RESEARCH ARTICLE

Major Congenital Metabolic Disorders in the First 12 years of Life in 79,100 Consecutively Born Children in Qazvin Province

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Abstract

Objective

Deficient enzyme activity may cause congenital metabolic defects. These defects are inherited in an autosomal recessive, autosomal dominant, and X-linked patterns. This study was aimed at investigating the occurrence of metabolic diseases in Qazvin Province.

Materials & Methods

This cross-sectional study was performed on 79,100 children aged 12 years or less between 2000 and 2010. Clinical manifestations, laboratory findings, and all other essential information were assessed to precisely diagnose the metabolic diseases. The sorted information on congenital metabolic defects of the patients, information included in a checklist, and data were analyzed using SPSS.

Results

A total of 57 metabolic disorders were recorded. The difference in the prevalence of metabolic disorders between male (29 cases) and female (28 cases) was not statistically significant. The most frequent congenital metabolic disorder among our patients was phenylketonuria (PKU; 5 per 1,000 cases), and the least common disorder was galactosemia (3 per 1,000 cases).

Conclusion

Timely detection and management of congenital metabolic disorders can help save the affected children. Prenatal screening programs, molecular gene therapy, and counseling for consanguineous marriage can play important roles in reducing the rate of metabolic disorders in this province.

Keywords: Congenital metabolic disorders; prevalence; population; Qazvin

Introduction

Congenital metabolic defects develop when a specific functional enzyme is absent, and this can be caused by several mechanisms (1). More than 350 different congenital metabolic diseases have been described to date, most of which are rare (2). A recent survey conservatively estimated that the incidence of metabolic disorders is approximately 1/2,500 births or 10% of all monogenic conditions in children (3) Most metabolic disorders are congenital and inherited in an autosomal recessive pattern, i.e., the disorder develops when two mutant alleles are present. The carrier state is usually not associated with morbidity (4). However, children born of a consanguineous marriage are at an increased risk of developing metabolic disorders and of early mortality (5). With a decrease in the incidence of fatal infectious diseases, congenital metabolic defects may be one of the main causes

of infant mortality in the future. Because large systemic studies of metabolic disorders have not been performed in Iran, we assessed the prevalence rate of metabolic diseases in patients who admitted to hospitals in Qazvin province with congenital complaints.

Materials & Methods

We designed a prospective cross-sectional study to evaluate disease prevalence, causes, and clinical presentation in 79,100 patients aged 12 years or less who were registered at the genetics division of the Ghods Major Pediatric Hospital between 2000 and 2010. We chose this hospital because it is affiliated to Qazvin University of Medical Sciences and provides emergency services to a large part of the province. Furthermore, demographic information and clinical findings at birth were collected from the maternal records maintained at Kosar Hospital as well as from the parents at the initial patient evaluation from 2000 to 2004. Patients were referred to us because of neurological signs, seizures, mental retardation, jaundice, organomegaly, and skeletal disproportion.

The metabolic diseases in the probands were confirmed by reviewing of the pedigree of the family and the family's genetic records; population screening; review of the mode of inheritance; assessment by geneticist; assessment of the patients' clinical characteristics, including complete blood count, creatinine level, FBS, calcium level, electrolyte levels, plasma TSH level, total and direct bilirubin levels, liver transaminase level, creatine kinase level, alfa fetoprotein level, urinary amino acid levels, reticulocyte count, and lipid profile; fluorescent spot test screening; high-performance liquid chromatography determination of plasma amino acid levels, and assessment of Guthrie test findings. Plasma acylcarnitine profile and urine organic acid levels were assessed if metabolic acidosis, hyperammonemia, and lactic acidosis were detected. On the basis of the diagnosis, the patients were classified into 3 categories (Table 1). Disease incidence rate per 1,000 patients was calculated. Patient data were analyzed using SPSS software (v.11.5; Chicago, IL).

Results

This study presents the results, frequencies, and analyses of congenital metabolic disorders of 57 of the 79,100 children. The diagnoses are summarized in Table 1.

The prevalence of metabolic diseases was 0.072% (57 cases), with no statistically significant difference between the prevalence in male (29 cases) and female (28 cases). The results were double-checked using hospital registration information related to the study period (Fig. 1).

Discussion

The results of the present study are discussed in light of our recent findings (from 2000 to 2004) (6) of increased incidence of congenital metabolic diseases in Qazvin Province.

The most frequent disorder among our patients was phenylketonuria (PKU) (41 patients, 0.05%) (Figure 1). The frequency of PKU is approximately 1 in 10,000 births (7). However, the rate of PKU in this study (0.05%) was less than the previously reported rate. The enzyme responsible for the disorder is phenylalanine hydroxylase, which catalyzes the hydroxylation of phenylalanine to tyrosine in healthy individuals. In the absence of this enzyme, phenylalanine levels increase, which is believed to be toxic. PKU is the most common congenital metabolic disorder in Tehran (8), Fars Province (9,10), Mashhad (11), and Isfahan (12). The incidence of PKU in Iran is higher than that reported in other countries (12).

Classic galactosemia occurs in approximately 1 in 60,000 live births. However, the incidence varies from 1 in 30,000–40,000 live births in Europe (13) to 1 in 1 million live births in Japan(14); the estimated incidence in the U.S. is 1 in 53,000 live births (15). In our report, the prevalence of galactosemia in the referred patients was approximately 1 in 27,000, a rate that is lower than that observed in previous studies in other countries.

The incidence rate reported for all types of mucopolysaccharidosis (MPS) ranges from 1 in 25,000 to 1 in 46,000 live births (16). Thirteen patients of the 79,100 symptomatic patients who were assessed for congenital metabolic disorders had MPS, and the prevalence rate was 1 in 6,000 among the referred patients. This incidence and prevalence rate are lower than the corresponding values reported in the general population.

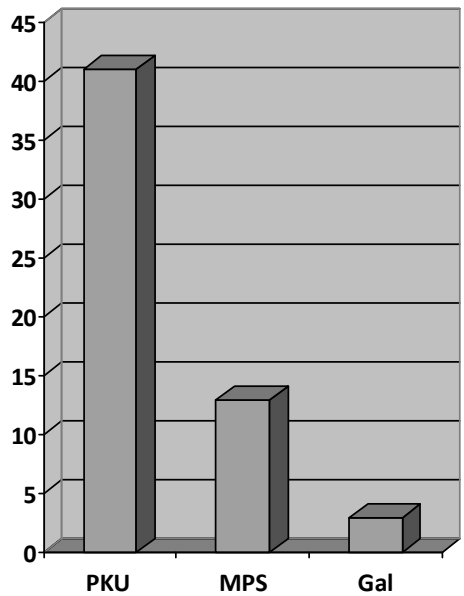
In this study, a large number of patients (68%) were children born from consanguineous marriages. We recommend that prenatal diagnosis be offered to consanguineous couples with recessive genes, since there is a 25% risk of the child being affected. In some countries, the current percentage of consanguineous marriages is higher and even exceeds 50%,while in many others, the percentage is not more than 1% (17,18). Many researchers have indicated that consanguinity causes autosomal recessive/metabolic disorders (4,19). On the basis of the findings obtained in our previous study, we estimated the incidence of congenital metabolic disorders to be higher in children born of consanguineous marriages (38.57%) than in children born of non-consanguineous marriages (7.26%) (20). Every year, over 130 million infants are born worldwide (18), and 13.5 million of these children are born of consanguineous marriages.

Taking the above findings into account, we concluded that newborn screening, prenatal diagnosis for congenital metabolic disorders, and somatic gene therapy can help treat affected infants. In addition, molecular screening has opened new avenues of diagnosis and become a promising new means for treatment. Various other factors, such as different geographical distribution, ethnicity, diet, socioeconomic differences, and consanguineous marriage should be considered for the accurate diagnosis and treatment of congenital metabolic disorders.

Table 1: Prevalence of congenital metabolic diseases in Qazvin Province

Disease	Male	Female	Cases	Percentag (%)
Galactosemia	2	1	3	0.0037
MPS	5	8	13	0.016
PKU	22	19	41	0.050
Total	29	28	57	-

MPS: Mucopolysaccharidosis, PKU: Phenylketonuria



MPS: Mucopolysaccharidosis, PKU: Phenylketonuria,Gal: Galactosemia

Fig 1. Number of cases of congenital metabolic disorders in our study

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