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Prevalence and profile of inherited metabolic disorders in Libya: single center experience

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Abstract

Background: Inherited Metabolic Disorders (IMDs) are collectively common, particularly in a highly consanguineous population. Early diagnosis and prompt treatment are crucial to prevent permanent damage to the central nervous system as well as other devastating irreparable damage and even death. This study was conducted to determine the prevalence of IMDs in children seen at the Pediatric Department, Faculty of Medicine, Misurata University, Libya.

Methods: In this cross-sectional study, medical records of all patients with IMDs over 6 years' experience were studied. Related information to age, gender, consanguinity, family history, disorder type, diagnostic criteria and disease outcomes were extracted and analyzed. *RESULTS:* 57 patients were included in this study; 39 patients were male (68.4%) and 18 patients were females (31.6%) [M: F= 2.17:1] and the mean age at diagnosis was 1.9 years. Consanguinity was reported in 47 patients (82.5%), with family history being found in 71.9% of patients. 16 patients have mucopolysaccharidosis (28.1%), 11 patients have Glycogen storage diseases (19.3%),4 Nieman pick disease (7%), while the rest constitute the small molecular weight disease.

Conclusion: IMDs are an up growing field of medicine, initial baseline diagnostic tools could take place in any specialized center and newborn screening should be established in Libya because of the high prevalence of IMDs. The lysosomal storage diseases are particularly common; however, many were still undiagnosed.

Keywords: Inborn Errors; Inherited; Metabolic Diseases; Prevalence

1. Introduction

Inborn errors of metabolism (IEM) are individually rare, but collectively numerous [1]. Inherited metabolic disorders (IMDs) are a complex and heterogeneous group of monogenic disorders, usually resulting from deficient activity in a single pathway of intermediary metabolism [2].

The classical inborn errors of metabolism are defects in enzymes of the metabolism of amino acids, carbohydrates, and fatty acids or in mitochondrial energy metabolism. These disorders are often dynamic; they fluctuate with changes in the metabolic state of the patient and frequently allow successful therapeutic intervention. Most of them are readily

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diagnosed through basic metabolic investigations, which include blood gases, glucose, lactate, ammonia, plasma amino acids, urinary organic acids, and an acylcarnitine profile [3].

Several initiatives at establishing a classification of inherited metabolic disorders have been published previously, some focusing on pathomechanisms, others on clinical manifestations, while yet another attempted a simplified approach of a comprehensive nosology. Some of these classifications suffered from shortcomings, such as lack of a mechanism for a continuous update in light of a rapidly evolving field, or lack of widespread input from the metabolic community at large [4]. Our classification is based on the pathophysiological perspective of the following three diagnostically useful groups.

- Group 1: Disorders that Give Rise to Intoxication.
- Group 2: Disorders Involving Energy Metabolism.
- Group 3: Disorders Involving Complex Molecules [1].

We should suspect an inborn error of metabolism (IEM) in patients with neurologic abnormalities (eg, developmental delay, hypotonic baby, or feeding difficulties), especially in those patients with multisystem involvement who appear with acute symptoms. The early and specific diagnosis of IEMs and prompt initiation of appropriate therapy are still the best determinants of outcome for these patients. Delay in diagnosis may have serious consequences resulting in acute metabolic decompensation, progressive neurologic injury, or death [5].

Multidisciplinary care should place patients and their families at the center of care services planning and to respond to their complex needs, including not only health-related but also other (psychological, social, educational, vocational) issues [6].

The specific metabolite testing includes Amino acid (AA) and urine organic acid (OA) analysis which helps in diagnosing mostly aminoacidopathies as well as organic acidemias. Plasma AA analysis by ion exchange chromatography (IEC) is a state-of-the-art technique for the quantitative analysis of AAs in various body fluids like plasma, urine and cerebrospinal fluid (CSF). Multiple AAs and their metabolites can be analyzed in each run. Likewise, urine OA analysis on gas chromatography mass spectrometry (GCMS) is an excellent state-of-the-art technique for detecting various organic acidemias. Final confirmation relies on enzyme and genetic analyses [7].

In IEM, the recent application of tandem mass spectrometry (tandem MS) to newborn screening and prenatal diagnosis has enabled presymptomatic diagnosis for some IEM. However, for most, neonatal screening tests are either too slow, too expensive or unreliable and, as a consequence, a simple method of clinical screening is mandatory before the initiation of sophisticated biochemical investigations [1]. Improved testing technology is leading many states to expand newborn screening for genetic metabolic disorders. The National Newborn Screening and Genetics Resources Center provides information on each state's screening practices.

If an inherited metabolic disorder is not detected at birth, it is often not diagnosed until symptoms appear. Once symptoms develop, specific blood or DNA tests are available to diagnose most genetic metabolic disorders. Referral to a specialized center (usually at a university) increases the chances of a correct diagnosis [8].

There are different treatments tailored to the specific inherited metabolic disease. A common treatment is diet modification. Other possible treatments include enzyme replacement therapy (ERT), hematopoietic stem cell transplantation (HSCT), and organ transplantation [9].

2. Material and methods

2.1. Study setting

Our outpatient follow up clinic started since 2016,during this journey years we follow all patient diagnosed in our pediatric and neonatology department in misurata medical centre and that referred to us from different speciality, In this cross-sectional study, medical records of all patients with IMDs over 6 years' experience were studied. Related information to age, gender, consanguinity, family history, disorder type, diagnostic criteria and disease outcomes were extracted and analyzed.

2.2. Inclusion criteria

All pediatric patients visit and had a regular follow-up at the metabolic clinic.

2.3. Exclusion criteria

Phenyl ketonuria was excluded because of their special clinic foundation.

2.4. Statistical analysis

The collected data were analyzed by SPSS software version 18 and the results were summarized as frequencies and percentages. Statistical analysis was performed using one sample Chi-square test. Results were accepted as significant level (p .0.05).

3. Results

Table 1 Disease Diagnosis

Disease diagnosis	IEM		P. value
	N.	%	
MPS1 (Mucopolysaccharidosis 1)	9	15.8	< 0.001*
MPS2 (Mucopolysaccharidosis 2)	7	12.3	
GSD1 (Glycogen storage disease 1)	6	10.5	0.009*
GSD3 (Glycogen storage disease 3)	5	8.8	
MSUD (Maple syrup urine disease)	7	12.3	0.041*
NCHCU (Non classical homocystinuria)	2	3.5	NS
TYR (Tyrosinemia)	3	5.3	NS
CPT (Carnitine palmitoyl transferase deficiency)	2	3.5	NS
FAOD (Fatty acid oxidation defect)	2	3.5	NS
BKT (Beta-ketothiolase deficiency)	1	1.8	NS
MMA (Methylmalonic acidemia)	2	3.5	NS
PA (Propionic acidemia)	2	3.5	NS
H lip (Familial hyperlipidemia)	4	7	NS
NPD (Neiman pick disease A&B)	4	7	NS
UCD (Urea cycle defect)	1	1.8	NS

The majority of patients are MPS1 (15.8%), MPS2 (12.3%), MSUD (12.3%), and UCD (1.8%), and that is statistically non-significant

Table 2 Type of Disease

Type Disease	IEM		P. value
	No	%	
GR1	21	36.8	0.004*
GR2	5	8.8	
GR3	31	54.4	

The majority of patients are GR3 (54.4%), and that is highly statistically significant

Table 3 Sex Distribution

Gender	IEM		P. value
	No	%	
Male	39	68.4	0.034*
Female	18	31.6	

The majority of patients are male (68.4 %), and that is highly statistically significant

Table 4 Family History

Family History	IEM		P. value
	No	%	
Yes	41	71.9	0.026*
No	16	28.1	

Family history was revealed in (71.9%), and that is highly statistically significant

Table 5 Consanguinity status

Consanguinity	IEM		P. value
	No	%	
Yes	47	82.5	< 0.001*
No	10	17.5	

Family history was revealed in (82.5%), and that is highly statistically significant

4. Discussion

The field of inherited metabolic diseases has changed from a limited group of rare, untreatable, often fatal disorders to an important cause of acutely life-threatening but increasingly treatable illness. Unchanged is the orphan nature of these disorders with mostly relatively nonspecific initial clinical manifestations.

The patient does not come to the physician with the diagnosis; the patient comes with a history, symptoms, and signs. 2. Our first effort in our center is to register these patients who follow up regularly with a confirmed diagnosis according to the international standards for specific disease diagnosis.

Our clinic was diagnosed and follow 57 patients with a mean of their age 6.6years, the index patient mostly diagnosed late after referral from other pediatric clinics, no newborn screening program was introduced in our country, because of the high rate of consanguinity marriage among our patients and the nature of autosomal inheritance in IMD, the consanguinity was found in a large number of our patients which is about (82.5%).with the support of patient education about the disease and possibility of picking the affected early further siblings was diagnosed early, in which our registry the family history was about(71.9%), male to female ratio were equal to(m:f, 2.1:1).

In comparing, our registry to inherited metabolic disorders in Austria9. The upper hand of our patients was of disorders involving complex molecules which is about (54.4%) (Disorders that give rise to intoxication36.8%, and disorders involving energy metabolism8.8%). this is support community education more than physician support because of the nature of the disease, which is easy to pick up from facial complexion and its slow progression intoxication effect.

The registry provides a unique data collection of IMDs in any center to improve general understanding of IMDs and patient's treatment.

5. Conclusion

IMDs are an up growing field of medicine, initial baseline diagnostic tools could take place in any specialized center and newborn screening should be established in Libya because of high prevalence of IMDs. The lysosomal storage diseases are particularly common; however, many were still undiagnosed.

Recommendations

Because of the effects of ethnicity and consanguinity and increasing ascertainment. We recommend depending partially on this study to provide useful epidemiological information for those planning and providing services for patients with IMDs, including newborn screening, in Libya and similar populations.

Compliance with ethical standards

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Disclosure of conflict of interest

All authors declare that they have no conflicts of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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