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The epidemiology of inborn metabolic errors and challenges in Nigeria

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Abstract

Inborn errors of metabolism are a class of genetically based illnesses that are uncommon on their own but can be extremely serious when combined. The body is unable to convert food into energy correctly in this set of uncommon genetic (inherited) illnesses. Poor outcomes during pregnancy and infancy are linked to congenital birth abnormalities. In developed nations, next generation sequencing (NGS) and tandem mass spectrometry (MS/MS) are used to investigate inborn errors of metabolism. In developing nations, such as Nigeria, these disorders are rarely screened for because of a lack of resources and public and healthcare professional awareness. Because Nigeria has few or no screening programs in place, there is a lack of epidemiological data on inborn metabolic faults throughout the country's six geopolitical zones, which this research aims to fill. Lack of countrywide newborn screening, insufficient diagnostic facilities, and low healthcare provider awareness are some of the obstacles to the screening and detection of inborn metabolic abnormalities in Nigeria. However, there is evidence of inborn errors of metabolism in Nigeria, as evidenced by the case of a 14-month-old boy with Glycogen Storage Disease Type 111a. This highlights the need for significant clinical awareness of inborn errors of metabolism.

Keywords: Inborn errors, metabolism, Glycogen Storage Disease, congenital, birth defects.

Introduction

Reducing child mortality is still a major worldwide concern [1]. It is a measure of both the general social and economic development of a country and the well-being of its children [2]. Child survival rates continue to confront major obstacles even after the Millennium Development Goals (MDGs) were developed and put into practice. A total of 5.491 million child deaths occurred during the aforementioned period, of which 2.681 million occurred during the neonatal period, accounting for 45.1% of the total child mortality under five years of age [4], despite a 53% decrease in the mortality rate for children under five years of age [3]. According to data from the World Health Organization (WHO), the sub-Saharan African region accounts for seventy-four fatalities for every 1000 live births. There is significant disparity in child survival rates, as the rate is over fourteen times greater than those reported in North America and Europe. Sub-Saharan Africa and Southern Asia accounted for over 80% of the 5 million children under five who died worldwide in 2020. Notably, Nigeria, India, Pakistan, the Democratic Republic of the Congo, and Ethiopia accounted for half of these fatalities [5].

One of the major problems in pediatric populations is biochemical genetics, specifically Inborn Errors of Metabolisms (IEMs). A broad category of uncommon illnesses known as Inborn Errors of Metabolisms (IEMs) are caused by a single enzyme's inadequate performance within a metabolic pathway. These conditions frequently result from genetic changes that change the structure or activity of enzymes, which affects the body's capacity to carry out particular biochemical activities necessary for regular physiological function [6], [7]. One of the factors causing 5.1% of neonatal deaths and 3.5% of fatalities in children ages 1 to 59 months is congenital abnormalities [8]. According to the research that is currently

accessible, these illnesses are uncommon worldwide, occurring at a rate of about one in 100,000 births. On the other hand, the overall incidence of IEMs falls between 1 in 800 and 1 in 2,500 births. Despite the rarity of each condition, this larger view illustrates the substantial influence that various disorders can have when combined [8]. The overall birth prevalence of IEMs is 50.9 per 1,000,000 live births, citing the meta-analysis report [9]. According to reports, 1 in 2497 infants in India had IEMs [8]. IEMs affect many people from many demographic groups around the world and account for a significant amount of the global disease burden [8]. In regions where consanguineous marriages are more common, this disease is more common [10]. This high percentage accounts for 20–50% of marriages in several groups in North Africa, the Middle East, and West Asia, which constitute a wide belt that stretches from Afghanistan and Pakistan in the East to Morocco in the West, as well as in South India [12]. The frequency of IEMs is greatly increased by the genetic susceptibility brought about by consanguinity. According to studies, children of Pakistani, Turkish, Afghan, and Arab ancestry have a 25.5-fold greater frequency of IEMs. For instance, compared to Danish natives, the predicted prevalence of IEMs is 10.6 in 10,000 among Afghan children and 6.5 in 10,000 among Pakistani children [13].

A substantial percentage of child deaths that are not currently well represented in international modeling efforts are caused by inborn metabolic errors, which are a major contributor to global child morbidity and mortality [9]. According to recent IEM data, there are 1,015 IEMs overall, divided into 130 groups. While some of these illnesses only affect one organ, others affect several. It is crucial to realize that while all of these numbers reflect recorded data from different places, there are probably still unidentified cases that have not been reported or diagnosed. This disparity between reported and real cases highlights the need for better reporting procedures and diagnostic tools to guarantee that every instance is appropriately identified and handled.

Worldwide data

The population's racial and ethnic makeup, as well as the scope of screening initiatives, influence the overall incidence and frequency of specific diseases [6]. The range of overall rates is comparable to that of the United States. PKU was the most prevalent disease among the study participants (19.6%), according to a research by the Society for the Study of Inborn Errors of Metabolisms (SSIEM), which examined 15 hospitals that specialize in the treatment of people with IEMs [14]. Data pertaining to race, ethnicity, sex, and age Race: The prevalence of specific IEMs varies by race and ethnicity. For example, the Ashkenazi Jewish population has a higher prevalence of Gaucher Disease Type 1, Niemann-Pick Disease Type A, and Mucolipidosis IV, while patients of Finnish descent have been found to have higher rates of infantile neuronal Ceroid lipofuscinosis, Salla disease, and Aspartylglucosaminuria [15]. Sex: The ratio of afflicted persons who are male to female depends on the manner of heredity. Numerous IEMs come in a variety of shapes with varying inheritance patterns. When transmission occurs from mother to kid, the male to female ratio is 1:1 for autosomal recessive and 1:1 for autosomal dominant. Because males only have one X-linked chromosome, autosomal recessive X-linked IEMs are more common among them. Age: The onset of clinical symptoms can occur within hours of birth or very late in maturity, depending on the specific IEM and its variant forms. Presentation timing is dependent on either a substantial build-up of hazardous metabolites or a substrate shortage. Environmental factors including food and other illnesses may make the onset and severity worse. Energy production and protein or carbohydrate intolerance disorders typically manifest in the newborn period or early infancy and are often persistent and fast progressing. Less severe forms of these illnesses are typically episodic and manifest later in infancy or childhood. Infancy and childhood are typically when fatty acid oxidation abnormalities, glycogen storage, and lysosomal storage disorders first appear. Subtle neurologic or mental symptoms of disorders frequently do not show up or are not identified until adulthood.

Current inborn errors of metabolism in Nigeria

There is currently a lack of thorough information on the epidemiology of IEMs in Nigeria's six geographical zones. Although there are few studies that clearly demonstrate the prevalence of such evidence, there have been reports that provide insights into the existence of IEMs in Nigeria. Among these proofs are:

• A case study of Type IIIa glycogen storage disease: On January 11, 2016, a 14-month-old girl was referred to the pediatric gastroenterology clinic at the Lagos State University Teaching Hospital in Ikeja. She had experienced stomach swelling approximately three weeks prior to her presentation. She also suffered a two-week fever. There was no swelling in any other area of the body, but there was widespread, steadily growing abdominal edema accompanied by hard breathing. A collection of disorders known as glycogen storage disease (GSD) are brought on by inherited metabolic abnormalities in the synthesis or breakdown of glycogen in the muscles, liver, and other cell types [16]. Between 1 in 20,000 and 40,000 live babies is the estimated overall incidence of GSD [17]. More than 12 kinds of GSD have been identified based on the various enzyme abnormalities [17]. Every disease has a unique enzyme deficiency or failure. A condition that is autosomal recessive, GSD Type III is inherited. In honor of the scientists who first documented the disorder's characteristics, it is referred to as Forbes disease or Cori's disease. GSD Type III is caused by a lack of the enzyme amylo-1,6-glucosidase, which breaks down glycogen molecules completely [18]. GSD Type III is known as GSD Type IIIa when the enzyme shortage affects both the liver and the muscle, and GSD Type IIIb when it just affects the liver.

• Children's congenital abnormalities: One of the factors causing 5.1% of neonatal deaths and 3.5% of fatalities in children ages 1 to 59 months is congenital abnormalities. According to a study done at the University of Port Harcourt Teaching

Hospital, there are 20.73 serious congenital anomalies for every 1000 live births. Some congenital defects may be caused by underlying metabolic diseases, albeit they are not unique to IEMs.

• Increased morbidity and death among children under five: Studies have revealed that congenital diseases and inborn metabolic abnormalities are major causes of morbidity and mortality in Nigeria, yet they are still underdiagnosed and untreated.

Challenges

Nigerian IEMs deal with a number of difficulties. There are a number of reasons for this excessive workload and Nigeria's severe IEM data latency. These issues include under-reporting because of cultural beliefs and stigma, limited understanding among healthcare professionals, poor diagnostic and screening facilities, and restricted barriers to proper financing. The following should be implemented in order to lessen these difficulties:

To prevent missed diagnoses, concentrate on better access and raised clinician awareness. The ability of the healthcare system to manage and follow up on diagnosed instances should be strengthened.

To aid in the early detection and intervention of IEMs, newborn screening programs should be established. National newborn screening initiatives should be developed and implemented.

To enhance the number of newborn screening facilities available nationwide, more funding must be allocated to healthcare infrastructure and resources. This entails setting up screening facilities across the country, supplying the required equipment, and educating medical staff. O Providing policymakers with factual presentations that emphasize Nigeria's congenital illnesses, the necessity of developing a national policy in partnership with WHO to address the problem, and the measures the public should take to stop this quagmire.

More epidemiological study is required in order to ascertain the prevalence and range of IEMs in the various geographical areas.

Conclusion

It is evident from this research that there aren't many studies on IEM conducted in Nigeria. IEMs are a major contributor to child morbidity and mortality worldwide, accounting for a sizeable share of child fatalities that are not yet included in global modeling initiatives. Although there is a dearth of thorough information on the epidemiology of IEMs in Nigeria, the research that are now available demonstrate the prevalence of these conditions there. Therefore, the government, health organizations, medical professionals, and the general public must work together to address these issues related to IEMs in order to raise awareness, enhance the diagnostic resources available, and put in place efficient screening programs both domestically and internationally. To better establish the epidemiology of these disorders, particularly the epidemiology and rate of prevalence in Nigeria, more population-level research is necessary. Nigeria's public health system must effectively address the issues posed by this concerning trend now, not later.

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