Categories of the Patients Attending Metabolic Clinic, Queen Rania Al-Abdullah Children Hospital

WajdiAmayreh, MBBS, MRCPCH, Hanadi Al-Rimawi, MD, Mo'menAlakil, MD, Noor Migdadi, MD, SumaiaRababa'a, MD

ABSTRACT

Objective: To describe the different categories of patients who were seen at the metabolic clinic at QRACH; over a period of eight months; from January the 1st to the end of August 2018.

Methods: A retrospective evaluation of patients who attended the metabolic clinic at QRACH in the 1st eight months of 2018. The metabolic clinic receives different categories of patients from other pediatric clinics at QRACH, and pediatric clinics of other military and non-military hospitals. There were no age limitations. Data recorded were; age, gender, parents' consanguinity, affected family members or relatives, diagnosis and the primary referral clinic or hospital.

Results: 429 patients were included in this study; the ratio of male to female was 1.03:1. The mean age of patients was 5.62±0.55 years old. 56.9% were known to the metabolic clinic while the neurologic clinic led the referral clinics with 17.5%. Parental consanguinity was obviously noticed; 55.5% of the patients' parents were first cousins and only22.6% were not related.38% of the patients have a confirmed diagnosis, 15% of the patients have a clinical diagnosis and 47% of the patients have no specific diagnosis.

Conclusion: The metabolic clinic at QRACH is very busy with patients from pediatric clinics and hospitals everywhere in Jordan. Parents' consanguinity is very frequent. Lack of diagnosis is still a large troublesome issue that needs to be solved by the use of more advanced investigations.

Key words: Metabolic Clinic, Inborn errors of metabolism, genetic testing, inherited diseases, Jordan.

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Introduction

Metabolism is the set of life sustaining chemical reactions in organisms to preserve cellular activities and continue life (1). This process relies on specific metabolic pathways in its regulation in order to maintain vital activities (2). Each pathway has a group of specific enzymes that help it in its function (3). Accordingly, the inborn errors of the metabolism process (IEM) can be defined as disturbances that occur in any of the metabolic pathways due to the lack of activity of enzymes (4).

From the departments of:
Pediatrics medicine
Correspondence should be addressed to:Dr. WajdiAmayreh, MBBS

In other words, IEM are a series of uncommon diseases involving the production, function, and transportation of the enzymes (5). They are also considered genetic diseases and they are inherited in an autosomal recessive manner (6). They are all genetic disorders and can be inherited on nuclear DNA (autosomal or sex chromosomes) or mitochondrial DNA (7).

Proteins, lipids, carbohydrates, vitamins, minerals and complex compounds can be affected in the anabolic or the catabolic pathways (8). Therefore, these groups of diseases are expressed in different presentations and different age groups (9). Increase diagnostic facilities such as expanding newborn screening (NBS) programs, dry blood spot (DBS) testing and Tandem Mass spectrometry (MS-MS) has enabled making the diagnosis of such rare diseases with increasing rapidity (10).

IEM categories are based on various parameters. These parameters may be a predominant system such as neurologic, age of onset, symptoms, or acuity (11). The symptoms associated with the IEM disorders are categorized by laboratory tests, for the first category, it includes one organ (12).The second category has many disorders divided into three groups: intermediate metabolic disorders that affect small molecules, disorders that primarily involve energy metabolism, and disorders that involve complex molecules (12, 13, 14).

There are categories of patients with IEM who have a wide range of clinical symptoms, some of which are detected at birth and others that begin to appear during life (15). Jordanian national screening program screens for phenylketonuria only from all other IEM (16). This study was conducted to describe the categories of patients that were seen at the metabolic clinic, King Hussein Medical City, Queen Rania Abdullah Children's Hospital, Amman, Jordan. The information collected their primary clinic, parenteral consanguinity, specific diagnosis and developmental delay.

METHODS

The medical records of the patient who attended the metabolic clinic in the 1ST eight months of 2018 were reviewed. Ages ranged from birth to 24 years old. The recorded data included: age, gender, primary referral clinic or hospital, the family history; parents' consanguinity, affected other family members affected, deaths related to the same presentation; the presence of developmental delay or regression and the presence of a laboratory confirmed or clinical diagnosis or not. The family data were all related only to conditions that may have had the same disease as the index case. The data of the patients who were seen more than one time in the study period were recorded for only the last visit. Laboratory investigations were variable for each patient. Basic investigations such as; CBC, serum electrolytes, kidney and liver function tests, ammonia, lactate, venous blood gases were done at the laboratory of Queen Rania Abdullah Children Hospital. Aminoacids chromatography, organic acids chromatography and MS_MS tandem mass spectrometry were done at Princess Iman Research Center; King Hussein Medical City. Lysosomal enzymes activities were measured at Prince Haya Biotechnology Center; King Abdullah University Hospital. The genetic tests like Next-generation Sequencing (NGS) and Whole Exome Sequencing (WES) were applied outside of Jordan in cooperation with specialized private laboratories. IEM disorders that are mostly diagnosed at the metabolic clinic are classified into [1] Protein metabolic disorders including aminoacidopathies and organic acidemias. [2] Carbohydrate metabolic disorders with glycogen storage diseases are the most common. [3] Lipid metabolic disorders considering familial hyperlipidemias as a part of this category. [4] Mitochondrial and energy metabolic disorders. [5] Micro-organelles metabolic disorders with lysosomal storage diseases are the most common. [6] Other metabolic disorders which are less common like; Vitamins metabolic disorders and neuro-transmitters disorders.

RESULTS

A total of 429 patients were included in this study, 218 male and 211 female with male to female ratio of 1.03:1. The mean age of males was 5.57 ± 0.59 years old with a range from birth to 24 years. The mean age of females was 5.63 ± 0.53 years old with ages ranged from birth to 19.2 years old. The mean age of the total patients (429 patients) was 5.62±0.55 years old.

Table (1) summarizes the patients' primary clinics.242 (56.4%) of the patients were known to the metabolic clinic and came on a scheduled appointment. 127 (29.6%) males and 115(26.8%) females. The neurologic clinic had the most referrals with 76 (17.7%) patients. Military hospitals referred 9 (2%) patients, and governmental hospitals sent 21 (4.9%) patients to the metabolic clinic.

Parental consanguinity occurred in 333 (77.6%) of the patients' parents. First cousins were parents of 238 (55.5%) patients. Second cousins were parents of 39 (9.1%) patients. Far relatives; parents who are related farther from their grandparents; were parents of 49 (11.4 %) patients. Double cousins; cousins from both paternal and maternal sides; were parents of 7 (1.6%) patients. 96 (22.4%) patients were children of non-related parents. Figure (1) summarizes parental consanguinity and figure (2) summarizes the family history; the presence of affected family members or relatives and the presence of deaths due to the same condition.

Table (I): The patients' primary clinics:

Primary clinic	Gender	No. Of Patients	Total (percentage)
Metabolic clinic	Male	127	242 (56.4%)
	Female	115	
Neurodevelopmental Clinic	Male	37	76 (17.7%)
	Female	39	
Gastrointestinal Clinic	Male	3	10 (2.3%)
	Female	7	
Genetic Clinic	Male	3	9 (2.1%)
	Female	6	
Cardiac Clinic	Male	4	6 (1.4%)
	Female	2	
Neonatology Clinic	Male	7	10 (2.3%)
	Female	3	
Endocrinology Clinic	Male	4	6 (1.4%)
	Female	2	
Hematology Clinic	Male	1	3 (0.7%)
	Female	2	
General Pediatric Clinic	Male	2	7 (1.6%)
	Female	5	
Pediatric Orthopedic Clinic	Male	2	6 (1.4%)
	Female	4	
Pediatric Ophthalmic Clinic	Male	1	3 (0.7%)
	Female	2	
Other Clinics	Male	4	6 (1.4%)
	Female	2	
Military Hospitals	Male	4	9 (2%)
	Female	5	
Ministry Of Health Hospitals	Male	16	31 (7.2%)
	Female	15	
Other Hospitals	Male	2	4 (0.9%)
	Female	2	

Figure (1): Percentage consanguinity (related parents)

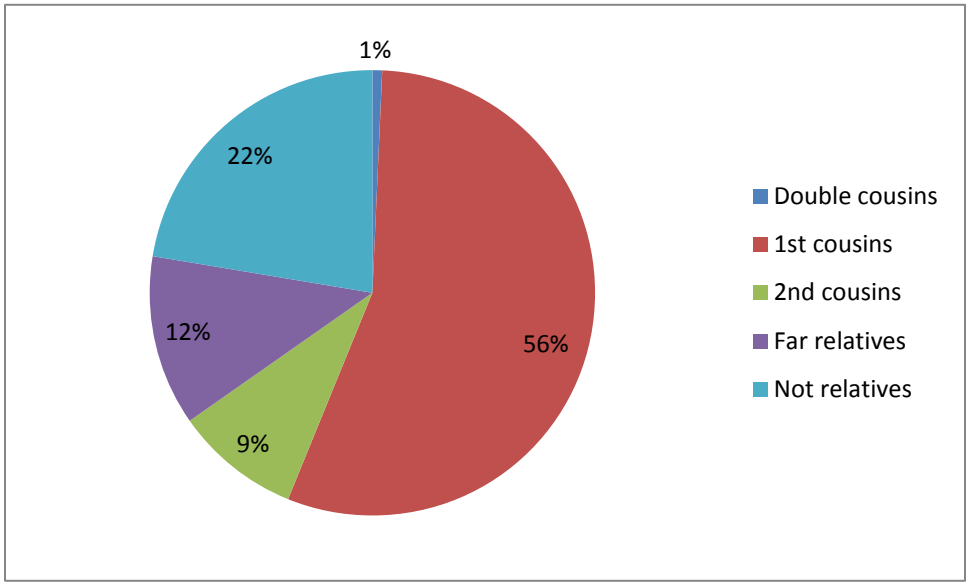
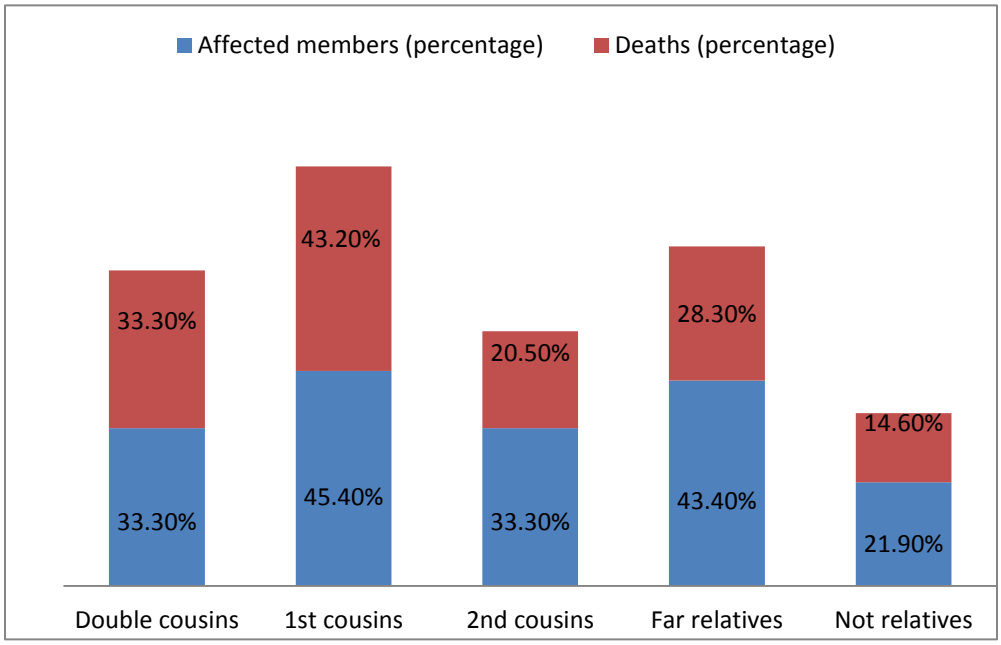


Figure (2): Affected family members and deaths by consanguinity (related parents)



Developmental delay and/or regression was the most common presenting symptom in the metabolic clinic. 103 (24%) male patients had a history of developmental delay and 80 (18.6%) patients had developmental regression. Female patients showed developmental delay in 85 (19.8%) patients and developmental regression in 66 (15.4%) patients. Table (2) summarizes the developmental history in the study patients.

Table (II): Developmental history in the patients:

	Developmental Delay		**Developmental Regression**	
Gender	***Male***	***Female***	***Male***	***Female***
No. of Patients	103 (24%)	85 (19.8%)	80 (18.6%)	66 (15.4%)
Total (Percentage)	188 (43.8 %)		146 (34%)	

A confirmed biochemical and/or genetic diagnosis was made in137 (31.9%) patients, while 89 (20.7%) patients had a clinical diagnosis. The rest of the patients; 203 (47.3%) have no diagnosis and are treated symptomatically at the metabolic clinic in cooperation with other relevant clinics. Table (3) summarizes whether patients have a confirmed or clinical diagnosis or not.

Table (III): Confirmed or clinical diagnosis or no diagnosis:

	Confirmed diagnosis		**Clinical diagnosis**		**No diagnosis**	
	Male	***Female***	***Male***	***Female***	***Male***	***Female***
No. of patients	71 (16.6%)	66 (15.4%)	43 (10%)	55 (12.8%)	99 (23.1%)	104 (24.2%)
Total	137 (31.9%)		98 (22.8%)		203 (47.3%)	

DISCUSSION

Inborn errors of metabolism (IEM) disorders are expressed at different ages and with a variety of phenotypes that make the parents search for medical treatment in multiple subspecialty clinics for their children's diagnosis (17). The clinical presentations of IEMs depend on several factors and the different types of disorders; because of this, there is a difference in the possibility and the timing of diagnosis, the availability of treatment options, the ability of a medical institution to provide care and the appropriate treatment intervention (18). Among the serious complications for patients diagnosed with IEM neurologic disability, mental retardation, difficulties in communication and learning, as well as death (19). Healthcare providers should be more aware of these disorders and manage them optimally until an early diagnosis is reached where possible. Good case management may prevent the deterioration of the patient's health and physical condition (20).

All IEM disorders are inherited and consanguinity is a major risk factor for new cases. Double cousins and first cousins have the greatest risk for offspring with metabolic disease and often have a positive history of other affected children and early deaths in their families. Newborn screening for some conditions may be the cornerstone for early diagnosis and management, which leads to prevention of deaths and permanent sequelae, especially when there is a family history of treatable disorders. Widening the newborn screening program can detect new cases earlier, even without a positive family history, leads to better management of patients (21).

Conclusion and Recommendations:

The metabolic clinic at Queen Rania Abdullah Children Hospital receives patients almost from all pediatric clinics and hospitals in Jordan. About 50% of the patients do not have a diagnosis and treated symptomatically. Awareness of IEM disorders between pediatricians is important and can lead to earlier diagnosis. The national newborn screening program needs to be expanded to include more early presenting and treatable disorders. Metabolic and genetic investigations are still challenging to be performed and/or analyzed by general physicians and pediatricians, hereafter, focusing on increasing genetic and metabolic teaching in universities and during the residential years may increase the awareness in the future physicians.

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