

Awareness of inborn errors of metabolism among general populations of Makkah city in Saudi Arabia.

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Abstract

Background: Inborn errors of metabolism (IEM) are single gene disorders resulting from the defects in the biochemical pathways of the body. According to the World Health Organization (WHO), prevalence of (IEM) globally is in the vicinity of 3-5%. Public awareness of IEM is critical for early diagnosis and effective management.

Objective: To assess the level of awareness about inborn errors of metabolism among the adult population in Makkah City, Saudi Arabia.

Methods: A cross-sectional survey was conducted using a self-administered online questionnaire distributed via convenience sampling to members of the general population (220 adults) in Makkah city. The questionnaire included 20 questions, comprised of both multiple-choice and dichotomous questions to evaluate the participants' general awareness and knowledge of inborn errors of metabolism. Data were analyzed using Statistical Package for the Social Sciences (SPSS).

Results: The study revealed major knowledge gaps. Only 32.3% knew enzymes regulate metabolism, while 43.2% didn't know. Regarding IEMs being hereditary, 33.6% said yes, but 41.4% were unsure. When asked if newborns can be affected, 33.6% said yes, while 44.1% were uncertain. On prevention, 31.8% said it's not possible, 25.5% believed it is, and 42.7% didn't know. These results highlight the urgent need for better public education on enzymes and genetic disorders.

Conclusion: The study highlights a significant deficiency in public awareness of inborn errors of metabolism (IEMs) in Makkah and emphasizes the need for accessible awareness initiatives and community-based interventions to enhance understanding and early detection.

Keywords: inborn errors of metabolism, IEM, knowledge, level of awareness, makkah, saudi arabia.

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Table of Contents

ABSTRACT	1374
ACKNOWLEDGEMENTS.....	1375
LIST OF TABLES.....	1377
LIST OF FIGURES.....	1378
LIST OF ABBREVIATIONS.....	1379
INTRODUCTION	1380
AIM OF THE STUDY:.....	1381
LITERATURE REVIEW	1382
MEDICAL HISTORY OF INBORN ERRORS OF METABOLISM:	1382
CLASSIFICATION OF INBORN ERRORS OF METABOLISM (IEMs):	1383
THE MOST COMMON DISEASES:	1383
METABOLIC DISEASES:	1393
ADVANCEMENTS IN NEWBORN SCREENING FOR METABOLIC DISORDERS:	1393
THE IMPORTANCE OF PARENTAL EDUCATION ON INBORN ERRORS OF METABOLISM (IEM):.....	1393
METABOLIC DISEASES AND THEIR RELATIONSHIP TO CONSANGUINEOUS MARRIAGE:.....	1394
DAMAGE CAUSED BY INBORN ERRORS OF METABOLISM (IEMs):.....	1394
METHODOLOGY	1394
RESULTS & DISCUSSION	1395
CONCLUSIONS.....	1419
RECOMMENDATIONS	1420
REFERENCES	1421
APPENDICES.....	1421
APPENDICES 1 (PUBLICATION).....	1426
APPENDICES 2 THE (10TH INTERNATIONAL SCIENTIFIC CONFERENCE)	1427
APPENDICES 3 (ENGLISH QUESTIONNAIRES)	1427
APPENDICES 4 (ARABIC QUESTIONNAIRES)	1431
APPENDICES 5 (STUDY LIMITATIONS)	1435

List of tables

Table (1) Do enzymes play a role in regulating metabolism in the body	1402
Table (2) There are hundreds of Inborn Errors of Metabolism (IEMs). Is the cause of these diseases generally a lack of enzymes that do not respond to the instructions they need to perform their function properly	1403
Table (3) Worldwide, Inborn Errors of Metabolism (IEMs) affect approximately 1 in every 2,500 births. How many people do you know who are affected by one of these inborn errors	1404
Table (4) Inborn Errors of Metabolism (IEMs) affect the body's ability to process one of the following from the food or drinks a person consumes, including	1405
Table (5) Can Inborn Errors of Metabolism (IEMs) be hereditary	1406
Table (6) Can Inborn Errors of Metabolism (IEMs) be related to consanguinity (marriage between relatives)	1407
Table (7) Each type of Inborn Error of Metabolism (IEMs) has a different genetic pattern, and therefore, symptoms vary from person to person	1408
Table (8) Can Inborn Errors of Metabolism (IEMs) be contagious	1409
Table (9) Are newborns affected by Inborn Errors of Metabolism (IEMs)	1410
Table (10) Is it important to diagnose Inborn Errors of Metabolism (IEMs) early after birth	1411
Table (11) Should you consult a doctor if someone in your family has one of the Inborn Errors of Metabolism (IEMs)	1412
Table (12) Inborn Errors of Metabolism (IEMs) can be diagnosed through the following screening tests	1413
Table (13) What treatment options are available for Inborn Errors of Metabolism (IEMs)	1414
Table (14) Can Inborn Errors of Metabolism (IEMs) be prevented	1415
Table (15) Adopting an organized lifestyle is one of the best solutions a person can adopt to cope with this disease. What questions would a patient likely ask	1416
Table (16) values of the correlation coefficients between the degree of each phrase and the degree of the questionnaire	1417
Table (17) values of the reliability coefficient of the questionnaire	1418

List of figures

Chart (1) shows (Do enzymes play a role in regulating metabolism in the body)	1402
Chart (2) shows (There are hundreds of Inborn Errors of Metabolism (IEMs). Is the cause of these diseases generally a lack of enzymes that do not respond to the instructions they need to perform their function properly)	1403
Chart (3) shows (Worldwide, Inborn Errors of Metabolism (IEMs) affect approximately 1 in every 2,500 births; How many people do you know who are affected by one of these inborn errors)	1404
Chart (4) shows (Inborn Errors of Metabolism (IEMs) affect the body's ability to process one of the following from the food or drinks a person consumes, including)	1405
Chart (5) shows (Can Inborn Errors of Metabolism (IEMs) be hereditary)	1406
Chart (6) shows (Can Inborn Errors of Metabolism (IEMs) be related to consanguinity (marriage between relatives))	1407
Chart (7) shows (Each type of Inborn Error of Metabolism (IEMs) has a different genetic pattern, and therefore, symptoms vary from person to person)	1408
Chart (8) shows (Can Inborn Errors of Metabolism (IEMs) be contagious)	1409
Chart (9) shows (Are newborns affected by Inborn Errors of Metabolism (IEMs))	1410
Chart (10) shows (Is it important to diagnose Inborn Errors of Metabolism (IEMs) early after birth)	1411
Chart (11) shows (Should you consult a doctor if someone in your family has one of the Inborn Errors of Metabolism (IEMs))	1412
Chart (12) shows (Inborn Errors of Metabolism (IEMs) can be diagnosed through the following screening tests)	1413
Chart (13) shows (What treatment options are available for Inborn Errors of Metabolism (IEMs))	1414
Chart (14) shows (Can Inborn Errors of Metabolism (IEMs) be prevented)	1415
Chart (15) shows (Adopting an organized lifestyle is one of the best solutions a person can adopt to cope with this disease. What questions would a patient likely ask)	1417

List of abbreviations

Medical Terminology	Abbreviations
Arginase Deficiency	ARG
Argininosuccinic Lyase Deficiency	ASL
Argininosuccinate Synthase 1 Deficiency	ASS1
Carbamoyl Phosphate Synthetase I Deficiency	CPS1
Hyperphenylalaninemia	HPA
Inborn Errors of Metabolism	IEM
Kearns-Sayre Syndrome	KSS
Low-Density Lipoprotein	LDL
Leber Hereditary Optic Neuropathy	LHON
Lysosomal Storage Diseases	LSDs
Myoclonic Epilepsy and Ragged-Red Fiber Disease	MERRF
Multiplex Ligation-Dependent Probe Amplification	MLPA
N-Acetylglutamate Synthase Deficiency	NAGS
Niemann-Pick Disease	NP
Ornithine Transcarbamylase Deficiency	OTC
Phenylalanine Hydroxylase	PAH
Phenylketonuria	PKU
Organization	Abbreviations
World Health Organization	WHO

Introduction

Inborn errors of metabolism (IEMs) are a large class of genetic disorders resulting from a defect in functioning of an intermediate metabolic pathway. (Phipps *et al.*,2019) Although individual IEMs are rare, they are common collectively and have a global prevalence of 50.9 per 100,000 live births. (Waters *et al.*,2018)

IEMs can result in severe symptoms, including seizures, organ failure, hypoglycemia, disabilities, and even death. This makes IEMs a major public health problem that requires attention and intervention. (Burton, B. K., 1998) The awareness should be a primary priority for the pediatric public health system. This can be achieved through the establishment of programs and the use of other media, such as social media. Based on many studies that evaluated the clinical symptoms and risk factors associated with some cases with the aim of raising awareness and establishing preventive programs for the community.

Inborn errors of metabolism also constitute an important health issue in pediatrics in the Kingdom of Saudi Arabia, but no studies have been conducted to assess the level of public awareness on this topic. The reason this issue was selected is because it is a major public health issue. Therefore, this research aims to address these concerns.

According to a previous research, "Awareness of Inborn Errors of Metabolism among Parents in Saudi Arabia," published in 1997, discovered that while parents were given a brief education about their children's illnesses in clinics and departments, the majority of them remained uninformed about various aspects of their conditions. (Al Essa *et al.*,1997) A survey questionnaire was distributed to parents who brought their kids to IEM clinics randomly. The findings showed that most parents, with the exception of those with advanced degrees, were ignorant of the significance of issues related to metabolic disorders in their kids. Then, in 2022, a new study on the awareness of ethical metabolic errors among male and female students at King Abdulaziz University was conducted. (Al qrahe *et al.*,2020) The study's findings suggested that more should be done to increase knowledge and raise awareness among medical and non-medical students in the Kingdom of Saudi Arabia by expanding the amount of widely shared materials on social media.

It is crucial to assess the public's level of knowledge and attitudes through studies, as this information will help determine if Interventions and public education are needed to address any knowledge deficits and misperceptions that may exist.

Study Problem:

Based on the high prevalence of genetic disorders faced by the Kingdom of Saudi Arabia, especially in inborn errors in metabolism, In appreciation of the Kingdom's challenges and efforts in this field The following questions have arisen:

- 1/ How aware are the residents of the Holy City of Makkah about inborn errors of metabolism?
- 2/ Is there a need for awareness programs for the residents of Makkah about the causes of inborn errors in metabolism?
- 3 / What is the impact of a cross-sectional study on educating the residents of Makkah to deal with inborn errors in metabolism at the present time?
- 4/ What is the impact of awareness programs with inborn errors on metabolism in the future?

Importance: The study aims to assess the level of population in the city of Makkah, with inborn errors in metabolism, and determine the extent to which they need an awareness program on this problem to deal with it.

Aim of the study:

- 1/ Assess the level of knowledge and attitudes of the public regarding inborn errors of metabolism.
- 2/ Determine whether interventions are needed to raise awareness of these diseases.

Research hypotheses:

- 1/ There is a significant need for health programs in the city of Makkah to raise awareness about IEM's
- 2/ There is a relationship between the type of awareness programs and inborn errors in the metabolic process.
- 3/ The selection of a cross-sectional study is based on its simplicity, speed, and the ability to quickly intervene in raising awareness among the population.
- 4/ There is an impact of the quality of targeted programs on Inborn Errors of Metabolism (IEM) in raising awareness among the population of Makkah.

Research procedures:

- A Cross Sectional Study Because it's quick and easy to conduct more representative of the general population.
- Questionnaire: a list of questions or items used to gather data from respondents about their attitudes, experiences, or opinions.

Terminology:

- Metabolism: Metabolism refers to the whole sum of reactions that occur throughout the body within each cell and that provide the body with energy.(Sánchez López de Nava, Raja, 2022)
- Inborn errors of metabolism: Inborn errors of metabolism (IEMs) are a group of disorders each of which results from deficient activity of a single enzyme in a metabolic pathway.(El-Hattab, 2015)
- Hypoglycemia: A condition in which the blood sugar (glucose) level is lower than normal.(Mayo Clinic, 2023)
- Genetic disorder: A genetic disorder is a disease caused in whole or in part by a change in the DNA sequence away from the normal sequence.(National Human Genome Research Institute, 2018)

Literature Review

1. Medical history of inborn errors of metabolism:

The term "inborn error of metabolism" was first introduced in 1908 by Sir Archibald Garrod to describe four specific disorders: alkaptonuria, pentosuria, cystinuria, and albinism. The foundational textbook on this subject, *The Metabolic Basis of Inherited Disease*, was first published in 1960, covering 80 disorders across 1,477 pages. Over time, as the field expanded, the book grew significantly, reaching 6,338 pages across four volumes in its eighth edition, encompassing over 1,000 disorders. Due to its extensive content, it was later transitioned into an online reference text, now featuring 259 chapters and continuing to expand. (Arnold G. L., 2018).

2. Classification of Inborn errors of metabolism (IEMs):

Metabolic diseases exhibit a wide range of symptoms, but they can be classified into three diagnostically useful groups:

- Group 1: Disorders of intermediary metabolism, which affect small molecules.
- Group 2: Disorders primarily related to energy metabolism.
- Group 3: Disorders involving complex molecules.(Saudubray & Cazorla, 2018)

3. The most common diseases:

3.1. Diabetes Mellitus:

Diabetes mellitus is the most prevalent metabolic disorder, affecting approximately 500 million people worldwide, according to estimates by the World Health Organization (WHO). Additionally, diabetes-related complications contribute to 1.5 million deaths annually. This condition is characterized by an impaired ability to regulate blood glucose levels due to either a deficiency or complete absence of insulin, a hormone produced by the pancreas. There are several types of diabetes, including:

3.1.1. Types of Diabetes mellitus:

Type 1 diabetes: This is an autoimmune disorder in which the immune system attacks the insulin-producing cells in the pancreas, causing irreversible damage and reducing insulin production. Individuals with type 1 diabetes must take daily insulin injections to regulate their blood sugar levels. (Cleveland Clinic, 2023)

Type 2 diabetes: This form of diabetes results from insulin resistance at the cellular level, leading to elevated blood glucose levels. It can develop at any age and is often linked to lifestyle factors such as poor diet, obesity, and physical inactivity. (Cleveland Clinic, 2023)

Gestational diabetes: This type occurs during pregnancy and typically resolves after childbirth. However, it increases the likelihood of developing type 2 diabetes later in life. (Cleveland Clinic, 2023)

3.2. Mitochondrial Disorders:

Mitochondria, often called the “powerhouse of the cell,” play a crucial role in processing oxygen and converting nutrients into energy. They are present in nearly every cell in the human body and generate approximately 90% of the energy needed for normal bodily functions. When cells do not receive sufficient energy, vital organs such as the heart and liver may not function properly. (Cleveland Clinic, 2023) Mitochondrial disease occurs when the mitochondria fail to produce enough energy, leading to inefficiencies or complete dysfunction in affected cells. The symptoms vary based on the number and location of affected cells, with high-energy-demanding organs such as the brain, muscles, liver, heart, and kidneys being the most impacted. In many cases, mitochondrial disorders worsen over time, potentially causing severe complications.

3.2.1. Symptoms of Mitochondrial Disease:

The symptoms of mitochondrial disease vary depending on the type and location of the affected cells. They can range from mild to severe and may include:

- Growth issues: Delayed development or difficulty gaining weight and growing properly.
- Muscle-related symptoms: Weakness, muscle pain, or low muscle tone.
- Neurological problems: Seizures, migraines, fainting episodes, and developmental delays.
- Gastrointestinal issues: Symptoms such as diarrhea, constipation, acid reflux, and difficulty swallowing.
- Respiratory complications: Breathing difficulties, including apnea.
- Sensory impairments: Vision and/or hearing loss.
- Metabolic disturbances: Lactic acidosis, which may lead to nausea, vomiting, fatigue, rapid breathing, and muscle cramps.

3.2.2. Inheritance Patterns of Mitochondrial Disease:

Mitochondrial diseases are genetic and can be inherited in various ways:

- Maternal inheritance: When the mutation is located in mitochondrial DNA (mtDNA), it is passed down from the mother.
- Nuclear inheritance: If the mutation occurs in nuclear DNA (nDNA), it may be inherited from either parent or both.
- Spontaneous mutations: In some cases, mitochondrial disease arises due to new genetic mutations without any prior family history.

3.2.3. Current Approaches to Treatment:

At present, there is no definitive cure for mitochondrial disease. Treatment is mainly supportive and aims to manage symptoms. For example, seizures can be controlled with medication. Additionally, healthcare providers may try to improve cellular energy production using co-factors and vitamins such as Ubiquinone (Coenzyme Q10), Thiamine, and Riboflavin (NHS, 2017).

3.2.4. Secondary Causes of Mitochondrial Dysfunction:

Mitochondrial dysfunction can also develop as a secondary result of several medical conditions, including:

- Alzheimer's disease
- Muscular dystrophy
- Type 1 diabetes
- Multiple sclerosis
- Cancer (Cleveland Clinic, 2023)

3.2.5. Common types of Mitochondrial Diseases:

There are several types of mitochondrial diseases, with some of the most common being:

- Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome.
- Leber hereditary optic neuropathy (LHON).
- Leigh syndrome.
- Kearns-Sayre syndrome (KSS).
- Myoclonic epilepsy and ragged-red fiber disease (MERRF). (Cleveland Clinic, 2023)

3.3. Phenylketonuria:

Phenylketonuria (PKU) is an autosomal recessive inborn error disorder resulting from a defect in the metabolism of the amino acid phenylalanine (Phe) due to a deficiency of the enzyme phenylalanine hydroxylase (PAH). Most cases of PKU and hyperphenylalaninemia (HPA) are caused by mutations in the PAH gene located on chromosome 12q23.2. If untreated, PKU can cause symptoms including delayed growth, hypopigmentation of the skin, microcephaly, seizures, delayed general development, and severe mental decline. However, since the introduction of early newborn screening programs and a strict diet, it has become possible for those affected to lead relatively normal lives. Advances in understanding the biochemistry, genetics, and molecular basis of this disorder have

led to the development of new treatment strategies to improve patients' quality of life. (Williams *et al.*,2008)

3.3.1. Symptoms of phenylketonuria (PKU):

- Developmental delay.
- Microcephaly.
- Epileptic seizures.
- Cognitive impairment due to the accumulation of toxic metabolites of phenylalanine.
- Tyrosine deficiency and consequent deficiency of:
 - Melanin, resulting in lighter skin, hair, and eyes.
 - L-thyroxine, affecting thyroid function.
 - Catecholamine neurotransmitters, affecting brain function. (Williams *et al.*,2008)

3.3.2. Diagnosis of phenylketonuria (PKU):

Conventional diagnosis of PKU relies on analyzing the patient's abnormal metabolic pattern. Genetic mutations and polymorphisms associated with the PAH gene can also be analyzed to identify carriers and perform prenatal diagnosis. Various molecular techniques are used to detect mutations, such as Southern blotting, restriction enzyme digestion, DNA sequencing, and multiplex ligation-dependent probe amplification (MLPA). (Williams *et al.*,2008)

3.4. Wilson's Disease

Wilson's disease is a rare hereditary metabolic disorder that leads to excessive copper accumulation in the liver, brain, and other essential organs. It is most commonly diagnosed between the ages of 5 and 35. Copper is vital for nerve development, bone growth, collagen formation, and melanin production in the skin. Under normal conditions, the body absorbs copper from food and eliminates excess amounts through bile secretion in the liver. However, individuals with Wilson's disease are unable to properly excrete copper, causing toxic accumulation that can become life-threatening without treatment. Early detection and appropriate management enable patients to live a normal life. (Mayo Clinic, 2023)

3.4.1. Symptoms of wilson's disease:

Wilson's disease is present from birth but remains asymptomatic until copper builds up in vital organs, particularly the brain, liver, or eyes. Symptoms vary depending on the affected organ and may include:

- General symptoms: Fatigue, loss of appetite, and jaundice (yellowing of the skin and eyes).
- Hepatic symptoms: Fluid accumulation in the legs or abdomen (ascites).
- Neurological symptoms: Difficulties with speech, swallowing, and coordination, as well as tremors, involuntary movements, and muscle stiffness.
- Psychiatric symptoms: Depression, mood swings, personality changes, sleep disturbances, and insomnia.
- Ophthalmologic symptoms: Presence of Kayser-Fleischer rings (golden-brown or copper-colored rings around the cornea). (Mayo Clinic, 2023)

3.4.2. Causes of wilson's disease:

Wilson's disease results from mutations in the ATP7B gene, which is responsible for regulating copper levels in the body. It follows an autosomal recessive inheritance pattern, meaning that a person must inherit two defective copies of the gene one from each parent to develop the disorder. Individuals with only one mutated copy are carriers and do not show symptoms but can pass the gene to their children. (Mayo Clinic, 2023)

3.4.3. Complications of wilson's disease:

If untreated, Wilson's disease can lead to severe complications, including:

- Liver cirrhosis: Damage to liver cells leads to scar tissue formation, impairing liver function.
- Liver failure: Can occur suddenly (acute liver failure) or develop over time, sometimes necessitating a liver transplant.
- Permanent neurological damage: While some motor symptoms improve with treatment, conditions such as tremors and speech difficulties may persist in certain patients.
- Kidney problems: Including kidney stone formation and abnormal amino acid excretion in urine.
- Mental health disorders: Personality changes, depression, bipolar disorder, and psychosis.
- Blood disorders: Copper toxicity may cause hemolysis (destruction of red blood cells), leading to anemia and jaundice. (Mayo Clinic, 2023)

3.5. Familial hypercholesterolemia

A hereditary metabolic disorder characterized by elevated blood cholesterol levels, particularly low-density lipoprotein (LDL) cholesterol. LDL is referred to as bad cholesterol because it accumulates in the artery walls, causing them to harden and narrow, which can lead to heart disease.(Mayo Clinic, 2023)

The Achilles tendon may thicken as a result of cholesterol buildup in certain tendons in the hands, as well as in areas of the epidermis. A corneal arcus, a white or gray ring surrounding the eye's iris, can develop as a result of elevated blood cholesterol levels.(Mayo Clinic, 2023)

3.5.1. Causes of Familial hypercholesterolemia:

Familial hypercholesterolemia is an inherited condition resulting from genetic mutations passed down from one or both parents. These mutations impair the body's ability to eliminate low-density lipoprotein (LDL) cholesterol, leading to its accumulation in the arteries and increasing the risk of heart disease.(Mayo Clinic, 2023)

3.5.2. Symptoms of Familial hypercholesterolemia:

High cholesterol typically presents no symptoms; the sole method of detection is through a blood test. (Mayo Clinic, 2023)

3.5.3. Risk factors of Familial hypercholesterolemia:

Factors that may increase your risk of unhealthy cholesterol include:

- **Poor diet:** Consuming excessive amounts of saturated or trans fat can elevate your cholesterol to unhealthy levels. Saturated fat is present in fatty cuts of meat and whole-fat dairy products. Trans fat is frequently located in packaged snacks or desserts.
- **Obesity:** If your body mass index is 30 or above, you're at risk for elevated cholesterol levels.
- **Smoking:** Smoking cigarettes may decrease your HDL.
- **Age:** Even small children can exhibit unhealthy cholesterol levels, but this issue is more frequently seen in individuals over the age of 40. As you grow older, your liver becomes less efficient at eliminating low-density lipoprotein (LDL) cholesterol.(Mayo Clinic, 2023)

3.6. Hereditary hemochromatosis

Hereditary hemochromatosis is an autosomal recessive genetic disorder that affects the body's ability to regulate iron levels. It is the most common inherited disease among white populations. Men are 24 times more likely than women to develop iron overload-related complications. Around 85–90% of individuals with clinical symptoms of hereditary hemochromatosis have two copies of the C282Y mutation in the HFE gene. However, only about 10% of those who are homozygous for this mutation experience significant organ damage or clinical symptoms. (Witte *et al.*,1996)

3.6.1. Symptoms of Hereditary hemochromatosis:

Early symptoms of hereditary hemochromatosis are often nonspecific or absent but may include:

- Weakness.
- Fatigue.
- Joint pain. (Witte *et al.*,1996)

As the disease progresses, more severe complications may develop, including:

- Joint pain.
- Osteoporosis.
- Cirrhosis.
- Liver cancer (hepatocellular carcinoma).
- Heart disease (cardiomyopathy, arrhythmias).
- Diabetes mellitus.
- Hormonal imbalances (hypogonadism). (Witte *et al.*,1996)

3.6.2. Diagnosis:

Diagnosis is confirmed by detecting elevated serum ferritin levels and increased transferrin saturation, regardless of whether symptoms are present. Genetic testing is used to classify the condition based on specific mutations. Serum ferritin levels are the most reliable indicator of disease severity. In cases where ferritin levels are significantly high or liver enzymes are abnormal, liver biopsy may be performed to assess fibrosis or confirm nonclassical hereditary hemochromatosis in patients with different genetic variations. (Witte *et al.*,1996)

3.7. Lysosomal storage diseases

Lysosomal storage diseases (LSDs) are a group of rare genetic disorders caused by the accumulation of toxic substances in the body's cells. These conditions occur due to a deficiency of

specific enzymes or the absence of substances that help enzymes function properly (enzyme activators or modifiers). Without these essential enzymes, the body is unable to break down fats, sugars, and other materials, leading to harmful buildup. (Cleveland Clinic, 2022) LSDs are classified as inborn errors of metabolism, where defective lysosomal function leads to excessive accumulation of substrates in various organs. This buildup results in organ dysfunction and contributes to significant morbidity and mortality. Although each LSD is rare individually, their collective prevalence is substantial. (Rajkumar & Dumpa, 2023) These diseases typically manifest during pregnancy or shortly after birth. In some cases, LSDs may develop in adulthood, with early-onset cases generally being more severe, while later-onset cases tend to be milder. (Cleveland Clinic, 2022)

3.7.1. Treatments of Lysosomal storage diseases:

Currently, there is no cure for lysosomal storage diseases, but available treatments can help manage symptoms and minimize organ and tissue damage (Cleveland Clinic, 2022).

3.7.2. Role of enzymes in Lysosomal function:

Enzymes play a crucial role in lysosomal metabolism by facilitating chemical reactions that break down:

- Carbohydrates (fiber, starches, and sugars).
- Lipids (fats).
- Proteins.
- Older or damaged cells (Cleveland Clinic, 2022)

Without these enzymes, substances accumulate within the cells, becoming toxic and leading to damage in multiple organs and systems, including:

- Brain.
- Central nervous system.
- Heart.
- Skeletal system.
- Skin. (Cleveland Clinic. 2022)

3.7.3. Types of Lysosomal storage diseases:

Researchers have identified more than 50 different lysosomal storage diseases, and the number

continues to grow. These disorders are generally classified into three main types based on the specific enzyme deficiency. (Cleveland Clinic, 2022)

3.8. Lipidoses:

Lipidoses occur when the body is missing an enzyme needed to break down fats. Examples of conditions in this category include:

- Cholesteryl ester storage disease.
- Wolman disease. (Cleveland Clinic, 2022)

3.9. Mucopolysaccharidoses:

Mucopolysaccharidoses occur when the body lacks an enzyme needed to break down complex sugar molecules (glycosaminoglycans). Examples of these conditions include:

- Hunter syndrome.
- Hurler's disease.(Cleveland Clinic, 2022)

3.10. Sphingolipidoses:

Sphingolipidoses occur due to a deficiency of an enzyme needed to break down sphingolipids, which are fatty substances that help protect cell surfaces and perform other important functions.

Conditions in this category include:

- Fabry disease.
- Gaucher disease.
- Krabbe disease (globoid cell leukodystrophy).
- Metachromatic leukodystrophy.
- Niemann-Pick disease (NP).
- Sandhoff disease.
- Tay-Sachs disease.(Cleveland Clinic, 2022)

3.11. Urea cycle disorders:

Urea cycle disorders are a group of genetic conditions that affect the function of proteins and enzymes responsible for removing ammonia from the blood. Since ammonia is toxic, its buildup can lead to severe, life-threatening complications. Managing protein intake through diet and using medications or supplements can help treat this condition. (Cleveland Clinic, 2022) The urea cycle is

the body's natural process for filtering out harmful toxins while maintaining essential substances. (Cleveland Clinic, 2022)

3.11.1. Types of Urea cycle disorders:

There are eight recognized types of urea cycle disorders, each resulting from a deficiency or malfunction of a specific enzyme or protein involved in the urea metabolism process. These include:

- N-acetylglutamate synthase (NAGS) deficiency
- Carbamoylphosphate synthetase I (CPS1) deficiency.
- Ornithine transcarbamylase (OTC) deficiency.
- Argininosuccinate synthase 1 (ASS1) deficiency, also known as Citrullinemia type I.
- Citrin deficiency, also referred to as Citrullinemia type II.
- Argininosuccinic lyase (ASL) deficiency.
- Arginase (ARG) deficiency.
- Ornithine translocase deficiency. (Cleveland Clinic, 2022)

3.11.2. Signs and symptoms of urea cycle disorders:

Symptoms often appear shortly after birth but can develop at any age. Early signs include:

- Lethargy or fatigue.
- Irritability in infants.
- Nausea or vomiting.
- Difficulty feeding. Abnormal breathing rate (too fast or too slow).
- Confusion (Cleveland Clinic, 2022)

Since urea cycle disorders cause excessive ammonia buildup in the blood (hyperammonemia), symptoms can vary in severity and may include:

- Problems with cognitive development and intellectual challenges.
- Cognitive and intellectual impairments.
- Behavioral changes.
- Developmental delays.
- Fluid buildup around the brain (cerebral edema).
- Muscle stiffness (spasticity).

- Seizures.
- Coma

Severe cases, especially those affecting brain function, can be life-threatening (Cleveland Clinic, 2022).

4. Metabolic diseases:

Metabolic diseases are a type of hereditary disorder caused by recessive genes, meaning that both parents must be carriers of the genetic trait for the disease to be passed on. In each pregnancy, there is a 25% chance that the child will inherit the disease, which equates to one affected newborn for every three unaffected ones. There are currently more than 400 known metabolic diseases, all of which result from a deficiency in specific enzymes from birth. These enzymes play a crucial role in the body by facilitating the conversion of food substances into other essential compounds across different tissues and organs. (Ministry of Health, 2024).

5. Advancements in newborn screening for metabolic disorders:

The introduction of tandem mass spectrometry (MS/MS) has significantly enhanced newborn screening (NBS), making it a mandatory public health measure in most developed and developing countries. This advanced technology enables the cost-effective detection of over 30 metabolic disorders using a single blood spot sample, with an estimated cost of around USD 10 per baby. Additionally, it offers high analytical accuracy and precision, with sensitivity reaching 99% and specificity up to 99.995%. (Mak *et al.*, 2013).

6. The importance of parental education on inborn errors of metabolism (IEM):

A recent study involving 500 parents revealed significant gaps in awareness regarding inborn errors of metabolism (IEMs), particularly among those with lower educational levels. Many parents are unfamiliar with the causes, symptoms, inheritance patterns, and treatments of these disorders, while those with higher education levels demonstrated slightly better awareness. This highlights the urgent need for comprehensive public health education programs to enhance knowledge and promote early referrals, especially for high-risk families with a history of metabolic diseases or unexplained infant deaths. (El-Hattab, 2015) For families with a previously diagnosed child, preventive measures can help reduce risks in future pregnancies. These include:

- Comprehensive prenatal counseling on the likelihood of having another affected child.
- Intrauterine diagnosis using advanced techniques, such as detecting abnormal metabolites in amniotic fluid.
- Delivering in specialized medical facilities equipped to manage metabolic disorders. (Al Essa *et al.*,1997)

7. Metabolic diseases and their relationship to consanguineous marriage:

Consanguineous marriage, particularly between first cousins, is a major risk factor for birth defects and inborn errors of metabolism (IEMs). A high degree of inbreeding can increase the likelihood of inheriting recessive genetic disorders, thereby exacerbating underlying genetic risk factors. (Al Bu Ali *et al.*, 2011) In countries where consanguineous marriages are common, the link between close-relative marriages and the prevalence of IEMs is particularly significant, emphasizing the need for genetic counseling and awareness programs to mitigate these risks. (Stein *et al.*,2017)

8. Damage caused by inborn errors of metabolism (IEMs):

During the neonatal period, inherited metabolic disorders can lead to severe liver dysfunction, manifesting as jaundice, coagulopathy, hepatosplenomegaly, and ascites. Given the liver's critical role in synthesis, metabolism, and excretion, IEM-related hepatic dysfunction is considered life-threatening. (Jeanmonod *et al.*,2023) Additionally, diabetes is one of the most common endocrine disorders in children, and while the exact link between IEMs and diabetes remains unclear, researchers propose three possible mechanisms:

- Toxic substance accumulation in the gland, damaging its structure and function.
- Disruption of energy availability, impairing hormone synthesis.
- Defects in complex molecules, affecting glandular function. (Alfadhel & Babiker, 2018).

Methodology

1. Study Design: a cross-sectional study will be used.
2. Study Area-setting: The study will be conducted in Saudi Arabia (in Makkah).
3. Study population: Adults in Makkah.
4. Sample size: According to the latest officially announced census, the number of people in Makkah between the ages of 20 and over 60 was 5388168 . By using the (Raosoft) sample size calculator,

with a margin of error of 5% and a confidence level of 95%, A total of 220 responses were collected. however, the target sample size of 385 could not be attained.

5. Sampling technique: The sample will be processed using a convenience technique.

6. Data collection tool: Data were collected using a structured, self-administered online questionnaire. The questionnaire included both multiple-choice and multiple-response questions and consisted of 20 questions divided into three sections. The first section included demographic information with five questions: age, area of residence, gender, marital status, and educational level. The second section consisted of 11 questions that measured participants' awareness of the topic. The third section consisted of 3 questions related to diagnosis, treatment, and coping the questions were translated into Arabic, and the estimated time to complete the questionnaire was 4 to 6 minutes. The validity and reliability of the questionnaire were assessed prior to data collection. Content validity was established by presenting the questionnaire to a panel of experts who evaluated the items for clarity, relevance, and comprehensiveness. Construct validity was examined by calculating the Pearson correlation coefficient between each item and the total questionnaire score to assess internal consistency. Reliability was evaluated using both Cronbach's alpha and the split-half method. The questionnaire demonstrated acceptable internal consistency. The questionnaire was generated using Google Forms and was distributed online through social media platforms, considering their widespread usage in the country. The following inclusion criteria were applied: participants had to be aged 20 years or older, reside in Makkah City, and provide voluntary consent.

7. Data entry and analysis: The data collected will be entered and analyzed using the Statistical Package for the Social Sciences (SPSS) descriptive statistics (frequencies, percentages, means, SD) were used to summarize participant characteristics and awareness levels.

Results & Discussion

These results indicate a clear deficiency in the level of awareness regarding inborn errors of metabolism among the residents of Makkah. The findings of the study revealed that 43.2% of participants were unaware of the significant role enzymes play in regulating metabolism. additionally, 24.5% of the participants responded that enzymes do not play a role in metabolic regulation, suggesting a gap in knowledge about how metabolic processes function in the body. while 41.4% were not aware of the genetic nature of these diseases, 25% of participants responded that Inborn Errors of Metabolism (IEMs) cannot be hereditary, indicating a lack of understanding about the

genetic transmission of these disorders. Based on these findings, the first hypothesis stating that “there is an urgent need for health programs in Makkah to raise awareness about inborn errors of metabolism” is confirmed. This highlights the necessity of developing effective awareness programs to enhance public knowledge about these diseases.

Table (1) Do enzymes play a role in regulating metabolism in the body

Do enzymes play a role in regulating metabolism in the body	Number	Percentage
Yes	71	32.3%
No	54	24.5%
I don't know	95	43.2%
Sum	220	100%

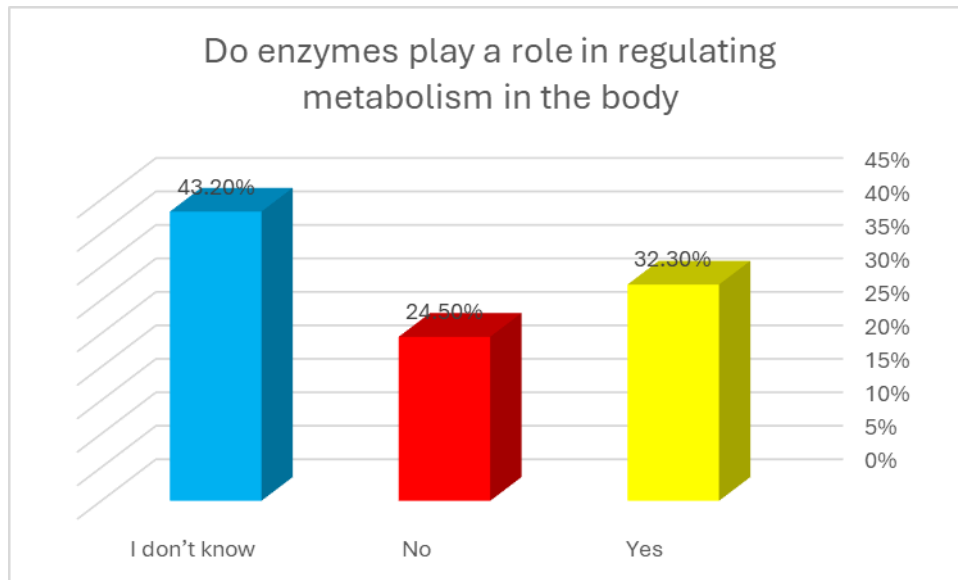


Chart (1) shows (Do enzymes play a role in regulating metabolism in the body)

Table (5) Can Inborn Errors of Metabolism (IEMs) be hereditary

Can Inborn Errors of Metabolism (IEMs) be hereditary	Number	Percentage
Yes	74	33.6%
No	55	25%
I don't know	91	41.4%
Sum	220	100%

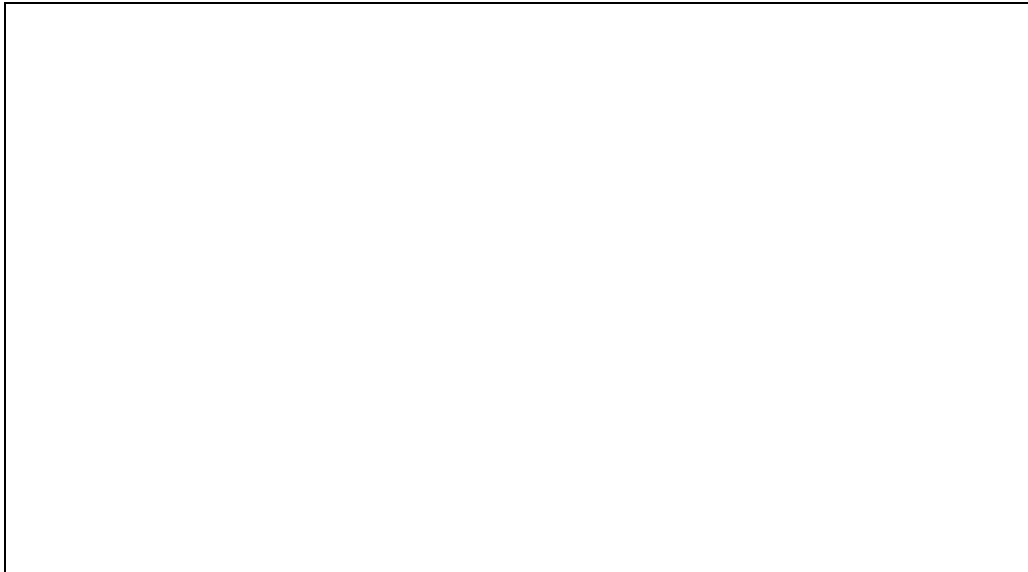


Chart (5) shows (Can Inborn Errors of Metabolism (IEMs) be hereditary)

These findings reveal variations in participants' knowledge of inborn errors of metabolism, underscoring the significance of awareness programs in correcting misconceptions and enhancing public understanding among Makkah residents. 42.7% of participants were uncertain about the possibility of preventing these diseases. Moreover, 53.2% of participants emphasized the importance of consulting a doctor if a family member is affected by these conditions, highlighting the role of awareness programs in guiding individuals toward making appropriate health decisions. Based on these data, it is evident that there is a correlation between the type of awareness programs and individuals' knowledge of inborn errors of metabolism. The more comprehensive and interactive these programs are, the higher the level of awareness among participants, which supports the validity of the second hypothesis. On the other hand, 26.4% of participants responded that it is not necessary to consult a doctor in such cases, which reflects a gap in understanding the importance of early medical intervention in managing genetic metabolic disorders.

Table (11) Should you consult a doctor if someone in your family has one of the Inborn Errors of Metabolism (IEMs)

Should you consult a doctor if someone in your family has one of the Inborn Errors of Metabolism (IEMs)	Number	Percentage
Yes	117	53.2%
No	58	26.4%
I don't know	45	20.4%
Sum	220	100%

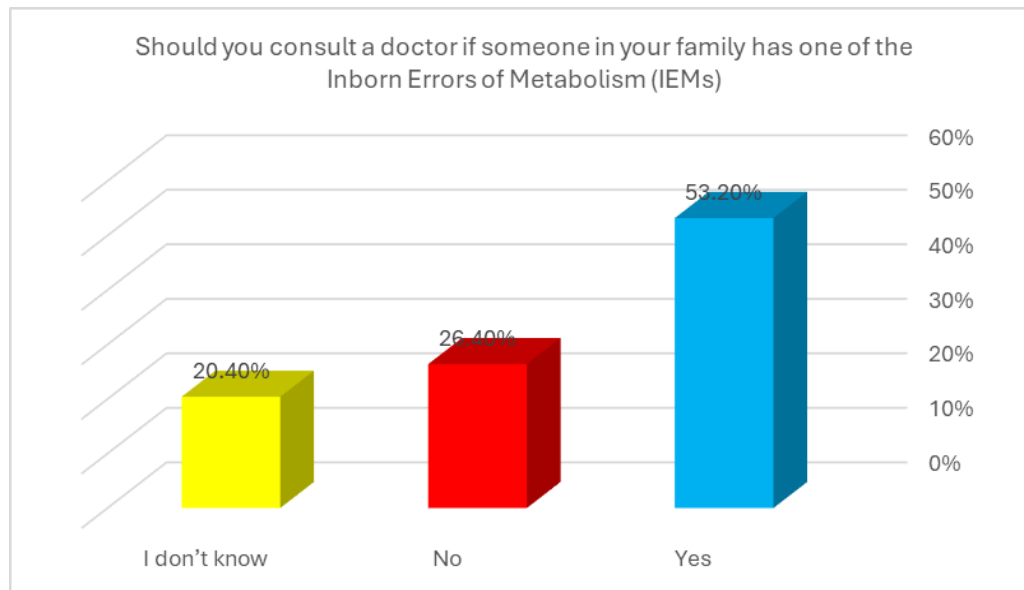


Chart (11) shows (Should you consult a doctor if someone in your family has one of the Inborn Errors of Metabolism (IEMs))

Table (14) Can Inborn Errors of Metabolism (IEMs) be prevented

Can Inborn Errors of Metabolism (IEMs) be prevented	Number	Percentage
Inborn Errors of Metabolism (IEMs) cannot be prevented because they result from genetic changes	70	31.8%
Yes, they can be prevented	56	25.5%
I don't know	94	42.7%
Sum	220	100%

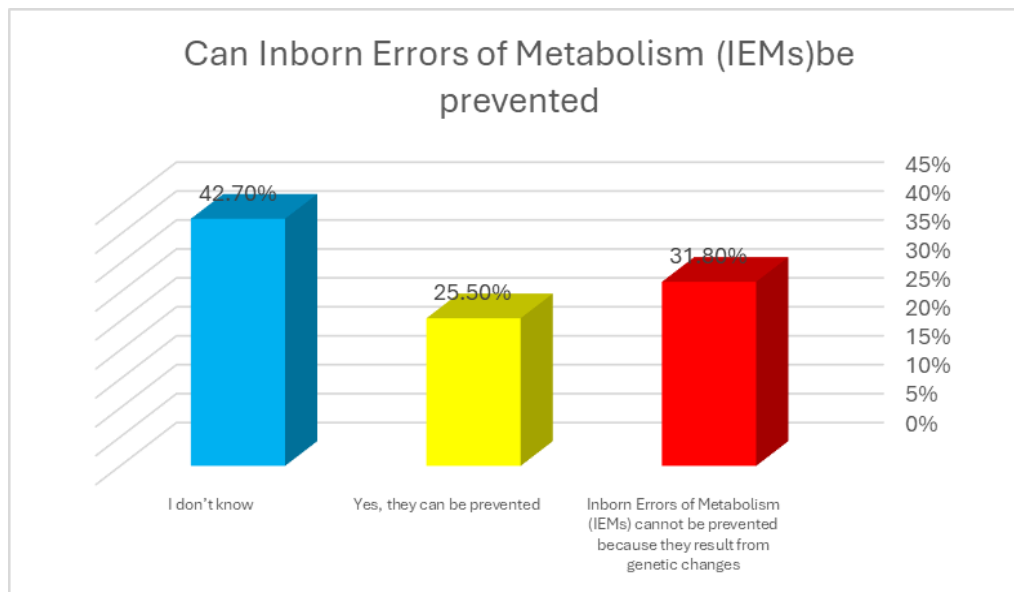


Chart (14) shows (Can Inborn Errors of Metabolism (IEMs) be prevented)

Based on the findings, it is evident that cross-sectional studies serve as an effective method for assessing public health awareness within a short timeframe. These studies provide precise data on the groups most in need of awareness, thereby enhancing the speed of response and enabling more efficient and targeted health program planning. The selection of a cross-sectional study design facilitates a rapid intervention to raise awareness among the population. The study results showed that adopting a cross-sectional approach contributed to the quick assessment of participants' awareness levels. The data revealed a significant lack of knowledge regarding inborn errors of metabolism (IEMs). This indicates that the cross-sectional study was an effective tool for identifying knowledge gaps in a short time, allowing for immediate intervention through targeted awareness programs.

These findings indicate that the effectiveness of awareness programs plays a fundamental role in increasing knowledge about inborn errors of metabolism. The more comprehensive these programs are incorporating accurate information and modern interactive methods the better their ability to correct misconceptions and enhance individuals' awareness. The results showed that 46.8% of participants emphasized the importance of early diagnosis of inborn errors of metabolism (IEMs) after birth, highlighting the crucial role of effective health education in raising awareness and enabling individuals to make informed health decisions. However, 17.7% of participants believed that early diagnosis is not important, while 35.5% stated that they were not sure, indicating a significant gap in

awareness regarding the value of early detection and its role in managing such conditions. additionally, 41.4% of participants were unaware of the genetic nature of these diseases, 25% of participants responded that Inborn Errors of Metabolism (IEMs) cannot be hereditary. reflecting a knowledge gap that may stem from the low quality of existing awareness programs or their inability to effectively convey essential information. Based on these data, the fourth hypothesis is confirmed, as it becomes evident that the quality of awareness programs directly influences the level of public awareness of IEMs among Makkah residents. Well-structured programs that rely on advanced educational methods and present information in a clear and engaging manner have a greater impact on improving the community's understanding of these diseases and how to manage them effectively.

Table (10) Is it important to diagnose Inborn Errors of Metabolism (IEMs) early after birth

Is it important to diagnose Inborn Errors of Metabolism (IEMs) early after birth	Number	Percentage
Yes	103	46.8%
No	39	17.7%
I don't know	78	35.5%
Sum	220	100%

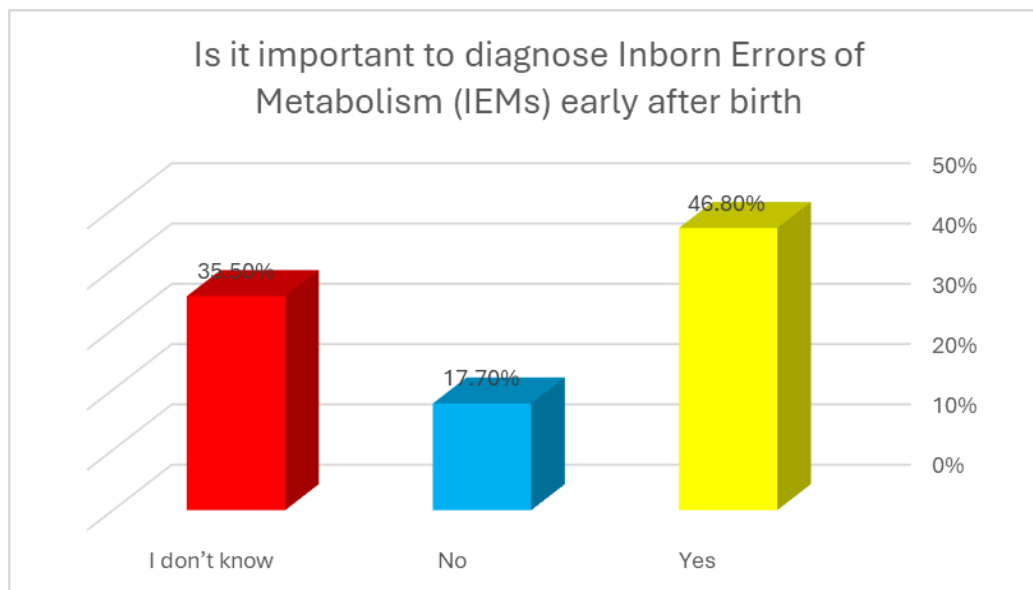


Chart (10) shows (Is it important to diagnose Inborn Errors of Metabolism (IEMs) early after birth)

Table (5) Can Inborn Errors of Metabolism (IEMs) be hereditary

Can Inborn Errors of Metabolism (IEMs) be hereditary	Number	Percentage
Yes	74	33.6%
No	55	25%
I don't know	91	41.4%
Sum	220	100%



Chart (5) shows (Can Inborn Errors of Metabolism (IEMs) be hereditary)

Analysis of the data collected from the study showed there were discrepancies in how participants comprehended the functions of enzymes. The results indicate that as many as 32.3% of the participants understand that enzymes regulate metabolism, which reflects the definition of enzymes as proteinaceous substances which facilitate metabolism by catalyzing biochemical reactions in the body and is involved in regulating various processes. However, 24.5% of participants selected "No," which could suggest a lack of knowledge or confusion about the biological roles of enzymes. A significant knowledge gap in this area is evident from the 43.2% of participants who answered "I do not know." This highlights the significance of encouraging scientific literacy in the community about basic biological concepts, such as the function of enzymes in metabolic processes. Given the link between these ideas and a better comprehension of Inborn Errors of Metabolism (IEMs), these findings emphasize the necessity of creating clear and thorough educational programs to increase people's awareness of the role of enzymes and their effects on the body.

Table (1) Do enzymes play a role in regulating metabolism in the body

Do enzymes play a role in regulating metabolism in the body	Number	Percentage
Yes	71	32.3%
No	54	24.5%
I don't know	95	43.2%
Sum	220	100%

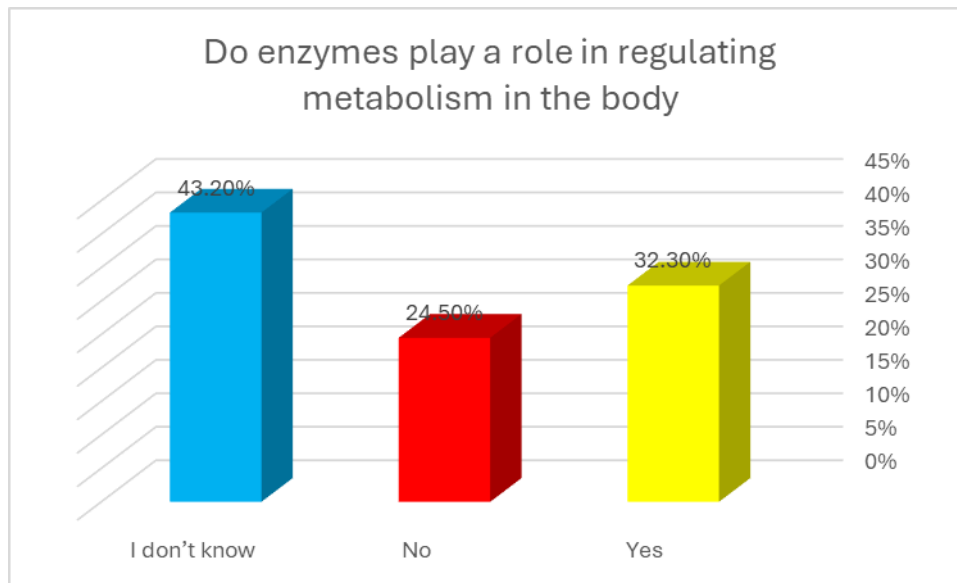


Chart (1) shows (Do enzymes play a role in regulating metabolism in the body)

The results indicated that 42.3% of participants responded “Yes” to the question: “Are Inborn Errors of Metabolism generally caused by a lack of enzymes that do not respond to the instructions necessary to perform their functions?” This suggests a moderate level of awareness regarding the nature of these disorders, as many metabolic conditions result from genetic mutations that cause a deficiency or dysfunction in the enzymes responsible for processing substances in the body. In contrast, 21.8% of participants responded “No,” which may reflect a limited understanding of the molecular basis of these disorders. Additionally, 36.8% of participants answered “I don’t know,” highlighting a significant knowledge gap among a large portion of the community concerning the biological causes of IEMs. These findings highlight the need to enhance public scientific awareness regarding the mechanisms of these diseases and to simplify genetic and medical information, enabling individuals to better understand the nature of these disorders, their causes, and how to address them proactively.

Table (2) There are hundreds of Inborn Errors of Metabolism (IEMs). Is the cause of these diseases generally a lack of enzymes that do not respond to the instructions they need to perform their function properly

There are hundreds of Inborn Errors of Metabolism (IEMs). Is the cause of these diseases generally a lack of enzymes that do not respond to the instructions they need to perform their function properly	Number	Percentage
Yes	93	42.3%
No	48	21.8%
I don't know	81	36.8%
Sum	220	100%

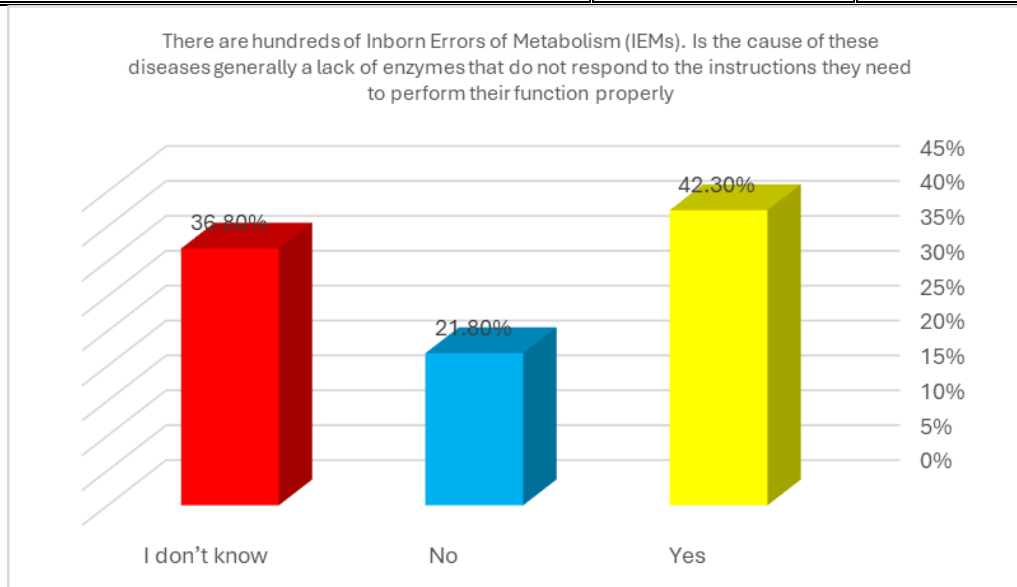


Chart (2) shows (There are hundreds of Inborn Errors of Metabolism (IEMs). Is the cause of these diseases generally a lack of enzymes that do not respond to the instructions they need to perform their function properly)

The results shown in the table and chart indicate that 34.1% of the research sample reported knowing between one and three individuals affected by Inborn Errors of Metabolism (IEMs). Additionally, 26.8% stated they know more than seven affected individuals, suggesting a notable prevalence of these conditions within the community. In comparison, 21.4% reported knowing between four and six cases, while only 17.7% indicated they do not know anyone affected. These findings demonstrate the widespread nature of these genetic disorders and emphasize the need for greater community awareness, particularly regarding diagnosis and psychosocial support.

Table (3) Worldwide, Inborn Errors of Metabolism (IEMs) affect approximately 1 in every 2,500 births. How many people do you know who are affected by one of these inborn errors

Worldwide, Inborn Errors of Metabolism (IEMs) affect approximately 1 in every 2,500 births. How many people do you know who are affected by one of these inborn errors	Number	Percentage
None	39	17.7%
1-3	75	34.1%
4-6	47	21.4%
More than 7	59	26.8%
Sum	220	100%

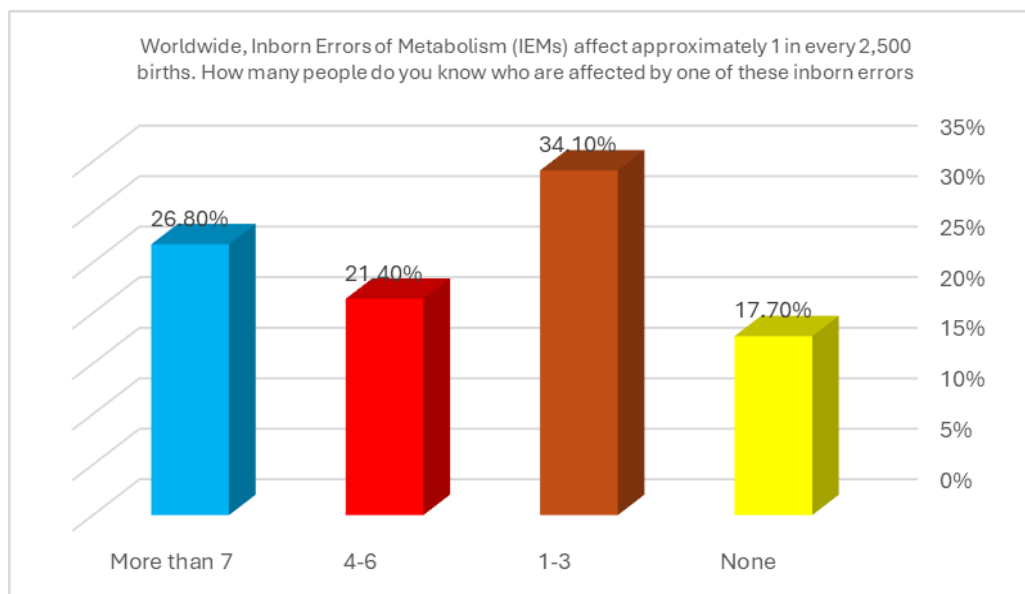


Chart (3) shows (Worldwide, Inborn Errors of Metabolism (IEMs) affect approximately 1 in every 2,500 births; How many people do you know who are affected by one of these inborn errors)

The results shown in the table and graph reveal that a significant portion of the research sample (30.9%) are unaware of which types of nutrients can be affected by Inborn Errors of Metabolism (IEMs), pointing to a knowledge gap within the community regarding these conditions. A total of 27.7% of participants identified proteins, 23.2% selected carbohydrates, and 18.2% chose fats. These variations in responses may indicate differing levels of public awareness and understanding of how IEMs influence the body's ability to metabolize various nutrients. These findings highlight the need to strengthen public education and awareness about IEMs and their potential impact on dietary metabolism.

Table (4) Inborn Errors of Metabolism (IEMs) affect the body's ability to process one of the following from the food or drinks a person consumes, including

Inborn Errors of Metabolism (IEMs) affect the body's ability to process one of the following from the food or drinks a person consumes, including	Number	Percentage
Carbohydrates	51	23.2%
Proteins	61	27.7%
Fats	40	18.2%
I don't know	68	30.9%
Sum	220	100%

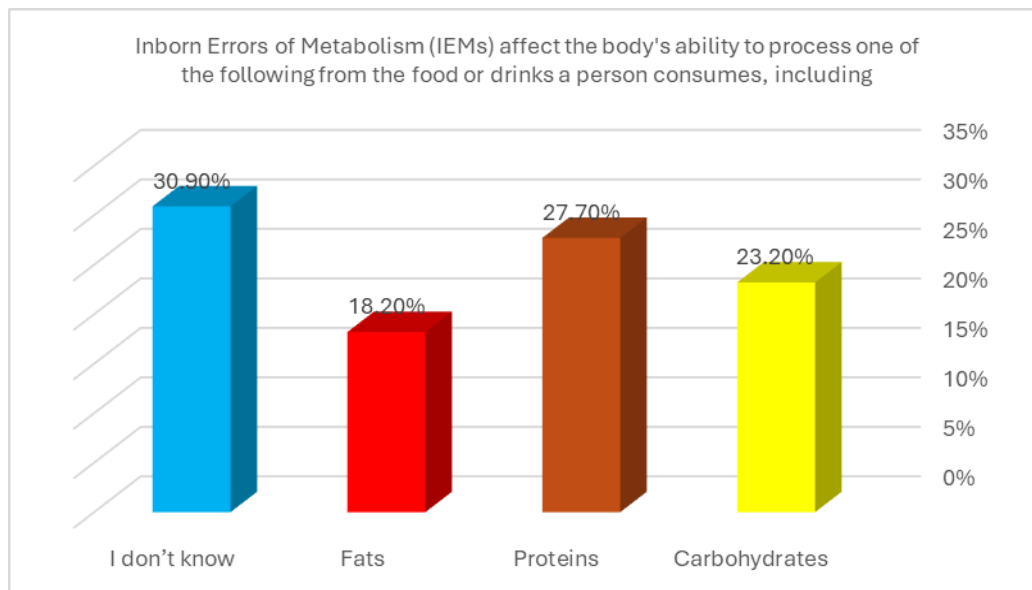


Chart (4) shows (Inborn Errors of Metabolism (IEMs) affect the body's ability to process one of the following from the food or drinks a person consumes, including)

The data shown in the table and graph reveal that 41.4% of the participants are unsure whether Inborn Errors of Metabolism (IEMs) are hereditary, indicating a gap in knowledge or awareness about the genetic nature of these conditions. On the other hand, 33.6% believe that IEMs can be inherited, which reflects a certain level of awareness likely influenced by medical exposure or personal experience. Additionally, 25% responded with “No,” suggesting a misunderstanding or lack of knowledge about the genetic origins of these disorders. These results highlight the need for improved health education and increased public awareness about genetic conditions like IEMs, which are typically inherited and often identified in early childhood.

Table (5) Can Inborn Errors of Metabolism (IEMs) be hereditary

Can Inborn Errors of Metabolism (IEMs) be hereditary	Number	Percentage
Yes	74	33.6%
No	55	25%
I don't know	91	41.4%
Sum	220	100%

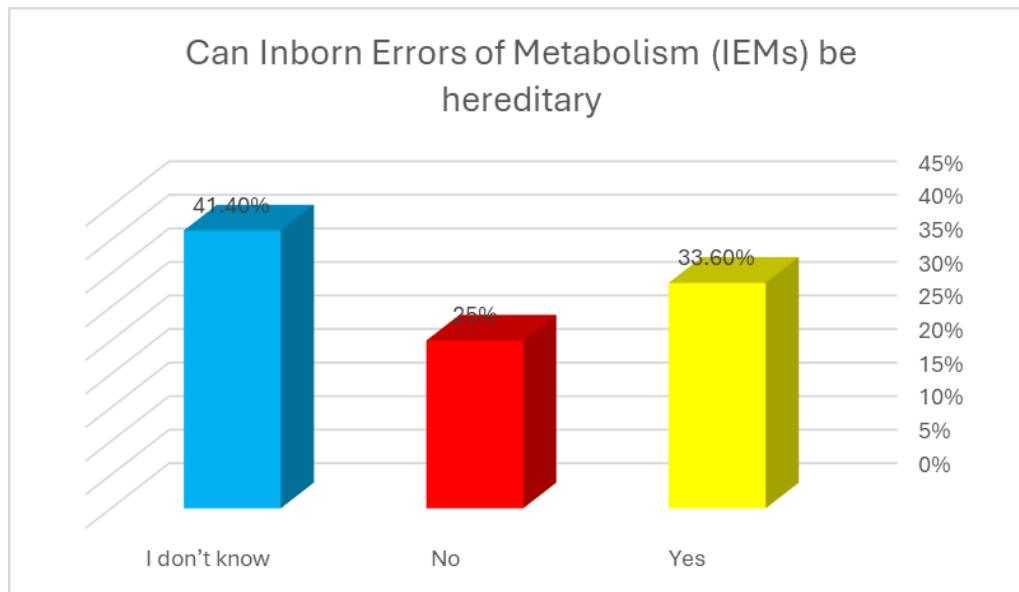


Chart (5) shows (Can Inborn Errors of Metabolism (IEMs) be hereditary)

The data presented in the table and graph show that 46.4% of the participants believe there is a relationship between Inborn Errors of Metabolism (IEMs) and consanguineous marriage, suggesting a reasonable level of awareness about the genetic risks linked to such unions. In contrast, 32.3% responded with “No,” which may reflect limited understanding of the genetic factors that can lead to these disorders. Additionally, 21.3% answered “I don’t know,” highlighting a significant knowledge gap among the participants. These findings emphasize the importance of promoting community awareness about premarital genetic screening, particularly in regions where consanguineous marriage is prevalent, as it can help reduce the risk of hereditary conditions like IEMs.

Table (6) Can Inborn Errors of Metabolism (IEMs) be related to consanguinity (marriage between relatives)

Can Inborn Errors of Metabolism (IEMs) be related to consanguinity (marriage between relatives)	Number	Percentage
Yes	102	46.4%
No	71	32.3%
I don't know	47	21.3%
Sum	220	100%

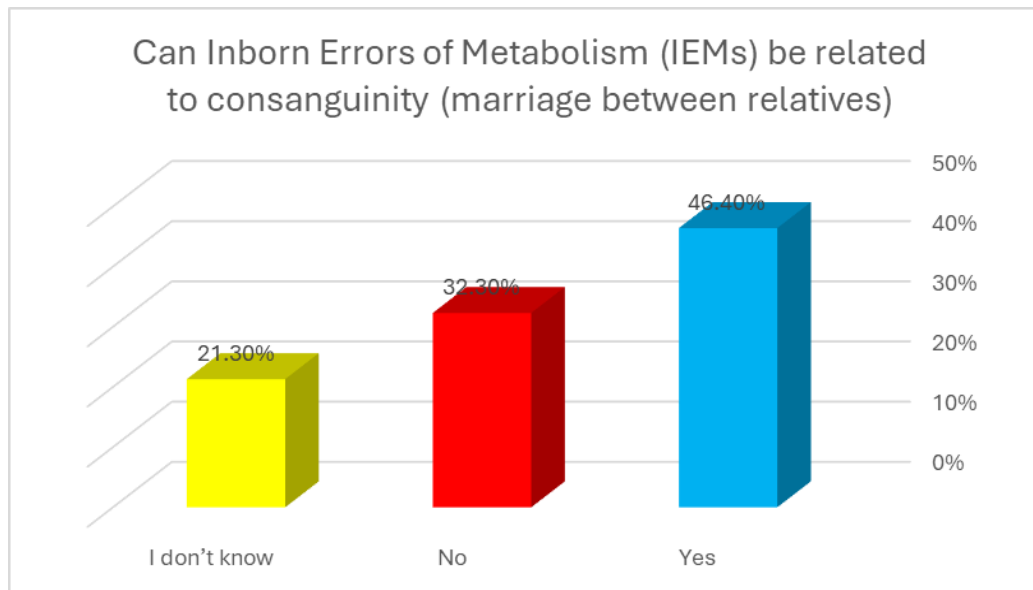


Chart (6) shows (Can Inborn Errors of Metabolism (IEMs) be related to consanguinity (marriage between relatives))

The table and graph show that 43.6% of participants do not believe that each type of Inborn Error of Metabolism (IEM) has its own distinct genetic pattern, indicating a lack of awareness about the genetic diversity of these disorders and how it affects the variation in symptoms among individuals. This reflects a limited understanding of the fact that different mutations can lead to different clinical presentations, even within the same disorder. In comparison, only 24.5% of the participants recognized this scientific reality, while 31.8% responded with “I don’t know,” pointing to a significant knowledge gap in understanding the link between genetics and symptom variation. These findings highlight the urgent need to strengthen health education on genetic conditions by providing accurate, simplified information to improve public understanding.

Table (7) Each type of Inborn Error of Metabolism (IEMs) has a different genetic pattern, and therefore, symptoms vary from person to person

Each type of Inborn Error of Metabolism (IEMs) has a different genetic pattern, and therefore, symptoms vary from person to person	Number	Percentage
Yes	54	24.5%
No	96	43.6%
I don't know	70	31.8%
Sum	220	100%

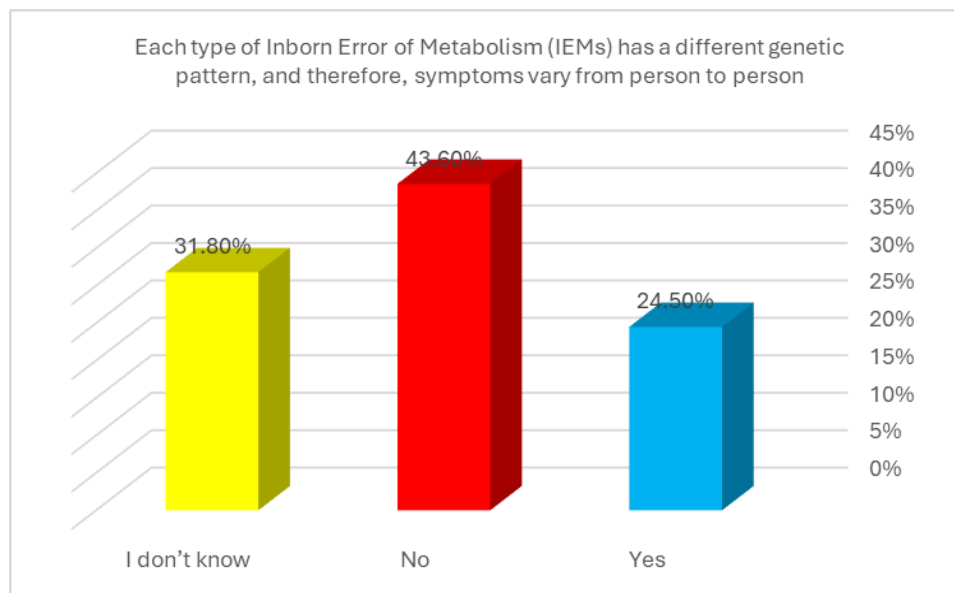


Chart (7) shows (Each type of Inborn Error of Metabolism (IEMs) has a different genetic pattern, and therefore, symptoms vary from person to person)

The data presented in the table and graph reveal that 38.2% of the study participants mistakenly believe that Inborn Errors of Metabolism (IEMs) are contagious, highlighting a prevalent misunderstanding about these conditions. In contrast, 45.9% correctly responded “No,” demonstrating a greater level of awareness regarding the non-contagious nature of these genetic disorders. Additionally, 15.9% selected “I don’t know,” indicating a noticeable knowledge gap within a segment of the population. These findings underscore the importance of raising public awareness about genetic diseases and their modes of transmission, in order to dispel misconceptions and the common confusion with infectious illnesses, as such confusion may lead to unwarranted social stigma against affected individuals and families, resulting in isolation or discrimination in schools and workplaces.

Table (8) Can Inborn Errors of Metabolism (IEMs) be contagious

Can Inborn Errors of Metabolism (IEMs) be contagious	Number	Percentage
Yes	84	38.2%
No	101	45.9%
I don't know	35	15.9%
Sum	220	100%

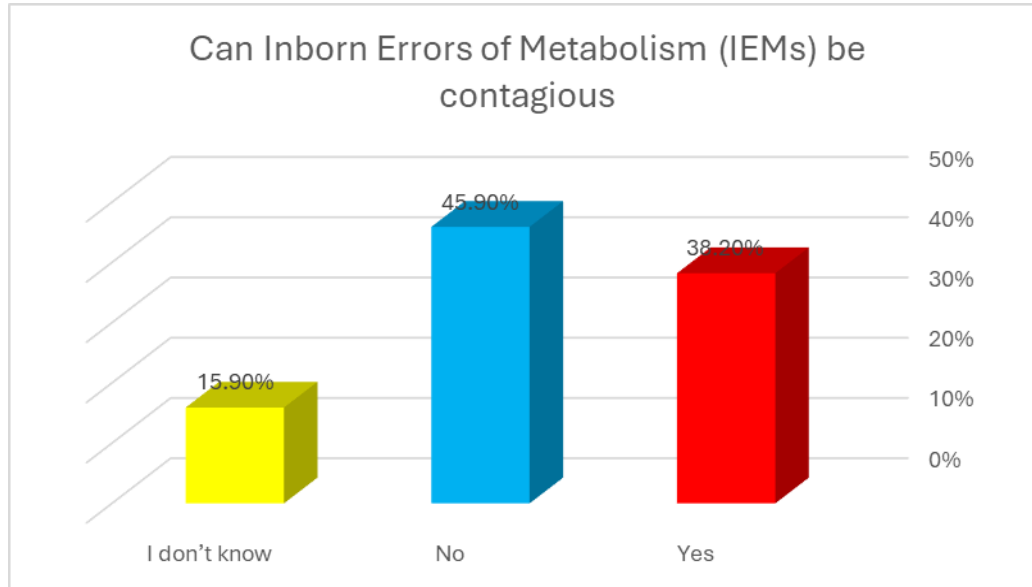


Chart (8) shows (Can Inborn Errors of Metabolism (IEMs) be contagious)

The data illustrated in the table and graph reveal that 44.1% of participants are uncertain about whether newborns can be affected by Inborn Errors of Metabolism (IEMs), highlighting a significant gap in public awareness regarding these rare but critical conditions. In comparison, 33.6% acknowledged that newborns can indeed be affected, indicating a moderate level of awareness among part of the population. On the other hand, 22.3% responded “No,” which may reflect either a lack of information or doubt concerning the association between metabolic disorders and newborns. These results stress the need to enhance health education and public awareness about the effects of IEMs on newborns, as well as the importance of early detection for timely and effective treatment. This underscores the vital role of neonatal screening programs, which aim to identify such metabolic conditions shortly after birth, allowing for early interventions that can significantly improve health outcomes and prevent severe complications.

Table (9) Are newborns affected by Inborn Errors of Metabolism (IEMs)

Are newborns affected by Inborn Errors of Metabolism (IEMs)	Number	Percentage
Yes	74	33.6%
No	49	22.3%
I don't know	97	44.1%
Sum	220	100%

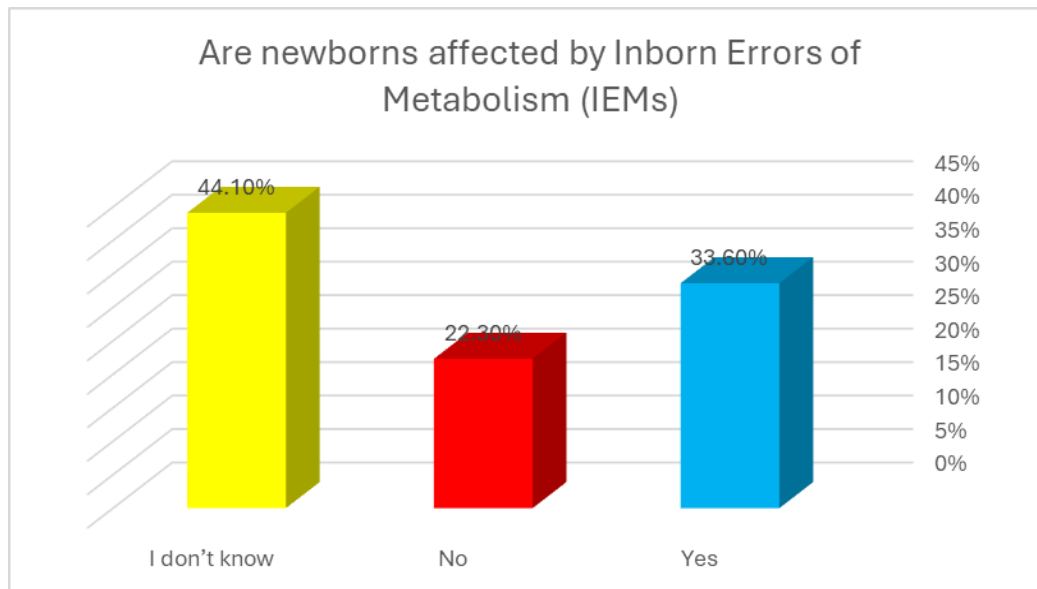


Chart (9) shows (Are newborns affected by Inborn Errors of Metabolism (IEMs))

The data indicate that 46.8% of participants recognize the importance of diagnosing Inborn Errors of Metabolism (IEMs) shortly after birth, reflecting a commendable level of awareness regarding the benefits of early detection in enhancing treatment outcomes and minimizing complications. Conversely, 35.5% of respondents selected “I don’t know,” highlighting a significant portion of the community that may lack sufficient knowledge about the critical role of early diagnosis in managing these genetic conditions. Meanwhile, 17.7% considered early diagnosis unimportant, suggesting the presence of misconceptions or limited understanding about the nature of IEMs. These findings underscore the necessity of bolstering public education and awareness initiatives focused on the value of early newborn screening for IEMs and the substantial health advantages it provides.

Table (10) Is it important to diagnose Inborn Errors of Metabolism (IEMs) early after birth

Is it important to diagnose Inborn Errors of Metabolism (IEMs) early after birth	Number	Percentage
Yes	103	46.8%
No	39	17.7%
I don't know	78	35.5%
Sum	220	100%

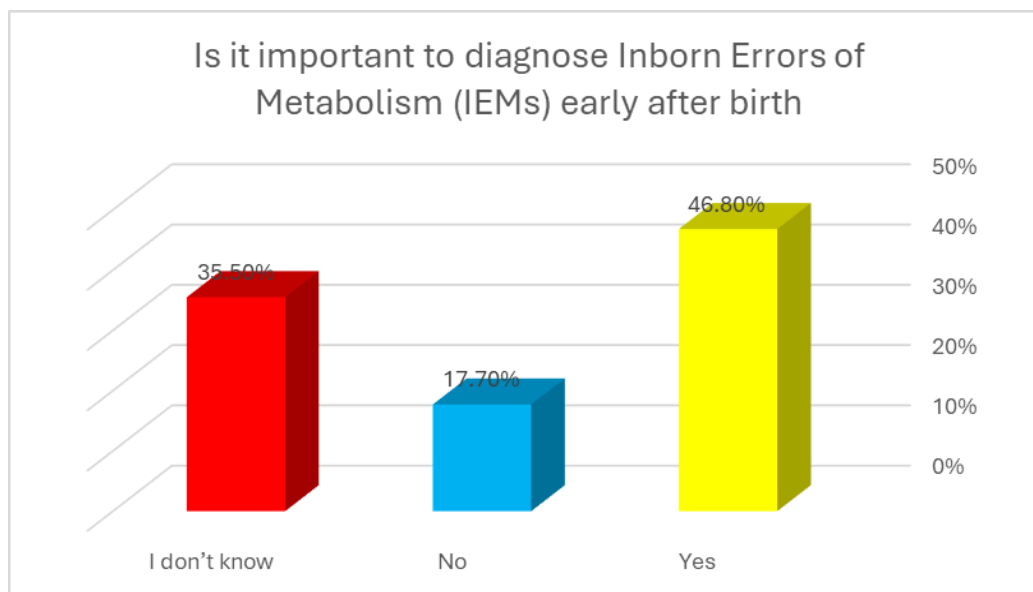


Chart (10) shows (Is it important to diagnose Inborn Errors of Metabolism (IEMs) early after birth)

The results indicate that more than half of the participants, specifically 53.2%, emphasized the importance of consulting a physician in the event that a family member is diagnosed with one of the Inborn Errors of Metabolism (IEMs). This response reflects a positive level of health awareness among community members regarding the necessity of early medical assessment and intervention in such genetic conditions. On the other hand, 26.4% of participants responded with “No,” which may suggest a lack of sufficient understanding about the seriousness of these inherited metabolic disorders and their potential implications for other members of the family. Additionally, 20.4% of the participants answered with “I don’t know,” which highlights a clear gap in knowledge and points to the need for enhanced health education efforts that focus on the importance of timely medical follow-up in cases involving genetic diseases, particularly those related to metabolism. These findings collectively emphasize the urgent need for comprehensive public awareness campaigns that address the hereditary nature of such disorders and reinforce the significance of consulting healthcare professionals to help prevent further transmission within affected families.

Table (11) Should you consult a doctor if someone in your family has one of the Inborn Errors of Metabolism (IEMs)

Should you consult a doctor if someone in your family has one of the Inborn Errors of Metabolism (IEMs)	Number	Percentage
Yes	117	53.2%
No	58	26.4%
I don't know	45	20.4%
Sum	220	100%

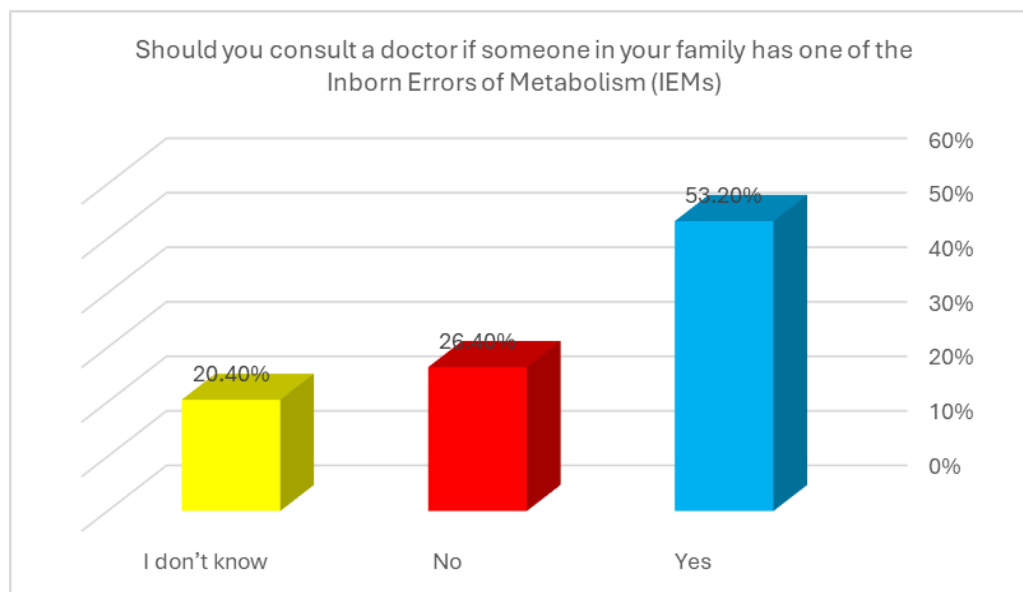


Chart (11) shows (Should you consult a doctor if someone in your family has one of the Inborn Errors of Metabolism (IEMs))

The results illustrated in both the table and the graph demonstrate that the largest proportion of participants, amounting to 41.9%, identified blood testing as the method by which Inborn Errors of Metabolism (IEMs) can be diagnosed. This indicates a satisfactory level of knowledge among respondents regarding the importance of blood analysis in identifying metabolic disorders. Furthermore, 27.4% of participants selected urine testing as a diagnostic approach, which reflects a moderate level of awareness about its role in certain screening or exploratory procedures. In contrast, 20.9% of the participants believed that physical examination could serve as a diagnostic method. This perception suggests that some individuals rely on visible clinical symptoms, despite the fact that physical examination alone is not sufficient for confirming metabolic disorders. Additionally, 9.8% of participants responded with “I don’t know,” highlighting the presence of a knowledge gap in the community concerning accurate diagnostic methods. These findings emphasize the need to strengthen

public health literacy by educating individuals about the most reliable diagnostic tools for IEMs, particularly the significance of both blood and urine tests in confirming diagnosis.

Table (12) Inborn Errors of Metabolism (IEMs) can be diagnosed through the following screening tests

Inborn Errors of Metabolism (IEMs) can be diagnosed through the following screening tests	Number	Percentage
Blood test	124	41.9%
Urine test	81	27.4%
Physical examination	62	20.9%
I don't know	29	9.8%
Sum	296	100%

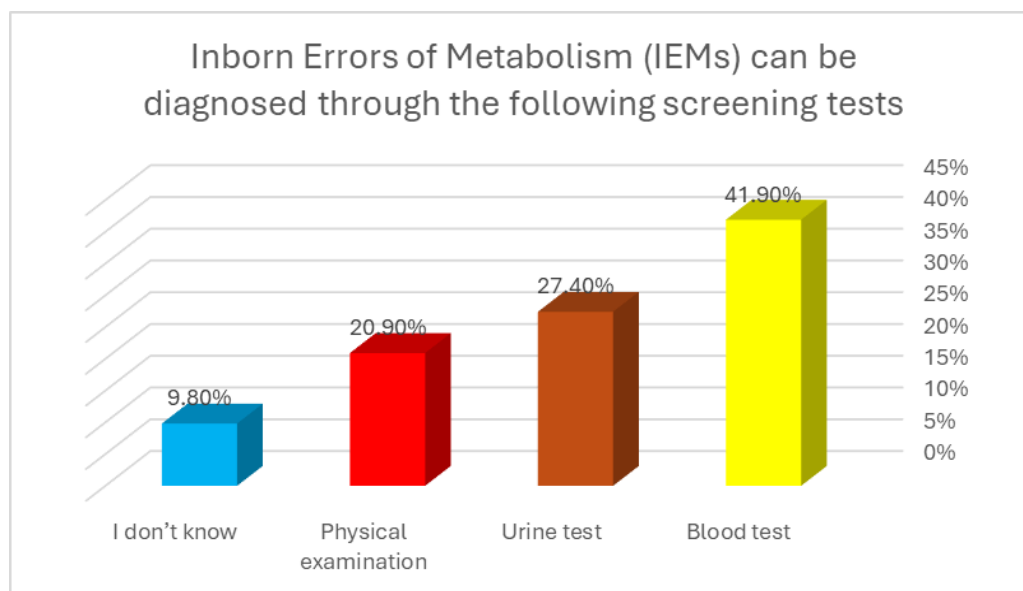


Chart (12) shows (Inborn Errors of Metabolism (IEMs) can be diagnosed through the following screening tests)

The study revealed that participants demonstrated varying levels of awareness regarding the treatment options available for Inborn Errors of Metabolism (IEMs). About 26.2% recognized dietary changes as a key treatment strategy, indicating a moderate understanding of the importance of nutritional management in addressing many of these conditions. Furthermore, 22.5% identified the use of specific medications as an effective form of treatment. In terms of interventional approaches, 10.9% mentioned liver transplantation as a potential option for certain cases, while 8.8% pointed to bone marrow transplantation, typically considered for more severe cases that do not respond to conventional therapies. Additionally, 17.6% of participants acknowledged dialysis as a possible treatment method. Overall, these findings suggest a basic level of public awareness regarding

treatment options for IEMs, but they also emphasize the need for enhanced health education to improve understanding of the nature of these disorders and the various therapeutic approaches available, especially given their wide-ranging types and complexities.

Table (13) What treatment options are available for Inborn Errors of Metabolism (IEMs)

What treatment options are available for Inborn Errors of Metabolism (IEMs)	Number	Percentage
Taking specific medications	84	22.5%
Changing the diet	98	26.2%
Liver transplant for some diseases	41	10.9%
Bone marrow transplant	33	8.8%
Undergoing dialysis	66	17.6%
I don't know	52	13.9%
Sum	374	100%

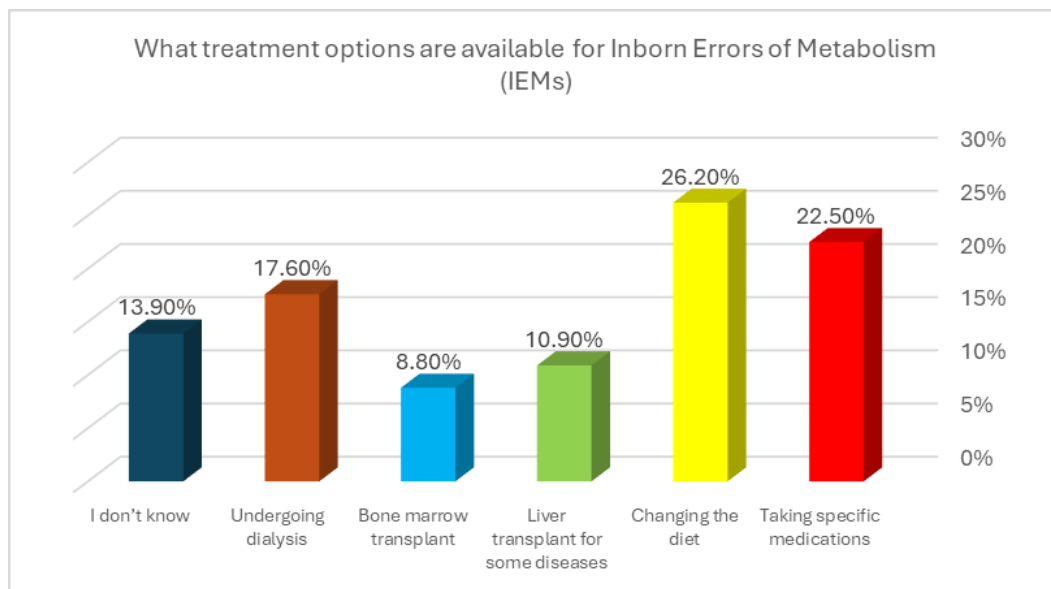


Chart (13) shows (What treatment options are available for Inborn Errors of Metabolism (IEMs))

When participants were asked whether Inborn Errors of Metabolism (IEMs) can be prevented, the results revealed a clear variation in their responses. A total of 31.8% stated that these disorders cannot be prevented, as they are caused by genetic mutations. While this belief is accurate in terms of the underlying genetic cause, it overlooks the role of possible preventive interventions. On the other hand, 25.5% believed that prevention is possible, reflecting an awareness of indirect preventive measures such as premarital screening programs, early newborn screening, and genetic counseling all of which can help reduce the occurrence or recurrence of such conditions in high-risk families. Notably, a significant portion of participants 42.7% responded with “I don't know,” indicating a considerable

knowledge gap regarding the preventive aspects of these disorders. This result highlights the importance of improving public education on available preventive measures, especially in communities with high rates of consanguineous marriage, which increases the risk of passing on rare genetic mutations. These findings emphasize the urgent need to develop more effective awareness programs that focus on the preventive aspects of genetic disorders and clarify the role of genetic testing and medical counseling in reducing their spread.

Table (14) Can Inborn Errors of Metabolism (IEMs) be prevented

Can Inborn Errors of Metabolism (IEMs) be prevented	Number	Percentage
Inborn Errors of Metabolism (IEMs) cannot be prevented because they result from genetic changes	70	31.8%
Yes, they can be prevented	56	25.5%
I don't know	94	42.7%
Sum	220	100%

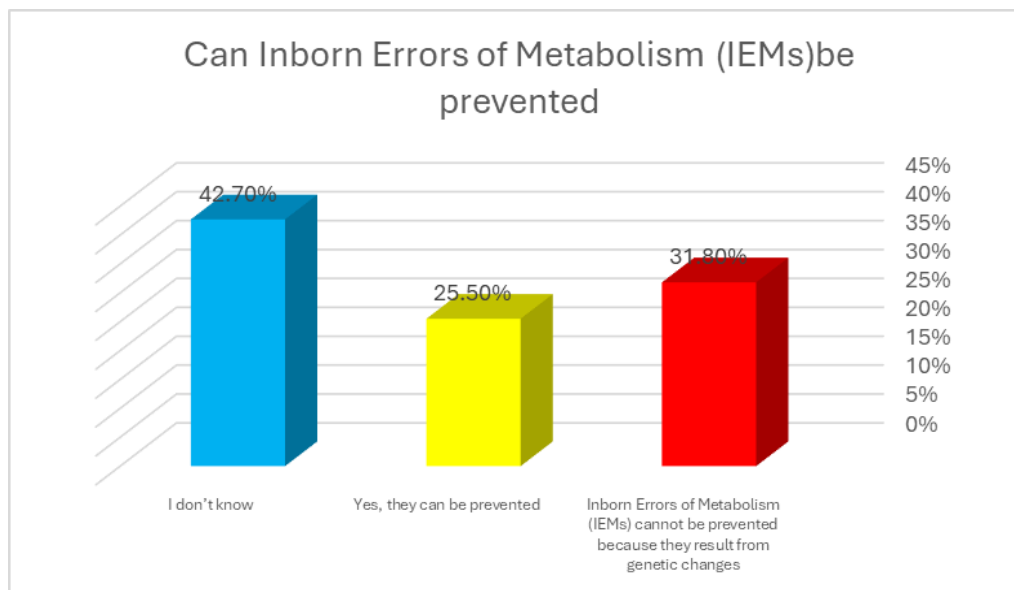


Chart (14) shows (Can Inborn Errors of Metabolism (IEMs) be prevented)

The study findings indicated that maintaining a well-structured lifestyle is one of the most effective strategies for patients coping with Inborn Errors of Metabolism (IEMs). To better understand patients' perspectives, a series of questions representing common concerns were presented to reflect the inquiries individuals might have when confronted with such conditions. The most frequently selected question, chosen by 29.8% of participants, was: "What treatment plans are available for this condition?", highlighting a strong patient interest in understanding available therapeutic options. This underscores the need to raise awareness about various treatment strategies, including dietary

modifications, specific medications, and, in some cases, interventions such as liver transplants or dialysis. Additionally, 20.8% of respondents were concerned about how the disorder would affect their daily lives and how the treatment plan might impact their symptoms, reflecting attention to day-to-day functioning and the psychosocial challenges of living with a chronic condition. Furthermore, 19.8% expressed a desire to join support groups with others who have similar conditions, emphasizing the importance of psychological and social support in managing rare and lifelong diseases. From a medical and scientific standpoint, 15.9% of participants wanted to understand the potential complications of leaving the disorder untreated, indicating an awareness of long-term consequences and a motivation to adhere to treatment. Meanwhile, 13.6% asked about the specific type of IEM they had, demonstrating a need for clearer education about the classifications and subtypes of these disorders. Overall, these findings highlight the importance of creating comprehensive, patient-centered educational programs that go beyond clinical treatment to address the psychological, social, and informational needs of individuals and families affected by chronic metabolic disorders.

Table (15) Adopting an organized lifestyle is one of the best solutions a person can adopt to cope with this disease. What questions would a patient likely ask

Adopting an organized lifestyle is one of the best solutions a person can adopt to cope with this disease. What questions would a patient likely ask	Number	Percentage
Can I join a support group with other people who have the same condition	77	19.8%
How will this disorder affect daily life? What is the impact of the treatment plan on the symptoms of this disorder	81	20.8%
What treatment plans are available for this condition	116	29.8%
What are the potential complications of this disorder if left untreated	62	15.9%
What type of disorder or (Inborn Error of Metabolism) is it	53	13.6%
Sum	389	100%

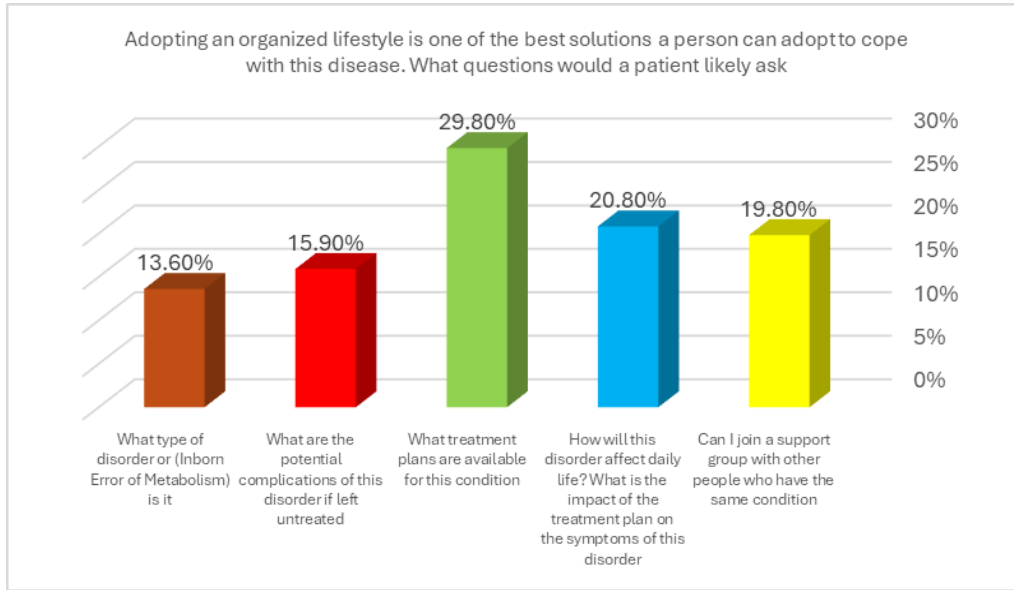


Chart (15) shows (Adopting an organized lifestyle is one of the best solutions a person can adopt to cope with this disease. What questions would a patient likely ask)

Table (16) values of the correlation coefficients between the degree of each phrase and the degree of the questionnaire

No	Correlations	Sig
1-	0.881	0.01
2-	0.702	0.01
3-	0.635	0.05
4-	0.813	0.01
5-	0.914	0.01
6-	0.790	0.01
7-	0.736	0.01
8-	0.608	0.05
9-	0.621	0.05
10-	0.855	0.01
11-	0.937	0.01
12-	0.820	0.01
13-	0.961	0.01
14-	0.758	0.01
15-	0.640	0.05

It is clear from the table that all the correlation coefficients are significant at the level (0.01- 0.05) because they are close to the whole one, which indicates the validity and homogeneity of the questionnaire phrases.

Reliability means the test accuracy in the measurement and observation, not a contradiction with itself, and its consistence in providing us with information about the examiner's behavior, and it is the ratio between the score difference on the scale, which refers to the actual performance of the examiner. The reliability has been calculated by:

- 1- Alpha Cronbach coefficient
- 2- Split-half method

Table (17) values of the reliability coefficient of the questionnaire

	Cronbach's Alpha	Split-half
Reliability of the questionnaire as whole	0.891	0.854 – 0.933

It is clear from the previous table that the all values of the reliability coefficients: the Alpha coefficient, the Split-half are significant at the level of 0.01 and that indicates the reliability of the questionnaire.

The results of this study revealed a clear deficiency in the level of awareness among the residents of Makkah regarding inborn errors of metabolism (IEMs), which is consistent with previous studies in this field. When compared to the findings of Alqrache et al. (2020), which targeted students at King Abdulaziz University – Rabigh branch, the level of knowledge among university students appeared to be higher. In their study, 63.5% of participants stated that these disorders are genetic, whereas in the current study, 41.4% of participants responded with “I don’t know,” and 25% answered “No” to the same question. (Alqrache et al., 2020) This indicates a larger knowledge gap within the general population compared to the university demographic. The reason for this difference in awareness may be due to the variation in the target populations. Our study focused on the general public, which includes individuals with diverse educational backgrounds, whereas their study was conducted among university students, including those in medical and non-medical fields. Therefore, the higher awareness observed in their findings could be attributed to the participants’ exposure to health-related information, especially among medical students, unlike the general population who may have limited knowledge about such disorders. Furthermore, awareness of the importance of early diagnosis was not high among participants, with only 46.8% considering it necessary. This contrasts with Alqrache’s findings, which highlighted participants’ recognition of the value of early screening and recommended the use of social media to spread awareness (Alqrache et al., 2020). This discrepancy may be attributed to university students having direct access to educational health resources, unlike

the general public, who may lack exposure to accurate information. Similarly, the study by Al Essa et al. (1997), which included parents of children diagnosed with metabolic disorders, found that many parents were unaware of the nature of their children's conditions despite receiving medical explanations. This lack of understanding was linked to lower levels of education (Al Essa et al., 1997). These findings align with our study, where a lower level of awareness was observed among participants with limited educational backgrounds. The results also revealed several misconceptions, such as the belief that these disorders are contagious, which was held by 38.2% of participants. Additionally, 22.3% believed that these diseases do not affect newborns, and 20.9% believed that physical examination alone is sufficient for diagnosis. These misconceptions emphasize the need to enhance public understanding of the nature of these conditions. Accordingly, there is a clear need for comprehensive awareness programs targeting the general population. These programs should focus on correcting false beliefs and delivering information in a simplified and accessible manner, using modern tools and platforms that are easily reachable by the public.

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Conclusions

This study highlights a noticeable deficiency in public awareness of inborn errors of metabolism (IEMs) among adults in Makkah. The findings point to widespread misconceptions and limited understanding of the genetic basis, causes, and prevention methods of these disorders. This underscores the urgent need for innovative and accessible awareness initiatives that utilize simplified educational approaches and digital media platforms to reach a broader audience. The study recommends future research to focus on community-based interventions and assess their effectiveness in improving knowledge and encouraging early detection and proper management of IEMs.

Recommendations

As part of the Kingdom of Saudi Arabia's efforts to improve quality of life and prevent diseases, the National Newborn Screening Program was launched in August 2005, becoming one of the foundational pillars of the preventive healthcare system. This program aims to preserve community health by enabling the early detection of selected genetic disorders, particularly inborn errors of metabolism and congenital endocrine diseases. It contributes to reducing morbidity, mortality, and disability rates. By utilizing modern technologies, the program allows for the detection of diseases before symptoms appear, which enables early medical intervention and prevents serious complications such as intellectual disabilities, physical impairments, or even early death. This initiative is part of the Kingdom's ongoing efforts to support public health and aligns with Vision 2030 goals in the areas of prevention, early detection, and enhancement of healthcare quality.

The findings of this study underscore the need for a multifaceted public health approach to raise awareness of inborn errors of metabolism:

A. Strengthen digital and media-based health education:

- Survey results revealed a significant lack of awareness among community members regarding Inborn Errors of Metabolism (IEMs).
- There is an urgent need to adopt innovative strategies that go beyond traditional health education methods.
- Social media can serve as a powerful platform for disseminating interactive awareness content, such as short videos using simple language and engaging visuals.
- Educational applications targeting children and families can be developed, featuring interactive games and quizzes.
- Storytelling is a powerful method for raising awareness. Sharing real-life stories of individuals affected by IEMs helps create an emotional connection with the audience.
- Augmented Reality and Virtual Reality offer immersive learning experiences. Virtual Reality and Augmented Reality align with current digital trends and contribute to more engaging and effective education.

- Collaboration with streaming platforms or television series can help raise awareness, as dramas or documentaries may spark public interest, stimulate conversations, and encourage people to take these conditions more seriously.

B. Encourage school-based and community education:

- Efforts should be directed toward enhancing health education and increasing public understanding of these rare and complex disorders.
- Entertaining school workshops can play a key role in early education.
- Interactive activities and educational theatrical performances can present scientific concepts in a memorable and impactful way.

C. Enhance inter-sectoral coordination and policy support:

- Cooperation between key stakeholders such as the Ministry of Health, the Ministry of Media, and other relevant authorities is essential to ensure effective messaging.
- Official support through government platforms can boost community engagement and enhance the impact of awareness campaigns.
- Integrating modern and innovative approaches with government and media collaboration can build comprehensive health awareness.

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Appendices 1 (Publication)

<p>Tanta University Faculty Of Specific Education</p>		<p>جامعة طنطا كلية التربية النوعية</p>
<p>المجلة العلمية لعلوم التربية النوعية إفــادــة</p>		
<p>Dr. Alanoud Omur A. Mehder Food Process Engineering Associate Professor Environmental and Occupational Health Department Faculty of Public Health and Health Informatics</p>		
<p>تحية طيبة وبعد ،،، تفيد إدارة المجلة العلمية لعلوم التربية النوعية بأن البحث المقدم من سيادتكم تحت عنوان : Awareness of inborn errors of metabolism among general Title: populations of Makkah city in Saudi Arabia</p>		
<p>الاشتراك مع</p>		
<p>Hanaa Mubark Al-Harbi Layan Mamdouh Al-Manabre Manar Ali Al-Elyani Rahaf Abdullah Bushnaq Waad Aali Al-Qurashi</p>	<p>Department of Health Education & Health Promotion, Faculty of Public Health & Health Informatics, Umm Al-Qura University, Ministry of Education Department of Health Education & Health Promotion, Faculty of Public Health & Health Informatics, Umm Al-Qura University, Ministry of Education Department of Health Education & Health Promotion, Faculty of Public Health & Health Informatics, Umm Al-Qura University, Ministry of Education Department of Health Education & Health Promotion, Faculty of Public Health & Health Informatics, Umm Al-Qura University, Ministry of Education Department of Health Education & Health Promotion, Faculty of Public Health & Health Informatics, Umm Al-Qura University, Ministry of Education</p>	
<p>تم قبوله بعد التحكيم وسوف يتم نشره في العدد الواحد والعشرون يونيو ٢٠٢٥ بالمجلة العلمية لعلوم التربية النوعية .</p>		
<p>ويمكن الإطلاع على البحث من خلال موقع بنك المعرفة المصري : https://www.ekb.eg/web/guest/journals أو من خلال موقع المجلة : https://sjsep.journals.ekb.eg والترقيم الدولي الموحد المطبوع: 2735-3893. والترقيم الإلكتروني: 2735-363X.</p>		
<p>وتفضلوا سيادتكم بقبول وافر التحية والإحترام ،،،</p>		
<p>عميد الكلية ورئيس مجلس إدارة المجلة</p>  <p>أ.د/ رانيا عبده الإمام</p>	<p>وكيل الكلية للدراسات العليا والبحوث ورئيس تحرير المجلة ونقيب رئيس مجلس الإدارة</p>  <p>أ.د/ السيد محمد مزروع</p>	<p>مسئول إدارى المختص</p>  <p>م/ فاطمة سليمان على</p>
<p>Fax: 0403307190 Tel: 0403314225</p>	<p>TP0SED0R0M0I020100</p>	<p>طنطا - كلية التربية النوعية - شارع بطرس</p>

Appendices 2 The (10th international scientific conference)



Appendices 3 (English questionnaires)

Dear Ms/Mrs

Metabolism in the human body refers to a series of chemical processes that convert the food and drinks you consume into energy.

There are what are known as Inborn Errors of Metabolism (IEMs), which are genetic disorders that affect the body's ability to convert food into energy. These errors occur when the body is unable to complete these chemical processes as expected, leading to various health complications. The purpose of this survey is to assess the level of awareness among the residents of Mecca regarding Inborn Errors of Metabolism (IEMs), and to determine their need for a program that enhances their knowledge and awareness of these genetic disorders and how to cope with them. The survey includes three sections: demographic and personal information, participants' awareness of the topic, methods for diagnosing and managing the condition. The researchers in the Department of Health Promotion and Health Education at the College of Public Health and Health Informatics, Umm Al-Qura University, present this survey to help us understand the risks associated with Inborn Errors of

Metabolism (IEMs). The ultimate goal is to design a program that assists the Meccan community in recognizing the prevalence of these disorders and understanding how to manage them optimally.

We deeply appreciate your cooperation in answering the survey questions, and we highly value your time and input.

Thank you for your support and participation.

First part: Demographic information

1. Age?

From 20 to 25 years

From 26 to 35 years

From 36 to 45 years

From 46 to 50 years

From 51 years or more

2. Are you a resident of Mecca?

Yes

No

3. Gender?

Male

Female

4. Marital status?

Single

Married

Divorced

Widowed

5. Education?

Preparatory school certificate or less

High School

Bachelor's Degree / Postgraduate

Second part: Participants' Awareness of the Topic

1. Do enzymes play a role in regulating metabolism in the body?

Yes

No

I don't know

2. There are hundreds of Inborn Errors of Metabolism (IEMs). Is the cause of these diseases generally a lack of enzymes that do not respond to the instructions they need to perform their function properly?

Yes

No

I don't know

3. Worldwide, Inborn Errors of Metabolism (IEMs) affect approximately 1 in every 2,500 births. How many people do you know who are affected by one of these inborn errors?

None

1-3

4-6

More than 7

4. Inborn Errors of Metabolism (IEMs) affect the body's ability to process one of the following from the food or drinks a person consumes, including?

Carbohydrates

Proteins

Fats

I don't know

5. Can Inborn Errors of Metabolism (IEMs) be hereditary?

Yes

No

I don't know

6. Can Inborn Errors of Metabolism (IEMs) be related to consanguinity (marriage between relatives)?

Yes

No

I don't know

7. Each type of Inborn Error of Metabolism (IEMs) has a different genetic pattern, and therefore, symptoms vary from person to person?

Yes

No

I don't know

8. Can Inborn Errors of Metabolism (IEMs) be contagious?

Yes

No

I don't know

9. Are newborns affected by Inborn Errors of Metabolism (IEMs)?

Yes

No

I don't know

10. Is it important to diagnose Inborn Errors of Metabolism (IEMs) early after birth?

Yes

No

I don't know

11. Should you consult a doctor if someone in your family has one of the Inborn Errors of Metabolism (IEMs)?

Yes

No

I don't know

Third part: Diagnosis, Treatment, and Coping

1. Inborn Errors of Metabolism (IEMs) can be diagnosed through the following screening tests?

Blood test

Urine test

Physical examination

I don't know

2. What treatment options are available for Inborn Errors of Metabolism (IEMs)?

Taking specific medications

Changing the diet

Liver transplant for some diseases

Bone marrow transplant

Undergoing dialysis

I don't know

3. Can Inborn Errors of Metabolism (IEMs) be prevented?

Inborn Errors of Metabolism (IEMs) cannot be prevented because they result from genetic changes

Yes, they can be prevented

I don't know

4. Adopting an organized lifestyle is one of the best solutions a person can adopt to cope with this disease. What questions would a patient likely ask?

Can I join a support group with other people who have the same condition

How will this disorder affect daily life? What is the impact of the treatment plan on the symptoms of this disorder

What treatment plans are available for this condition

What are the potential complications of this disorder if left untreated

What type of disorder or (Inborn Error of Metabolism) is it

Appendices 4 (Arabic questionnaires)

عزيزي/ عزيزتي

إن عملية التمثيل الغذائي في جسم الانسان (Metabolism): عبارة عن سلسلة من العمليات الكيميائية التي تحول ما تأكله وتشربه إلى طاقة.

وهناك ما يعرف بالأخطاء الخلقية في التمثيل الغذائي (Inborn Errors of Metabolism (IEMs)، أو الاضطرابات الوراثية التي تؤثر على قدرتك على تحويل الطعام إلى طاقة (عملية التمثيل الغذائي) فتحدث بعض الأخطاء بحيث لا يتمكن جسمك من إكمال هذه العمليات الكيميائية كما هو متوقع.

والهدف من هذه الاستبانة هو: تقييم مستوى معرفة سكان مكة المكرمة بالأخطاء الخلقية في التمثيل الغذائي (Inborn Errors of Metabolism (IEMs)، ومدى حاجتهم لبرنامج يعزز معرفتهم ووعيهم بهذه الأمراض الوراثية وكيفية التعايش معها. ويتضمن الاستبيان الإجابة على ثلاثة أقسام: المعلومات الشخصية والديموغرافية، وحي المشاركين بالموضوع، طرق تشخيص المرض والتعايش معه.

وتضع الباحثات في قسم التعزيز والتنقيف الصحي بكلية الصحة العامة والمعلوماتية الصحية بجامعة أم القرى، هذه الاستبانة بين أيديكم للتعرف على خطورة هذه الأخطاء الخلقية في التمثيل الغذائي (Inborn Errors of Metabolism (IEMs)، وبالتالي تصميم برنامج يساعد المجتمع المكي على التعرف على مدى انتشار نوعية هذه الأمراض، وكيفية التعامل معها على الوجه الأمثل. وتقبلو جل الشكر والتقدير على تعاونكم معنا في الإجابة على بنود الاستبيان، مقدرين وقتكم الثمين ..

القسم الاول: المعلومات الشخصية والديموغرافية

١. العمر؟

من ٢٠- ٢٥

من ٢٦- ٣٥

من ٣٦- ٤٥

من ٤٦- ٥٠

أكبر من ٥١

٢. هل انت من سكان مكة؟

نعم

لا

٣. الجنس؟

ذكر

انثى

٤. الحالة الاجتماعية؟

اعزب

متزوج

مطلق

أرمل

٥. المستوى التعليمي؟

ابتدائي

متوسط

ثانوي

بكالوريوس

دراسات عليا

القسم الثاني: مدى وعي المشاركين حول الموضوع

١. هل تلعب الإنزيمات دوراً في تنظيم عملية التمثيل الغذائي في الجسم؟

نعم

لا

لا أعلم

٢. هناك مئات من الأخطاء الخلقية في عملية التمثيل الغذائي (IEMs) Inborn Errors of Metabolism هل سبب هذه

الأمراض بشكل عام هو نقص الإنزيم الذي لا يستجيب للتعليمات التي يحتاجها للقيام بعمله كما ينبغي؟

نعم

لا

لا أعلم

٣. على مستوى العالم تؤثر الأخطاء الخلقية في التمثيل الغذائي (IEMs) Inborn Errors of Metabolism على ما يقدر ١ من

كل ٢٥٠٠ ولادة، كم شخص تعرفه مصاب بأحد الأخطاء الخلقية؟

لا يوجد

٣-١

٦-٤

أكثر من ٧ أشخاص

٤. تؤثر الأخطاء الخلقية في التمثيل الغذائي (Inborn Errors of Metabolism (IEMs على قدرة الجسم على معالجة أحد العناصر التالية من الأطعمة أو المشروبات التي يتناولها الشخص، بما في ذلك:

الكربوهيدرات

البروتينات

الدهون

لا أعلم

٥. هل يمكن أن تكون الأمراض/ أو الأخطاء الخلقية في عملية التمثيل الغذائي (Inborn Errors of Metabolism (IEMs وراثية؟

نعم

لا

لا أعلم

٦. هل يمكن أن تكون الأمراض/ أو الأخطاء الخلقية في عملية التمثيل الغذائي (Inborn Errors of Metabolism (IEMs لها علاقة بزواج الأقارب؟

نعم

لا

لا أعلم

٧. كل نوع من العيوب الخلقية في التمثيل الغذائي (Inborn Errors of Metabolism (IEMs له شكل مختلف بالوراثة وبالتالي تختلف الأعراض من شخص لآخر؟

نعم

لا

لا أعلم

٨. هل يمكن أن تكون الأمراض/ أو الأخطاء الخلقية في عملية التمثيل الغذائي (Inborn Errors of Metabolism (IEMs معدية؟

نعم

لا

لا أعلم

٩. هل تتأثر الفئة العمرية لحديثي الولادة بالأمراض/ أو الأخطاء الخلقية في عملية التمثيل الغذائي Inborn Errors of Metabolism (IEMs) ؟

نعم

لا

لا اعلم

١٠. هل من المهم تشخيص الأمراض/ أو الأخطاء الخلقية في عملية التمثيل الغذائي Inborn Errors of Metabolism (IEMs) مبكراً بعد الولادة؟

نعم

لا

لا اعلم

١١. هل يجب استشارة الطبيب في حالة وجود أحد الأمراض/ أو الأخطاء الخلقية في عملية التمثيل الغذائي Inborn Errors of Metabolism (IEMs) في أحد أفراد الأسرة؟

نعم

لا

لا اعلم

القسم الثالث: التشخيص والعلاج والتعايش

١. يمكن تشخيص العيوب الخلقية في التمثيل الغذائي Inborn Errors of Metabolism (IEMs) من خلال اختبارات الفحص التالية: (يمكنك تحديد أكثر من خيار)

فحص الدم

اختبار البول

الفحص البدني

لا اعلم

٢. ما هي طرق العلاج المتاحة للأمراض/ أو الأخطاء الخلقية في عملية التمثيل الغذائي Inborn Errors of Metabolism (IEMs) ؟ (يمكنك تحديد أكثر من خيار)

تناول أدوية خاصة

تغيير النظام الغذائي

زراعة الكبد في بعض الأمراض

زراعة نخاع العظم

الخضوع لغسيل الكلى

لا اعلم

٣. هل يمكن منع الأخطاء الخلقية في التمثيل الغذائي (IEMs)؟

لا يمكن منع الأخطاء الخلقية في التمثيل الغذائي لأنها نتيجة لتغيرات جينية

نعم يمكن ذلك

لا اعلم

٤. تبني نمط حياة منظم هو من أفضل الحلول التي يمكن للشخص اللجوء إليها للتعايش مع هذا المرض، ماهي الاسئلة التي

سيرغب المريض بالسؤال عنها؟ (يمكنك تحديد أكثر من خيار)

ما هو نوع الاضطراب أو الخطأ الخلقي في عملية التمثيل الغذائي؟

ما هي خطط العلاج المتاحة لهذه الحالة؟

ما هي نسبة تأثير خطة العلاج على أعراض هذا الاضطراب؟

كيف سيؤثر هذا الاضطراب على ممارسة الحياة اليومية؟

هل يمكن الانضمام إلى مجموعة دعم تضم أشخاصاً آخرين يعانون من نفس الحالة؟

Appendices 5 (Study Limitations)

- A. The cross-sectional design limits the ability to assess changes in awareness over time.
- B. Convenience sampling may introduce bias.
- C. Reliance on self-reported data may lead to social desirability bias.
- D. Results may not be generalizable to other regions of Saudi Arabia.
- E. Limited demographic diversity.
- F. The sample size did not reach the ideal number based on statistical calculation.