study population

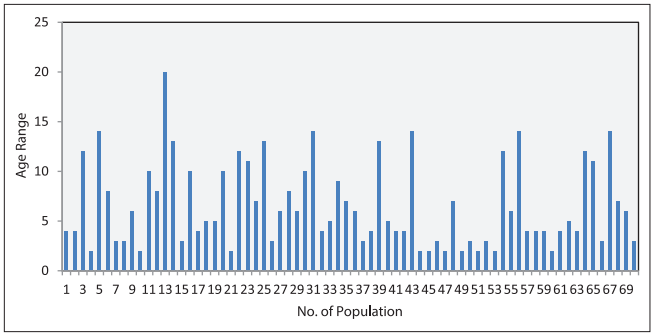

Figure 2: Age range

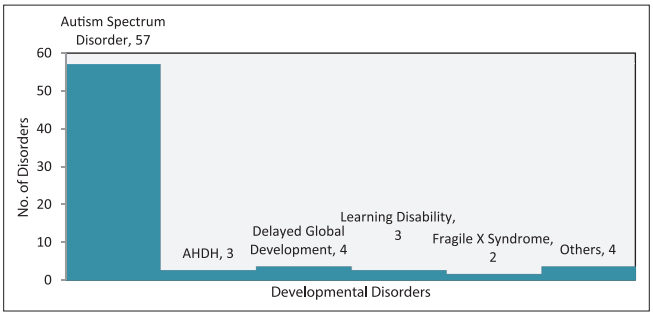

Figure 3: Types of developmental disorders

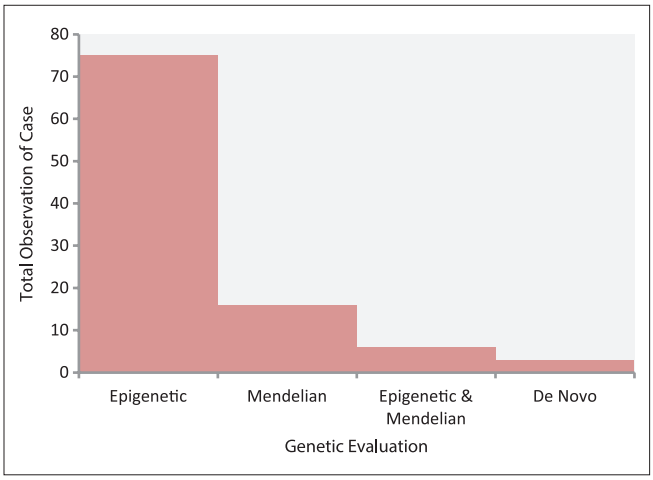

Figure 4: Genetic evaluation of disorder

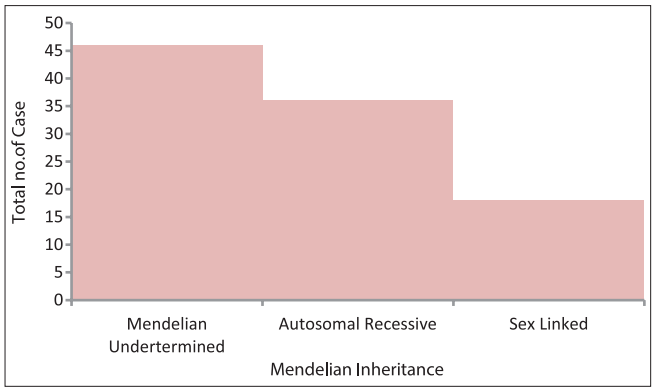

Figure 5: Mendelian inheritance

The developmental delay in most of the study population was found to be from the age of 1.5 years. In Indian population the developmental delays were observed from 1.5 years to 2 years and the diagnosis was made by the age of 3 to 4 years.[13-15] This indicates that symptoms of developmental disorders become pronounced from the age of 1.5 years.

During genetic evaluation of the cases it was observed that 75% of the cases were epigenetic, 16% were mendelian and 3% were de novo mutation (Figure 4). While 6% showed combination of epigenetic and mendelian inheritance. In the mendelian inheritance, 36% of cases were of autosomal recessive mutation, 18% were sex-linked and 46% were undetermined. The cause of these disorders may be due to combination of (a) rare genetic variants with high effect size, (b) common genetic variants with low effect size, and (c) environmental risk factors.[16-18] Therefore, in the present study, the cause of the disorder has been found to be combination of genetic variation with environmental risks due to which epigenetic changes might have taken place in prenatal stages in most of the cases. A study done by Perera and Herbstman[19] has shown evidence that prenatal exposure to diverse environmental risk factors dysregulates the fetal epigenome which can lead to developmental disorders and disease manifesting in childhood. Hence environmental factors like stress, nutrition, infections during pregnancy; can dysregulates the fetal epigenome leading to developmental disorders.

CONCLUSION

The present study shows that prenatal exposure to diverse environmental risk factors dysregulates the fetal epigenome which can lead to developmental disorders

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