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Diagnosis and Management of Pompe Disease in Saudi Arabia

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Abstract Pompe disease, firstly described in 1932 by J.C. Pompe, is a distinct form of glycogen storage disease (GSD) in which there is a generalized accumulation of glycogen within the lysosomes of heart, skeletal muscles, and nervous system. Pompe disease is a devastating condition in which there is progressive muscle weakness, organomegaly, respiratory failure, and ultimately death. In the Middle East, especially Saudi Arabia, a higher prevalence of genetic diseases was observed compared to reported rates from European countries and the United States (U.S). However, published data on the characteristics and treatment patterns of Pompe patients in Saudi Arabia are still lacking. Therefore, the present manuscript aimed to present an overview of the Pompe disease situation in Saudi Arabia by bringing together a panel of Saudi experts to share their views on current trends and practice in Saudi Arabia regarding Pompe disease. The panel agreed that there are no reliable data regarding the incidence of Pompe disease in Saudi Arabia, and future multicentre studies are needed. Besides, they recommended that the implementation of a nationwide screening program is essential for accurate estimation of the burden of Pompe disease and early diagnosis of the patients. The diagnosis of Pompe disease is challenging as the disease is obscure, even to general neurologists. Clinical diagnosis of LOPD has a place but can be unreliable because different manifestations share the same phenotypes. Novel screening methods involving NGS, such as whole-exome sequencing, are preferred for the diagnosis of Pompe disease etiologies. The experts recommended awareness campaigns to familiarize neurologists with Pompe disease. The availability of treatment for Pompe disease is critical in making newborn screening effective. Health care providers may play a role in providing treatment at an affordable cost in different centers in Saudi Arabia.

Keywords Pompe, Glycogen storage disease, NGS, Saudi Arabia

1. Introduction

Glycogen storage diseases (GSD) are a group of inborn errors of metabolism that is characterized by impaired glycogenesis or glycogenolysis pathways due to genetic defects in the involved enzymes [1]. Pompe disease, firstly described in 1932 by J.C. Pompe, is a distinct form of GSD in which there is a generalized accumulation of glycogen within the lysosomes of heart, skeletal muscles, and nervous system; hence, Pompe disease considered as a form of lysosomal storage diseases (LSD) [2]. The condition develops secondarily to a significant deficiency in acid α-glucosidase (GAA); to date, up to 582 gene mutations were identified as potential causes of GAA deficiency [3]. The incidence of Pompe disease varies widely across different regions and age groups; previous reports showed that the incidence of Pompe disease is 1 in 40,000 live births in the United States (U.S), 1 in 14,000 in live births among African American, 1 in 145,000 in live births in Australia, and 1 in 17,000 in live births in Taiwan [4–6]. Broadly, Pompe disease classified according to the age of onset and severity of the disease into infantile-onset (IOPD) and late-onset (LOPD).

Pompe disease is a devastating condition in which there is progressive muscle weakness, organomegaly, respiratory

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failure, and ultimately death [7]. Symptoms of Pompe disease usually develop when the GAA enzyme level becomes below 1%. The diagnosis of Pompe disease can be made through GAA assay, whether through a blood sample or cultured fibroblasts from skin or muscle biopsy. In patients with low GAA levels, the mutational cause of Pompe disease can be confirmed by gene sequence analysis [8]. Recent reports demonstrated that newborn screening programs targeting Pompe disease could have beneficial long-term outcomes in the affected patients [9]. The introduction of enzyme replacement therapy (ERT) has revolutionized the management of Pompe disease; currently, ERT is the most reliable treatment option [10].

In the Middle East, especially Saudi Arabia, a higher prevalence of genetic diseases was observed compared to reported rates from European countries and the United States (U.S) [11]. The high rate of consanguinity postulated as the main contributing factor to this high incidence [12]. However, published data on the characteristics and treatment patterns of Pompe patients in Saudi Arabia are still lacking. Therefore, the present manuscript aimed to present an overview of the Pompe disease situation in Saudi Arabia by bringing together a panel of Saudi experts to share their views on current trends and practice in Saudi Arabia regarding Pompe disease.

2. Consensus Development

The present manuscript developed as a part of the Saudi experts' efforts to address the current situation of Pompe disease in Saudi Arabia and to reach a national consensus in the diagnosis and management of Pompe disease. One advisory board meeting planned and engaged six medical geneticists and two neurologists from different geographical distribution. The Saudi experts represented current practice in different healthcare sectors across Saudi Arabia. The advisory board meetings took place in Riyadh on April 11th, 2019. The agreement of all experts reached the consensus statement in each aspect.

3. Incidence of Pompe Disease in Saudi Arabia

The global incidence of Pompe disease reported being 1 in 40,000 live births. Nevertheless, the current body of evidence shows wide geographical and ethnic variations in the incidence of Pompe disease. The highest incidence of Pompe disease reported among African Americans (1 in 14:000 live births) [4]. On the other hand, the incidence of the disease in Europe and Australia reported being as low as 1 in 283,000 and 1 in 145,000 in live births, respectively [13,14]. Among descents from South Asia, the incidence of Pompe disease reported being 1 in 17,000-50,000 live births [5,15].

Arab world represents one of the leading regions in terms of the incidence of congenital and genetic disorders; a growing body of published literature reported notable trends towards a higher incidence of congenital and genetic diseases, compared to other parts of the world [16]. High consanguinity rates that reach up to 60% in some regions, high prevalence of hemoglobinopathies and metabolic disorders, relatively high maternal and parental age, and lack of proper genetic screening reported as contributing factors for this high prevalence of genetic disorders in the Arab world [16–18]. In Saudi Arabia, the situation appears to be no different as previous retrospective studies showed a relatively high incidence of genetic diseases such as inborn error of metabolism.

The first retrospective study, which reported the incidence of inborn errors of metabolism in Saudi Arabia, utilized the data from the Saudi Aramco Medical Services Organization (SAMSO) that provides comprehensive health care residents of the Eastern Province. Out of 165,130 live births during this period, 248 cases had metabolic diseases, with 17 of these cases were GSD patients. The overall incidences of GSD and GSD type II (Pompe disease) were 1 in 9737 and 1 in 50,000 live births, respectively [19].

More recently, AlFadhel et al. [20] reported the number of cases with inborn errors of metabolism who presented at the Pediatric Department of King Abdulaziz Medical City in Riyadh from 2001 to 2014. The incidence of GSD type II was 2 in 110,601 live births. Besides, Al-Sannaa and colleagues [21] performed a hospital-based retrospective analysis to evaluate the incidence of LSDs in the Eastern Province of Saudi Arabia between 1983 and 2016. The incidence of GSD type II was 3.31 per 100,000 live births.

Of note, these figures appear to be similar to other retrospective charts from the Arab region. for example, Al-Jasmi et al. [22] reported that the incidence of GSD type II was 2.02 per 100,000 live births in the United Arab Emirates.

If we combined the incidence rate of Pompe disease in the abovementioned studies, we could conclude that the incidence of Pompe disease in Saudi Arabia is near 4 cases per 100,000 live births, which highlights the notable high prevalence of this disorder in Saudi Arabia, compared to other parts of the world.

However, the experts raised concerns about the generalizability of the published retrospective studies from Saudi Arabia on the total population of the Kingdom; the published reports included the liver births from one institution or one district of the Kingdom. Therefore, there is a need for multicentred studies to reflect the real epidemiology of Pompe disease in Saudi Arabia.

Another concern is the lack of a nationwide newborn screening program, which can help accurate estimation of the incidence of Pompe disease in Saudi Arabia.

As mentioned earlier, Pompe disease classified according to the age of onset and severity of the disease into IOPD and LOPD. The current body of evidence shows that LOPD is more common that IOPD [23]. In Saudi Arabia, the

published literature is scarce regarding the distribution of Pome disease subtypes; previous reports were confined to IOPD [24] or LOPD [24] only.

Consensus Statement: Most cases of Pompe disease clustered in the Northern and Southern areas of the Kingdom. Nonetheless, the exact prevalence of Pompe disease in Saudi Arabia is unknown. To date, there are no reliable data regarding the incidence of Pompe disease in Saudi Arabia, and future multicentred studies are needed. Also, there is an issue of undiagnosed patients, especially for LOPD, in which muscle weakness can be mistakenly recognized as usual aging effects. The experts suggested that Saudi Arabia has a higher prevalence of IOPD cases than LOPD, which is in contrast with the global figures. Therefore, the implementation of a nationwide screening program is essential for accurate estimation of the burden of Pompe disease and early diagnosis of the patients.

4. Diagnosis of Pompe Disease in Saudi Arabia

4.1. Clinical Presentation

Infants with IOPD usually present within the first few weeks of life with typical features of muscle disorder. Progressive weakness of skeletal muscle is the main cardinal feature of IOPD in which there is hypotonia, weak suckling, and motor delay. Besides, infants with IOPD usually have cardiomegaly (commonly hypertrophic cardiomyopathy). Other features of IOPD are hepatomegaly and macroglossia. As the disease progress, IOPD patients can develop respiratory failure, cardiac failure, and, eventually, death [25]. The differential diagnosis of IOPD includes infantile causes of hypotonia (such as hypoxic-ischemic encephalopathy, congenital myopathies, and congenital muscular dystrophies) and cardiomyopathy (such as storage diseases, endocardial fibroelastosis, myocarditis, and idiopathic hypertrophic cardiomyopathy) [2].

On the other hand, the LOPD usually develops after 12 months of age, with a mean onset of 29-33 years old. Patients with LOPD present mainly with muscular weakness of variable phenotypes; limb-girdle muscle weakness, weakness of neck flexion, scapular winging, and waddling gait are common phenotypes of LOPD. Less common phenotypes include scoliosis, osteoporosis, spinal rigidity, ptosis, dysphagia, and idiopathic hyperCKemia. Cardiac involvement in LOPD cases are less prominent than IOPD; previous reports showed that patients with LOPD are at higher risk of Wolff–Parkinson–White syndrome and cerebral aneurysm [26–28]. Nonetheless, cardiac involvement in LOPD remains uncertain. Other rare manifestations of LOPD include hearing loss and pre-symptomatic hyperCKemia [29,30]. The clinical diagnosis of LOPD is more complicated than IOPD due to features overlap with other causes of muscular dystrophy and myopathies [25].

4.2. Diagnostic Algorithm

4.2.1. Laboratory Evaluation

Patients with Pompe disease usually exhibit a high level of serum creatine kinase, up to 15 times than average values. Also, some patients show a high level of liver enzymes and lactate dehydrogenase, which usually correlated with the severity of the disease. Nevertheless, previous reports showed than almost 10% of Pompe disease patients had a reasonable level of serum creatine kinase, with or without elevated liver enzymes [31].

4.2.2. Electromyography

In patients with IOPD, electromyography (EMG) can reveal myotonic or pseudomyotonic discharges, alongside other abnormalities like repetitive discharges and fibrillation potentials. On the contrary, adult patients rarely show myotonic discharges on EMG studies; however, they can exhibit typical patterns of myopathy (small amplitude, short-duration, polyphasic motor unit action potentials) that involve proximal muscles mainly [32].

4.2.3. Cardiac Evaluation

The vast majority of infants with Pompe disease show cardiomegaly on chest radiography. Besides, the echocardiographic study usually reveals intra or biventricular septal thickness with left ventricular outflow obstruction. Shortened PR interval, inverted T wave, and a vast QRS complex may be present on electrocardiography (ECG). On the contrary, patients with LOPD rarely show cardiac abnormalities [33].

4.2.4. Pulmonary Function Tests

As the disease progress, the respiratory functions of the patients deteriorated due to diaphragmatic weakness; this weakness is evident when there is a>10% drop in the forced vital capacity (FVC) when the patient turns from upright to supine positions. Polysomnography should be considered in all patients due to the high incidence of sleep-disordered breathing [34,35].

4.2.5. Muscle Biopsy

Under the light microscopy, skeletal muscle biopsy usually exhibits vacuolated fibers filled with glycogen, the lysosomal source of this glycogen established by positive acid phosphatase stain. There is also free glycogen in the sarcoplasm. Mitochondrial abnormalities, such as Z-line streaming and thickening, can also be demonstrated [36]. Although muscle biopsy is an accurate method for diagnosis of Pompe disease, there is a high rate of false-negative results, especially in patients with LOPD. Previous reports indicated that a considerable proportion of adult patients show mild abnormalities in muscle biopsy; moreover, 20% of the LOPD patients show even standard muscle biopsy and glycogen content [31]. Other limitations of muscle biopsy include its invasiveness and a long time for results delivery

[2].

4.2.6. Confirmatory Tests

The definitive diagnosis of Pompe disease can be made through a GAA assay, whether through a blood sample or cultured fibroblasts from skin or muscle biopsy.

Measuring GAA activity within fibroblasts is an accurate method for diagnosis of Pompe disease; however, fibroblasts from skin biopsy take a long time to grow enough to measure GAA activity (4-6 weeks). On the other hand, fibroblasts from muscle biopsy grow faster, and the results can be obtained in less time than fibroblasts from skin biopsy; nevertheless, a muscle biopsy is not a complications-free procedure, especially in infants in whom general anesthesia is required [37].

The whole blood sample is an alternative, less invasive, a method for assessment of GAA activity. Lymphocytes are preferred over mixed leukocytes as neutrophils contain maltase glucoamylase (MGA), which leads to false-negative results. The purified lymphocytes preparation can provide a definitive diagnosis for Pompe disease without the need for muscle biopsy. However, the time window for isolation and purification of lymphocytes is only 30 minutes, which may preclude its utility in many centers that lack appropriate facility and trained personals [8].

Recently, the dried blood sample (DBS) has evolved as a new, non-invasive, and reliable technique for assessing GAA activity. The DBS technique depends on immunocapture, MGA inhibitors, or acarbose to stop the activity of MGA within the blood sample. Previous reports showed that DBS effectively identified adult patients with Pompe disease. Recent guidelines and consensuses recommend DBS as an initial screening test as negative test result likely excludes the diagnosis of Pompe disease. If the DBS shows reduced GAA activity, confirmatory testing should be performed by measuring GAA activity in cultures of fibroblasts or muscle tissue or by genetic testing [8,38,39].

4.2.7. Genetic Testing

Though the diagnosis of GSD can be established using traditional methods as mentioned above, identification of specific genetic mutations has become of great interest in recent years with the introduction of gene therapy. To date, up to 582 mutations in the *GAA* gene have been reported in individuals with Pompe disease [40]. Previous reports showed differences in the type of mutations across various ethnic groups [41]. Methods for detecting mutations include targeted mutational analysis, full sequence analysis, and deletion/duplication analysis; however, none of these have a 100% mutation detection frequency [42]. Next-generation sequencing (NGS) is a novel mutational analysis test that can generate a massive amount of data regarding DNA pairs through sequencing large numbers of genes in a single reaction. Owing to their advantages, the NGS has been introduced in the clinical field to identify genetic mutations in a wide range of disorders. Recent reports indicated high clinical utility, reduction in diagnostic delay, and reduction in sequence costs when NGS applied in the setting of inborn errors of metabolism [43]. Nevertheless, the use of NGS can be limited by technical difficulties and the need for trained personals [44].

4.3. CRIM Status Identification and Impact

Cross-reactive immunologic material (CRIM) status is an important prognostic factor during ERT. CRIM-negative patients are those who lack detectable, endogenous, GAA levels. CRIM-negative patients with classic IOPD usually develop neutralizing antibodies upon exposure to recombinant human GAA (rhGAA), which compromise the efficacy of ERT [45]. The currently published literature showed that CRIM-negative patients had a higher level of antibody titers, and they are more likely to experience progressive motor loss, mechanical ventilation, and death than patients with CRIM-positive status [46,47]. Thus, international guidelines recommend accurate identification of CRIM status before the initiation of ERT. The GAA genotype can predict the CRIM status if the patient's genotype has previously been associated with CRIM status [17] or by GAA Western blot analysis using cultured fibroblast lysates, a process that can take a few weeks [48]. The recent development of a blood-based assay for determining CRIM status expected to facilitate this process promptly [40].

Consensus Statement: The diagnosis of Pompe disease is challenging as the disease is obscure, even to general neurologists. Clinical diagnosis of LOPD has a place but can be unreliable because different manifestations share the same phenotypes. Novel screening methods involving NGS, such as whole-exome sequencing, are preferred for the diagnosis of Pompe disease etiologies. The experts recommended awareness campaigns to familiarize neurologists with Pompe disease.

5. Newborn Screening Program for Pompe Disease in Saudi Arabia

Pompe disease is a chronic, progressive disorder with multisystem affection and fatal disease course. Although patients with Pompe disease usually present with very distinctive physical features, most of the patients with Pompe disease are asymptomatic at birth [7]. Early diagnosis of Pompe disease can potentially reduce disease progression and improve the quality of life of the patients; thus, newborn screening methods are promising modalities for optimizing the outcomes of Pompe disease [49]. With the introduction and availability of tandem mass spectrometry (MS/MS) methods, it has become feasible to implement newborn screening programs for many metabolic disorders in both developed and developing countries. GSD screening programs have gained much attention recently, and pilot GSD programs conducted in many countries [50]. These

reports demonstrated that there are several feasible, effective, and affordable methods for Pompe disease screening programs, which can be extended to the larger population [49].

In the setting of GSD, different methods are available for early diagnosis of Pompe disease, based on the detection of the deficient enzyme activity using DBS punches. Conventional fluorimetric methods are one of the widely available techniques for the detection of enzymatic activity; however, it has limited value in testing multiple enzymes simultaneously [51]. MS/MS methods, which quantify the lysosomal enzyme activity, exhibited high diagnostic accuracy for the detection of GSD and high capacity for multiplex testing [52]. Recent reports have also introduced new, cheap, and feasible MS/MS-based methods for the mass detection of inborn errors of metabolism [53,54].

Such advances in the diagnostic methods have encouraged previous studies to conduct several Pompe disease neonatal screening programs; the aim of these studies was to evaluate the utility of neonatal screening for inclusion in primary screening programs. Using MS/MS technology, Scott et al. [49] assessed the enzymatic activity of 100,000 newborns from Washington State Newborn Screening Laboratory. A total of four cases of Pompe disease (incidence rate 1 in 27, 800 live births) and three carriers identified. Another neonatal screening study identified three cases of Pompe disease among 5055 anonymized newborn DBSs (1 in 8,657 live births) [55]. A newborn screening program since 2005 in Taiwan identified 13 (1 in 26,466) cases of LOPD [56]. The feasibility of newborn screening programs targeting Pompe disease was also reported in Austria and Hungary [5,57].

In Saudi Arabia, there are established national newborn screening program since 2005 that covers inborn error of metabolism, endocrine disorders, congenital heart defects, and hearing loss [58]. A recent 7-years retrospective study in 139 hospitals reported a high rate of inborn error of metabolism in Saudi Arabia compared to other parts of the world [59]. However, the inclusion of Pompe disease in the program has not been discussed yet. A previous Saudi consensus stated that a DBS screening test should be conducted in patients with unexplained weakness or suspected LOPD in the MENA region.

Consensus Statement:

The experts agreed that there is a need for a newborn screening program in Saudi Arabia that includes Pompe disease. The family screening will limit future siblings with Pompe disease and pick up on any undiagnosed relatives. However, there are a lot of local barriers to newborn screening in Saudi Arabia. The main barrier is the lack of precise data about the incidence rate and the absence of available treatment options that can make early diagnosis meaningful. Therefore, there is a need to provide reliable data about the incidence of Pompe disease before implementing newborn screening in Saudi Arabia. The availability of treatment for Pompe disease is critical in making newborn screening effective. Health care providers may play a role in providing treatment at an affordable cost in different centers in Saudi Arabia.

6. Management of Pompe Disease in Saudi Arabia

Ideally, effective treatment of Pompe disease should be able to prevent the intracellular accumulation of glycogen, slow disease progression, and restore enzyme activities. There are few treatment options available for the management of Pompe disease. In the early 1980s, hematopoietic stem cell transplantation (HSCT) introduced for the treatment of LSD, especially infants with Hurler syndrome [60]. However, previous reports showed that HSCT did not improve the clinical outcomes of Pompe disease patients [61]. Besides, HSCT is an invasive procedure with a high risk of mortality and morbidity [62].

More recently, ERT with rhGAA (alglucosidase alpha, Myozyme® , Genzyme Corporation, Framingham, MA) has emerged as a promising modality for Pompe disease management. In 2006, the rhGAA approved for the management of Pompe disease in the USA, Europe, Canada, and, subsequently, many countries [39]. The current body of evidence shows that the majority of CRIM-positive patients were stabilized or had improved CK levels and muscular and respiratory function following treatment with alglucosidase alfa [63]. A significant improvement in the quality of life, life expectancy, and survival observed after alglucosidase alfa treatment [45]. Various factors, including age and extent of muscle damage at the initiation of ERT, muscle fiber type, and defective autophagy, have been associated with varied responses to treatment [64].

In CRIM-negative patients, immune tolerance induction (ITI) can be initiated before ERT. The currently used ITI in clinical practice includes rituximab with plasma exchange and the combination of rituximab and methotrexate with or without intravenous gamma-globulin [46].

The current guidelines state that if a patient has secondary immunodeficiency (SID), suffers from hypertrophic cardiomyopathy, and has a positive DBS test with no feasible means of genetic testing is available; the patient should be treated as CRIM-negative (unless a sibling previously determined as CRIM-positive) [65].

Recently gene therapy was introduced as one of the promising options for many inherited diseases, including Pompe disease. The modality based on delivering the defective gene to the affected cells through a specific vector or injection [66]. In vitro studies using retro/lentiviral and adenoviral vectors showed an efficient expression of hGAA cDNA in human and murine myoblasts as well as secretion of GAA and reuptake by neighboring cells through MPR endocytosis [67,68].

Other novel experimental therapies for Pompe disease include substrate reduction therapy (SRT), anti-inflammatory therapy, and pharmacological chaperone therapy.

Consensus Statement:

ERT is the only approved modality for the treatment of Pompe disease in Saudi Arabia. In patients with LOPD, the experts agreed that MRI muscle changes and apparent clinical signs could be used to determine the start of treatment for LOPD. The experts recommended the establishment of a regional ERT center in the Kingdom, which would improve treatment outcomes. In contrast to global figures, the outcome of CRIM-positive IOPD patients is poor in Saudi Arabia. The Saudi experts agreed that the ITI should be initiated in CRIM-negative patients and patients with no defined CRIM status in a timely fashion. Miss-sense variant of uncertain significance (VUS) mutations are treated as CRIM-positive, whereas truncating mutations treated as CRIM-negative.

The experts also agreed that there is a need for Saudi consensus regarding the diagnosis and treatment of Pompe disease in Saudi Arabia. The consensus should be comprehensive and involve all specialties that deal with Pompe disease in order to share their ideas and suggestions. All key players must be invited to this type of meeting; the meeting can be conducted in the form of a national Pompe disease day. Another exciting idea is to develop a national day for rare diseases in which experts get together and hence move forward.

7. Discussion

Saudi Arabia is the largest country in the Arabian Peninsula, with a population of more than 28 million [69]. Despite healthcare being free to Saudi citizens, several potential barriers to healthcare access and individual healthcare-seeking have been reported [70,71]. While Pompe disease is a rare disease, its incidence in Saudi Arabia appears to be higher than in other parts of the world. Nevertheless, no previous nationwide study conducted to provide reliable data regarding the incidence and characteristics of Saudi patients with Pompe disease. The published literature is scarce regarding the treatment patterns and outcomes of Pompe disease in Saudi Arabia as well.

The Saudi experts held a consensus meeting to gather views from a panel of Saudi experts on current trends and practice regarding MPS in Saudi Arabia, and to compare their views with current global trends and practice. Panel members highlighted the need for a central, unified, and updated national registry to monitor the current trends of Pompe disease in the Kingdom.

Although measurement of GAA activity and molecular testing are considered essential diagnostic tools by the panel members, many Saudi healthcare facilities do not have access to GAA, and molecular tests and many samples are sent abroad for testing; thus, an average time for Pompe disease diagnosis and referral from the first presentation may be prolonged with the high possibility of false results due to malpractice during sample handling and transportation. The experts have also raised issues around the availability of drugs and their costs. Finally, the panel members recommended the development of educational and quality improvement programs to improve physicians' knowledge and awareness about Pompe disease.

8. Conclusions and Recommendations

There are no reliable data regarding the incidence of Pompe disease in Saudi Arabia, and future multicentred studies are needed. Besides, there is an issue of undiagnosed patients, especially for LOPD, in which muscle weakness can be mistakenly recognized typical aging effects.

Therefore, the implementation of a nationwide screening program is essential for accurate estimation of the burden of Pompe disease and early diagnosis of the patients.

The diagnosis of Pompe disease is challenging as the disease is obscure, even to general neurologists. Clinical diagnosis of LOPD has a place but can be unreliable because different manifestations share the same phenotypes.

Novel screening methods involving NGS, such as whole-exome sequencing, preferred for the diagnose of Pompe disease etiologies.

The experts recommended awareness campaigns to familiarize neurologists with Pompe disease.

The experts agreed that there is a need for a newborn screening program in Saudi Arabia that includes Pompe disease, However, there are a lot of local barriers to newborn screening in Saudi Arabia. The main barrier is the lack of precise data about the incidence rate and the absence of available treatment options that can make early diagnosis meaningful. Therefore, there is a need to provide reliable data about the incidence of Pompe disease before implementing newborn screening in Saudi Arabia.

The availability of treatment for Pompe disease is critical in making newborn screening effective. Health care providers may play a role in providing treatment at an affordable cost in different centers in Saudi Arabia.

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Conflict of Interest

Marwan ElBagoury and Yahia Aktham are employees of Sanofi Genzyme.

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