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Original Article

Clinical Characteristics of Pediatric Patients with Inborn Errors of Metabolism Admitted to Namazi Hospital, a Tertiary Referral Center in Shiraz, Southern Iran

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Abstract

Background: Inborn errors of metabolism (IEMs) are rare genetic disorders that usually cause disease by blocking a metabolic pathway. Delayed diagnosis often occurs due to nonspecific symptoms. This study assesses the demographic and clinical characteristics of pediatric patients with IEMs admitted to Namazi hospital, a referral center in southern Iran.

Methods: All 1-month-old to 18-year-old patients who were admitted to the pediatric ward at Namazi hospital, a referral center in southern Iran, and diagnosed with IEMs were enrolled. Patients with incomplete information were excluded. Comprehensive demographic and clinical data, including age, sex, parental consanguinity, family history of IEM, presenting symptoms, number of hospitalizations, age of onset, and diagnosis of the disease, were collected. All the data were entered into SPSS version 22 and analyzed.

Results: Two hundred patients, 53.5% male and 46.5% female, were enrolled in the study. The predominant clinical symptoms observed were lethargy and vomiting. The most prevalent IEMs were aminoacidopathies, organic acidemia, and mitochondrial disease. Consanguinity was found in 57.5% of patients, while a family history of metabolic diseases was observed in 16.5%. A statistically significant association was identified between consanguinity and the type of disease.

Conclusion: The clinical symptoms of IEMs are nonspecific and may be misdiagnosed as other diseases, such as septicemia. We should always keep IEMs in mind to detect the disease earlier and prevent significant morbidities and mortality through appropriate and timely treatment. Due to the prevalence of family marriages in Iran, we should also consider metabolic screening.

Keywords: Inborn errors of metabolism, Children, Pediatric, Metabolic disease

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Introduction

Inborn errors of metabolism (IEMs) are genetic disorders known since 1902, causing diseases through the accumulation of toxic substrates, deficiency of certain products, or diversion to alternative pathways (1). The estimated incidence is 1:2500 individuals (2). These disorders can manifest with a variety of symptoms, including neurologic manifestations (seizure, developmental delay, and hypotonia), hepatic involvement (cholestatic jaundice, liver failure, and hepatomegaly with hypoglycemia), cardiac complications (cardiomyopathy), facial features, hydrops fetalis, and characteristic urine odor (3). Delayed diagnosis and treatment of IEMs lead to irreparable consequences and even death (4). Consanguinity is often associated with these autosomal recessive genetic disorders (5), and given the high rate of consanguineous marriages in Iran, the country has a higher prevalence of metabolic diseases (6,7). There is no exact assessment of the IEM incidence rate in Iran, and further studies are required to address this issue and develop strategies for early detection and prevention. Tandem mass spectrometry is a reliable method for newborn screening of metabolic disease soon after birth (4), and prenatal screening is another method (7).

In this cross-sectional descriptive study, we aim to evaluate the demographic characteristics and clinical presentations of patients diagnosed with metabolic diseases admitted to the pediatric ward at Namazi hospital between 2017 and 2021. By recognizing the clinical manifestation and looking for metabolic diseases at an

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Consanguinity marriage, observed in 57.5% of parents in our study, has been identified as a contributing factor to the occurrence of IEMs. In Iran, the overall rate of family marriage is estimated to be 38.6% (14). A significant association was seen between consanguinity and the type of metabolic disease. The incidence of IEM was higher among children born to parents with family marriage (5). In our study, all patients with fatty acid oxidation defects and 77.7% of patients with GSD were born in consanguineous marriages. The rates for other types of IEM are presented in Table 1. In a survey conducted in Oman, the rate of consanguinity among parents of pediatric patients with IEMs was 95%, including all patients with fatty acid oxidation defects and 96% of patients with GSD (15). In Bahrain, the rate of family marriage was estimated to be 11.4% (16). Another study in Bahrain reported consanguinity marriage in 84% of patients with IEMs (17).

In addition, a family history of previous affected children was observed in some patients with IEMs. In our study, the prevalence of family history of IEMs was 16.5%. However, higher rates were reported in a study in Libya (63.5%) and Saudi Arabia (57.2%) (18,19). It is important to note that screening older siblings of affected patients is crucial as they may be at risk of developing the same disease (20).

Patients with IEMs often require repeated hospital admissions. Among the patients in our center, 53% had more than one hospital admission, and those diagnosed with GSD had the highest rate of hospitalization. The other patients who had one hospital admission may require admission in the following years through follow-ups. Frequent hospitalization of these patients has significant economic implications for the healthcare system and society. Khneisser et al estimated at least one hospital admission in the first five years for early-detected IEM and at least three times for late-detected patients. They concluded that screening programs are economically beneficial despite IEM being a rare disease (21).

Limitations

The diagnosis of IEMs usually needs more time, and specific laboratory data preparation can be time-consuming. The follow-up of patients is essential for specific diagnosis in the unspecified diagnosis groups in our study. The participants in this study consisted of patients admitted to hospitals. Many IEM patients, such as those with Phenylketonuria (PKU), are diagnosed in early screening in Iran and usually do not need hospital admission. This study had no outpatient data.

Conclusion

Given the nonspecific clinical manifestations of IEMs and the wide range of diseases that may be considered in the differential diagnosis, it is essential to always consider the possibility of IEMs. Screening programs and early detection play a crucial role in ensuring timely and appropriate treatment, which can help prevent irreversible complications and long-term sequelae associated with these conditions. By maintaining a high index of suspicion for IEM and implementing effective screening strategies, we can improve outcomes and minimize the potential long-term impacts on patients' health.

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Authors' Contribution

Conceptualization: Homa Ilkhanipoor, Naser Honar, Hossein Moravej, Ali Nazemosadat, Hamide Barzegar.
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Competing Interests

The authors declare no conflict of interest.

Ethical Approval

The Medical Ethics Committee of Shiraz University of Medical Sciences approved the study protocol (ethics code: IR.SUMS.MED.REC.1400.023).

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