Original Article

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The Frequency of Hereditary Metabolic Diseases in Children Referred to Amirkola Children Hospital (2005-2015)

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ABSTRACT

BACKGROUND AND OBJECTIVE: Hereditary metabolic diseases are individually rare disorders, early diagnosis and treatment are very important which can prevent from permanent damage to the nervous system and mental retardation and other irreparable injury and even death in these patients. This study was done to evaluate the prevalence of hereditary metabolic diseases in children admitted to Amirkola children hospital 1384-94.

METHODS: In this cross-sectional study, medical records of patients with hereditary metabolism disorders from 1384 to 1394 were studied. Related information to age, gender, family relationship, family history, disorder type, diagnostic criteria and disease outcome were extracted and analyzed.

FINDINGS: In this study, 65 children were diagnosed with different types of metabolic disease research. The common disorders were maple syrup urine disease 14 patients (21.5%), methylmalonic acidemia 10 (15.3%), mitochondrial 8(12.3%) galactosemia 6(2.9%), respectively. Among children, 36 cases (55.4%) were male and positive family history of metabolic disorders was observed in 15 children (23.1%). Mortality of metabolic disorders was in 26 children (40%) and the rest of the 19 children (54.2%) had developmental delay.

CONCLUSION: In this study 19 different types of hereditary metabolic diseases were detected that more than 25% of patients had a positive family history of this disorder.

KEY WORDS: *Metabolism, Hereditary Disorders, Children, Frequency.*

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Introduction

Hereditary metabolic disorders are caused by the absence or abnormal function of an enzyme or its cofactor and leads to accumulation or loss of certain metabolites in the body (1). These disease are classified based on the size of metabolite to small molecule disorders such as amino acidopathy, urea cycle deficiency, galactosemia, organic acidemia, etc and other disorders such as glycogen storage disease, and lysosomal disorders (2).

The prevalence of metabolic disorders are separately rare, but generally metabolic disease prevalence accounted for 1 in 800 to 1 in 2500 live births that consequently have a high prevalence (1). In the study of Golbahar and colleagues, among the 144 patients, 43 cases of phenylketonuria, 6 cases of maple syrup urine disease and 15 tyrosinemia were identified. The prevalence of these diseases were 27.2, 9.4 and 4.7 per 100000 live birth (2).

In the study of Moammar and collaborators during the years of 2008- 1983, 268 patients were identified with the 55 metabolic disorder. Moreover, in this course, the prevalence of hereditary metabolic disorders was 150 cases per hundred thousand live births. The most common assessed disorders was the lysosomal storage disease with a prevalence of 30% and 20% organic acidemia, 16% amino acid disorders and 7% fatty acid oxidation disorders, respectively. Family history was positive in 36% of cases (3). The clinical diagnosis of these disease is difficult or impossible and requires specific biochemistry and genetics tests and on the other hand, early detection and treatment is very important to prevent from permanent damage to the nervous system and mental retardation and other irreparable injury and even death in these patients (7, 6, 4).

In many parts of the world for these types of patients neonatal screening programs are used, because timely diagnosis and treatment of these complications can be prevented or minimized them (9, 8, 6). The study of Devi and colleagues identified 51 cases of hereditary metabolic disorders among 2994 hospitalized newborns. The most common symptoms on admission were poor nutrition, decreased activity, jaundice, seizures and breathing problems and common metabolic disorder in this study were phenylketonuria (PKU) (11 cases), organic acidemia (8), maple syrup urine disease (5 cases), citrullinemia (5 cases), galactosemia (4 cases), nonketotic hyperglycemia (4 cases) and tyrosinemia. Of the 33 cases with detected metabolic abnormalities, 19 cases had process of natural evolution, 9 cases of developmental delay and 5 cases of cerebral palsy. Inheritance of this disorder is typically autosomal recessive (9), therefore, in societies with higher inbreeding coefficient are more common. This ratio in Canada is 0.0004-0.0008, 0.001 to 0.005 in America (10) and 0.024 in Saudi (3).

The rate of familial marriage and average inbreeding coefficient in our country has been reported 70-25% and 0.0185, respectively (4, 11). Thus the expected prevalence of these disorders must be higher in Iran compared with other societies such as America and Canada.

Unfortunately, to date, despite increasing our knowledge of the pathogenesis of metabolic diseases and factors affecting its incidence is still no consensus on screening for these disorders. For designing screening programs for metabolic disorders it is necessary the existing of country's overall statistics, but studies on its prevalence is low in Iran. Therefore, such studies are essential as a guide to determine the necessity or lack of necessity of screening programs. Therefore, this study aimed to determine the prevalence of metabolic disease and its consequences in Patient of pediatric hospital of Amirkola over a period of 10 years.

Methods

In this cross-sectional study, the medical records of patients referred to endocrine treatment center of Amirkola for follow up or treatment and diagnosed with metabolic disorders based on clinical symptoms and genetic and laboratory findings were considered. Referred patients during the period of this study were enrolled according to type of disorder and diagnostic criteria. In these patients, information regarding age, sex, parent's familial relationship, occupation of their parents, a family history of the disease and the complications of the disease were extracted from patients' files and were examined. Descriptive statistics were used to determine the frequency of complications and disorders.

Results

In this study, 65 children with diagnosis of metabolic disease referred for treatment to the endocrine clinic that the average age at diagnosis was 35.01± 14.02 months. The most common inherited metabolic disorder was maple syrup urine disease with frequency of 14 children (21.5%). Other common problems include methyl malonic acidemia, mitochondrial, galactosemia with frequency of 10 (15.3%), 8(12.3%), 6(9.2%), respectively (Figure 1). Of children with metabolic disorders, 36 patients (55.4%) were male.

Location of Parents in all children was at Mazandaran province, nearly half of them (28 cases) (43.1%) were from babol and its surrounds. Of the total patients, 3 cases of methyl malonic acidemia, 4 cases of mitochondrial, 9 cases of maple syrup urine disease , 3 cases of phenylketonuria (PKU), 3 cases of pompe disease were from babol and familial relationship of parents was observed in 33 cases (50.8%). Positive family history of metabolic disorders was found in 15 cases (23.1%) and deaths from complications of metabolic diseases were observed in 26 (40%) of the children and from the rest of the children, 19 cases (2.54 %) were diagnosed with developmental delay.

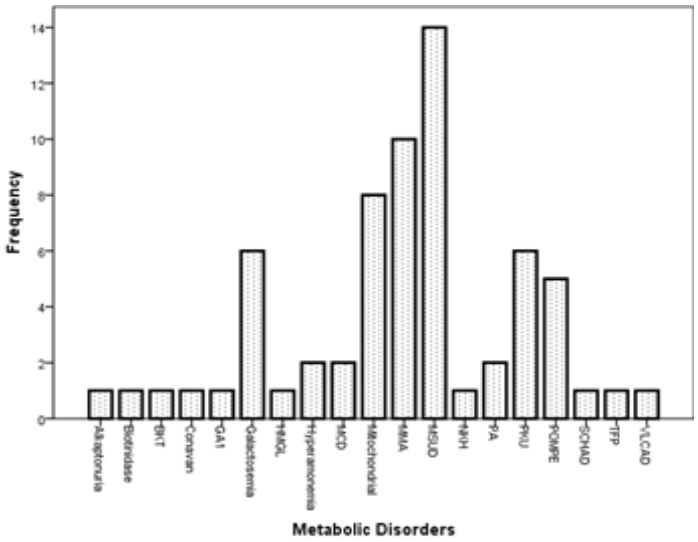

Figure 1. Frequency of metabolic disorder based on the disorder type

*Beta Ketothiolase, **Gluteric academia type I, ***Multiple carboxylase deficiency, ****3-Hydroxy- 3methyl GlutaricAridemia, *****Non ketotichyperglycinemia, ******Propionic academia, *******short chain hydrony any.coa dehydrogenase, ********Three functional protein, *********Very long chain acylcoa dehydrogenase

Discussion

This study found that more than half of the patients in the study suffered death or irreversible effects of the disease. Phenylketonuria (PKU), methyl malonic acidemia, maple syrup urine disease and galactosemia are the most prevalent inherited metabolic disorders in this region.

Today, patients with phenylketonuria associated with Favismand and congenital hypothyroidism are under newborn screening in the country. But other more common disorders are not covered by this program. The study of Zahedpasha and colleagues also showed that minimal frequency of maple syrup urine disease in Mazandaran is 1 in 26714 live births, which is higher compared with the all world (1 in 185,000 live births) (9). Golbahar and colleagues during a selective screening for metabolic disease in infants born in shiraz showed higher frequency of phenylketonuria (PKU), tyrosinemia and maple syrup urine disease, respectively, (2). Two studies in China show methyl malonic acidemia is one of common metabolic disease in the region (14, 13). Recent studies in the Middle East and North Africa countries showed that the prevalence of metabolic diseases in Qatar is 1 per 1300 live births (4).

In addition, in Saudi Arabia over a period of 25 years, 55 different metabolic disease were identified that frequency of these disorders was totally 1 from 667 live births (3). In Japan, according to the results of neonates screening program, prevalence of PKU and maple syrup urine disease, galactosemia, homocystinuria was 1:80000, 1:500000, 1:30000 and 1:80000, respectively (15, 7).

The results of the study show the prevalence, natural history, genetics and other features of inherited metabolic diseases are different in populations and different races and it is necessary that data be collected for each population (4). In this study 19 different types of hereditary metabolic diseases were detected that more than 25% of patients had a positive family history of this disorder. Due to the frequency of familiar marriage in the patient's parents, using screening tests for newborns in this area followed by prenatal diagnostic test for couples with a family history of congenital disorders, can be possible the timely diagnosis and treatment of many of these diseases and can prevent at least serious and

irreversible damages to patients. In addition to early detection and early treatment of disease, these programs could provide several useful achievements such as reducing hospitalization time, reduce the cost of unnecessary tests for patients.

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