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Assessment of Mitochondrial Dysfunction in Autistic Individuals by Measuring Plasma Lactate Levels

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ABSTRACT
Introduction: Autistic disorder, Asperger syndrome and pervasive developmental disorder-not otherwise specified comprise a heterogeneous group of neurodevelopmental disorders known as autism spectrum disorders (ASDs). ASDs are behaviorally defined by impairments in communication and social interaction along with restrictive and repetitive behaviors.
Objectives of the study: The main objectives of the study will determine the mitochondrial dysfunction in autistic individuals by measuring plasma lactate levels.
Material and methods: This cross sectional study was conducted in DHQ Hospital Sahiwal. This study will include 200 children aged 7 to 9 years. Randomly selected sampling technique will be used for the data collection. For the purpose of analysis of mitochondrial dysfunctionality we will collect the blood samples of each individual.
Results: The data was collected from 200 children. In this study, blood ammonia, serum lactate, AST, ALT and CK level were higher in 29(90%), 18(80%), 23 (30%), 20(20%) and 14 (40%) subjects of study group.
Conclusion: It is concluded that mitochondrial dysfunction occur in children with autism spectrum disorder children.

KEYWORDS: Dysfunction, Health, Mitochondria, Patients.

INTRODUCTION

Autistic disorder, Asperger syndrome and pervasive developmental disorder-not otherwise specified comprise a heterogeneous group of neurodevelopmental disorders known as autism spectrum disorders (ASDs). ASDs are behaviorally defined by impairments in communication and social interaction along with restrictive and repetitive behaviors[1]. An estimated 1 out of 110 individuals in the United States is currently affected with ASD, with a male-to-female ratio of 4.5:1[2].

The etiology of ASD is not known in most cases, but a genetic component, possibly involving 15 or more loci, is widely accepted to contribute to the development of ASD. However, the robust phenotypic and genotypic heterogeneity among individuals with ASD has limited the case for a purely genetic etiology[3]. Indeed, it is becoming apparent that many children with ASD have associated underlying medical comorbidities, such as epilepsy, sleep disruption, mitochondrial dysfunction and gastrointestinal (GI) abnormalities[4].

The etiology of ASD is complex and encompasses the roles of genes, the environment (epigenetics) and the mitochondria. Mitochondria are cellular organelles that function to control energy production necessary for brain development and activity[5]. Researchers are increasingly identifying mitochondrial abnormalities in young children with ASD since the most severe cases present early with features of ASD[6]. Better awareness and more accurate and detailed genetic and biochemical testing are now available for the younger patient presenting with developmental delay or behavioral problems[7].

Mitochondrial dysfunction has been implicated in several psychiatric and neurological disorders. Over 20 years ago, Coleman and Blass hypothesized that individuals with ASD may have an abnormality in carbohydrate metabolism, and in 1998 Lombard proposed that ASD may be a disorder of impaired mitochondrial function[8]. Over the past decade, evidence has accumulated that some individuals with ASD have concomitant mitochondrial dysfunction, and some have proposed a 'mitochondrial autism' subgroup. Several review articles have been recently published concerning mitochondrial dysfunction in ASD[9].

This cross sectional study will conducted to analyze the mitochondrial dysfunction in autistic individuals by measuring plasma lactate levels. Because a minority of cases of autism has been associated with several different organic conditions, including

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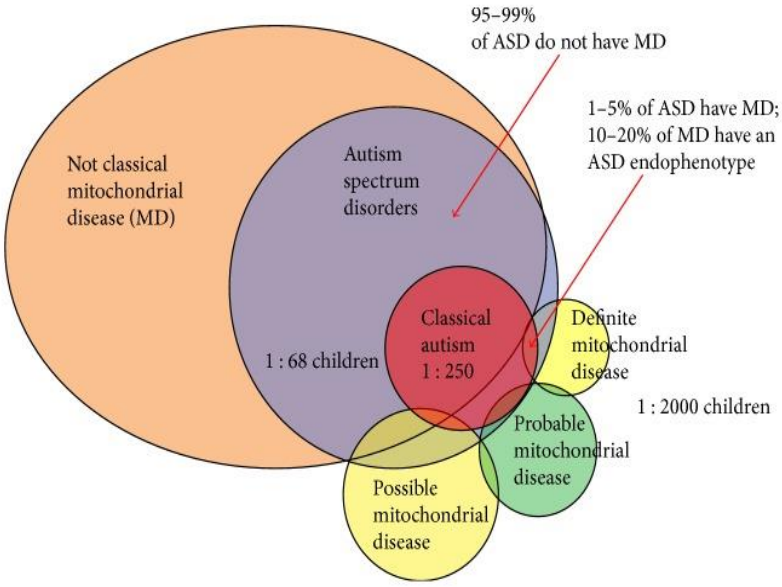
bioenergetic metabolism deficiency[10]. Autism is a childhood encephalopathy characterized by deficiencies in social interaction and communication, and by repetitive and stereotyped behaviors[11]. Its aetiology remains unknown, although several different specific organic conditions have been found to be associated with autism and autistic-like conditions in about 11 to 37% of cases[12].



Relationship between Mitochondrial dysfunction and autism

OBJECTIVES OF THE STUDY

The main objectives of the study will be:

1. To determine the mitochondrial dysfunction in autistic individuals by measuring plasma lactate levels.
2. To compare the prevalence of autism spectrum disorders and the frequency of associated pathologies.
3. Examine the clinical, biochemical and genetic characteristics of children diagnosed with mitochondrial dysfunction.

MATERIAL AND METHODS

Study Design

This cross sectional study was conducted in DHQ hospital Sahiwal during July 2021 to December 2021. The data was collected from 200 patients with the age range 7 to 9 years. The data was collected from both genders.

Inclusion criteria

1. All the children of age 7 to 9 years will be included in this study.
2. Plasma lactate and pyruvate levels will be included.

Exclusion criteria

Exclusion criteria included:

1. Individuals which suffer from any other dysfunction will be excluded from this study.
2. Age above 9 years will excluded.

Data collection

This study include 200 children aged 7 to 9 years. Randomly selected sampling technique was used for the data collection. For the purpose of analysis of mitochondrial dysfunctionality we collect the blood samples of each individual. Blood samples was used for the purpose of analysis of plasma lactate levels in autistic individuals. Lactate and pyruvate in plasma was measured enzymatically. Muscle respiratory chain complex activities in isolated deltoid muscle mitochondria was measured by double-wavelength spectrophotometry.

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Statistical analysis

Student's t-test was performed to evaluate the data. Two-way ANOVA was performed to study the contributions. A chi-square test was used to examine the difference in the distribution of the fracture modes (SPSS 19.0 for Windows, SPSS Inc., USA).

RESULTS

The data was collected from 200 children. In this study, blood ammonia, serum lactate, AST, ALT and CK level were higher in 29(90%), 18(80%), 23 (30%), 20(20%) and 14 (40%) subjects of study group. But blood ammonia level were higher in only 1(10%) and no rise of serum lactate, AST, ALT and CK level in control group respectively.

Table 01: Serum enzyme analysis in selected patients

Parameters	Neurodevelopmental disorder children (n= 100)	Healthy children (n= 1000)
blood ammonia	29 (90%)	10 (10%)
serum lactate	18 (80%)	10 (10%)
AST	23 (30%)	0 (0%)
ALT	20 (0%)	10 (10%)
CK	14 (40%)	0 (0%)

Table 2: Pooled statistics and meta-analysis of group differences for mitochondrial biomarkers in ASD compared with controls

Biomarker	***Total* N**	***Mean (95% CI)***	***Total* N**	***Mean (95% CI)***
Lactate (m l^{-1})	11	1.73 (1.61, 1.88)	114	0.91 (0.87, 0.96)
Pyruvate (n l^{-1})	24	0.12 (0.11, 0.14)	24	0.06 (0.06, 0.06)

DISCUSSION

Table 2 outlines the mean values (with CIs) of biochemical markers of mitochondrial dysfunction, along with meta-analysis statistics, for ASD and control groups. The present study was undertaken to observe some biochemical variables in children with autism spectrum disorder in order to evaluate their mitochondrial dysfunction. Mitochondrial dysfunction were assessed by measuring blood ammonia, serum lactate, creatine kinase (CK), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) level in autism spectrum disorder children[6]. All these variables were also studied in apparently healthy age and sex matched normal children for comparison. In this study, values of all the biochemical variables of healthy subjects were within physiological limit and were almost similar to those reported by different investigators abroad[7].

The etiology of ASD is complex and encompasses the roles of genes, the environment (epigenetics) and the mitochondria. Mitochondria are cellular organelles that function to control energy production necessary for brain development and activity. Researchers are increasingly identifying mitochondrial abnormalities in young children with ASD since the most severe cases present early with features of ASD. Better awareness and more accurate and detailed genetic and biochemical testing are now available for the younger patient presenting with developmental delay or behavioral problems[8].

Epidemiologic and family studies suggest that genetic risk factors are present. Monogenic causes are identifiable in less than 20 percent of subjects with ASD. The remaining subjects have other genetic or multigenic causes and/or epigenetic influences which are environmental factors altering gene expression without changing the DNA sequence[9]. Epigenetic factors in ASD have been reviewed by Grafodatskaya *et al.*. The recurrence risk for ASD varies by gender for the second child to be affected (4% if the first child affected is female and 7% if a male). The recurrence rate increases to 25-30% if the second child is also diagnosed with ASD. Studies have shown that among identical twins, if one child has ASD, then the other has a 60 to 95% chance of being affected[10].

CONCLUSION

It is concluded that mitochondrial dysfunction occur in children with autism spectrum disorder children.

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