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Correspondence

Serendipitous discovery of phenylketonuria in Iraq – How to identify and treat?

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Early Phenylketonuria (PKU) diagnosis and treatment is vital in order to prevent irreversible damage such as neurological impairment and intellectual disability [1]. Largely, PKU and other metabolic disorders have not been systematically evaluated and reported in Iraq including KRG (Kurdistan Region; Northern Iraq). Because of that, metabolic disorders, including PKU, have possibly been underestimated [2]. The purpose of this letter is to raise awareness and bring to the forefront the urgent need for prevalent NBS and appropriate treatment of children in Iraq and other economically developing countries, in addition to highlighting solutions for going forward.

With the high incidence of consanguine marriages in the Middle East there is increasing prevalence of PKU and other metabolic disorders. The overall worldwide prevalence of PKU is 6.002 per 100.000 neonates. The highest prevalence (38.13) was reported in Turkey, while the lowest (0.3) in Thailand [3]. Among Arab countries, Turkey and Iran, the prevalence of classical PKU in countries having national newborn screening (NBS) programs ranges from 0.005% to 0.0167%. The highest prevalence was reported for Turkey (0.0167%) and the lowest one for the UAE (0.005%) [2]. A study conducted in Iraq in 2013 indicated that from seven cases detected with PKU all of them have had consanguineous parents [4].

NBS has not yet become prevalent in Iraq thus the screening for metabolic disorders or a phenylalanine level is not normally requested until a patient is already experiencing symptoms. In some cases, symptoms are treated without even considering the possibility of a PKU diagnosis. In the Arab countries, only a few countries such as Saudi Arabia, UAE, Qatar, and Turkey have implemented comprehensive national NBS programs with relatively high coverage that aim for early detection of PKU along with other treatable disorders in an attempt to reduce disability rates [2]. The absence of NBS leaves the Iraqi population vulnerable to the delayed diagnosis of PKU and other metabolic diseases that could be detected early giving the person the opportunity to seek appropriate treated. Metabolic disorder screening is very important for symptomatic infants, children, and adults, especially in the absence of NBS. However, as with all chronic diseases, long-term management can be challenging and many adult patients with PKU become lost to follow-up. In the KRG, there are only two laboratories where measurements of amino acids can be done in addition to a panel that helps diagnose other rare metabolic disorders. The amino acid panel is crucial for the monitoring and adjustment of a patient's diet.

The central government in Baghdad is the official provider of the metabolic formulas to all the Iraqi territory, including the Kurdish area. Unfortunately, due to continuous conflicts inside the territory, the provision of formula from Baghdad is not consistent nor in sufficient quantities, increasing the frustration of the families and healthcare professionals dealing with PKU.

As a consequence of constant conflicts, the healthcare system has been disrupted and the university system adversely affected, resulting in a general lack of awareness and understanding regarding the diagnosis, treatment, and on-going management of PKU and other rare metabolic disorders among the local healthcare professionals.

In a recent effort by health workers from different international organizations to help families with children with special needs in KRG, some of these children were found to be positive for PKU. Since then, it has been discovered around thirty-three children in Kurdistan (Dohuk, Erbil and Sulaimania) needing help due to PKU. In this context, a nine year old boy diagnosed with cerebral palsy was mistreated with a high-protein diet for three years until the family changed doctors, and a PKU diagnosis was made. In the past three years of being on the PKU diet and formula, the boy has improved significantly. The frequency of seizures have decreased and the children is able to walk with some assistance. However, he is unable to talk, understand yes or no, or do any activities of daily living independently.

With the lack of specialists in Iraq, many families seek assistance in Iran and Turkey, which hinders the ability for regular follow-up due to travel restrictions and/or financial problems. Multiple parents have reported not following up with their physicians in Turkey or Iran for months, in some cases, over a year, due to not being able to travel. In one case, a child remained on the same diet plan for over a year, losing rather than gaining weight.

The American College of Medical Genetics and Genomics released medical guidelines to treat PKU in 2014 [1]. The guidelines contained evidence based and/or expert opinion on recommendations regarding diagnosis, treatment and care for patients with PKU of all ages. Implementing these guidelines, would improve access to screening, treatment and monitoring. Given large parts of the world fall behind in even basic standards for screening, management practices vary widely in PKU centers, countries and regions, making it even more critical that this

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detailed plan is implemented in economically developing countries. This plan would also include education about chronic conditions like PKU in displaced populations, accurate data collection, rebuilding and recruiting metabolic teams and focusing on standards of care for all by minimizing risk.

Considering the challenges and difficulties briefly mentioned here, the following measures are understood as urgent in favour of the Iraqi population:

- Implementation of prevalent NBS across Iraq, which would allow early PKU diagnosis and treatment;
- Establishment of local Health Agencies, specially in KRG and Sinjar due to their distance from Baghdad, responsible for receiving the metabolic formulas from Baghdad and distributing it to the the families with relatives diagnosed with PKU;
- Raising awareness about consanguine marriage and associated diseases including PKU;
- Development of programs for education and training of government officials and those in the healthcare system on the importance of NBS and the specialized PKU diet;
- Collaboration with international healthcare professionals and metabolic specialists for training and counseling of local healthcare professionals;
- Implementing the key recommendations for PKU management according to current guidelines from the American College of Medical Genetics and Genomics.

Further discussions and research is required to understand chronic health needs like PKU and effects on future generations. Due to the continuing crisis in Iraq, international assistance is needed to accomplish the previously mentioned goals.

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Daniele Suzete Persike de Oliveira[a,*], Kendra J. Bjoraker[b]

[a] *College of Pharmacy, University of Dohuk, Kurdistan Regional Government (KRG), Iraq*

[b] *3:1 Neuropsychology Consultants, PLLC, United States of America*

[*] Corresponding author.

E-mail addresses: daniele_persike@protonmail.com (D.S. Persike de Oliveira), bjorakerneuro@gmail.com (K.J. Bjoraker).