Molecular Genetics and Metabolism Reports 39 (2024) 101082

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism Reports

journal homepage: www.elsevier.com/locate/ymgmr

Editorial

Treating the whole patient: Facilitating health care for patients facing health inequity☆

ARTICLE INFO

Keywords:
Social determinants of health
Urea cycle disorders
Phenylketonuria
Socioeconomic barriers
Health inequity
Rare disease

ABSTRACT

Social determinants of health (SDOH) are conditions in which people are born, grow, live, work, and age. Variations in these conditions are largely responsible for health inequities, the differences in health status or distribution of health resources within a population. Despite recent increases in attention to SDOH in research and clinical practice, few, if any, resources exist to describe how these complex dynamics impact patients with inborn errors of metabolism. Recognizing the role real-life narratives have as a powerful educational tool, we compiled a series of 3 original cases, published as part of this special supplement, to illustrate challenges and learnings related to SDOH within the context of urea cycle disorders and phenylketonuria.

In the complicated landscape of managing inborn errors of metabolism (IEMs), such as urea cycle disorders (UCDs) and phenylketonuria (PKU), the significant impact of social determinants of health (SDOH) emerges as a pivotal yet intricate element. Health outcomes in patients with IEMs are profoundly shaped not only by the complex biochemical impacts of the IEM itself but also by the interplay of socioeconomic disparities, psychosocial intricacies, and health literacy barriers [1–5]. Challenges related to economic disparity and health inequity loom large within the IEM sphere, imposing barriers to diagnosing patients, accessing emergent care, and acquiring essential treatment/nutritional support critical for optimizing health outcomes [6–10]. In this issue of *Molecular Genetics and Metabolism Reports*, we explore SDOH-related hurdles within the context of UCDs and PKU. We examine a variety of barriers through invaluable narratives of patient case studies, shedding light on the socioeconomic and psychological intricacies that management plans must consider. This supplement illustrates how deeply SDOH influence the management of IEMs.

As improvements are made to addressing health inequities, progress can be found in areas such as state-run newborn screening (NBS) programs, more of which are including select IEMs [11,12]. Early identification and diagnosis of IEMs allows for prompt development of a management plan that can reduce the comorbidities and mortality associated with these disorders. However, individuals with limited health literacy obtain less information from disease state educational materials and may be less likely to undergo follow-up screening or pursue specialist referrals to properly manage their condition [3]. Although NBS is a notable example of public health success because it has saved and improved the lives of many individuals with IEMs, low socioeconomic status (SES) and economic factors, such as reliable transportation, prevent NBS alone from catching individuals who may fall through the cracks [13]. In the case presented by Andrews and McMinimee, PKU was identified successfully in an 8-year-old girl through NBS. Although she was responsive to sapropterin, maintaining metabolic control was hindered by lack of transportation. Data from the National Health Interview Survey (1997–2017) revealed that in 2017, 5.8 million people in the United States postponed medical care due to lack of transportation [13]. The patient's care was also hindered by her caregiver's variable employment status, lack of stable internet/phone, housing instability, homeschooling, and food insecurity. Families affected by housing insecurity frequently have challenges accessing medical care, which can be especially problematic for children with long-term health needs who are particularly vulnerable to the impact of inconsistent medical care [14]. Further, a family's economic hardships can be compounded by the cost of low-protein modified foods, which cost 2 to 8 times more than unmodified foods, making them extremely difficult to obtain for many individuals [8,9]. The authors illustrate how some common sources of aid, such as telehealth, school meal programs, and patient outreach events, were unable to meet the needs of this patient and that more tailored patient-centric approaches were necessary.

Health inequities can be particularly high-risk in emergent care settings, especially when there are health literacy or limited English proficiency barriers to communicating with health care professionals [7]. In the case presented by McNutt, a Black female patient with argininosuccinic aciduria (ASA) ultimately died of hyperammonemia after hospital providers did not treat her condition urgently, despite caregiver requests. The case explores how SDOH impact physicians' management decisions. Studies have shown that physicians are less likely to perceive patients with low SES as intelligent, responsible, or rational and believe

Abbreviations: ASA, argininosuccinic aciduria; IEM, inborn errors of metabolism; NBS, newborn screening; PKU, phenylketonuria; SDOH, social determinants of health; SES, socioeconomic status; UCD, urea cycle disorder.

☆ This paper is part of a Supplement supported by Amgen Inc.

https://doi.org/10.1016/j.ymgmr.2024.101082
Received 26 January 2024; Accepted 13 April 2024
Available online 18 April 2024

they are less likely than other patients to comply with medical recommendations and return for follow-up care [4,15,16]. Physicians also delay diagnostic testing, prescribe more generic medications, and avoid referral to specialists for patients with low SES versus other patients [17]. The patient in this case was additionally burdened by a long history of inadequate care at home and an unstable family environment, including her mother's substance abuse, housing insecurity, and unsafe living conditions. The patient's health worsened during a brief period in foster care because of inadequate communication about her disorder. When welfare agencies place children in out-of-home settings to facilitate safety and well-being, the children tend to display more behavioral, educational, and psychological difficulties than their peers [18]. Challenges associated with out-of-home settings are multiplied when coupled with a rare chronic illness for which experienced medical care is limited and a high level of health literacy is needed to achieve metabolic stability [3,10,19,20]. This case explores these facets of public health and raises thought-provoking questions regarding the complicated issues providers face when trying to provide the best care for patients with IEMs.

SDOH encompass far more than financial circumstances, and the inherent challenges caused by the physiological impacts of IEMs can exacerbate health inequities. This is illustrated in the case of a 7-year-old Burmese boy with neonatal-onset ASA presented by Vucko et al. In addition to financial hardships, the patient's immigrant parents faced language, health literacy, and cultural barriers to executing recommended management plans. For example, language barriers and cultural/linguistic nuances in communication via translators play a role in both the amount of time needed and level of understanding achieved during clinical visits [21]. This case illustrates how local resources are complex to navigate, particularly for nonnative speakers. Additionally, there are fewer translation resources for languages less commonly spoken in the United States (eg, Burmese) and immigrants often have inadequate social support networks, which further hinders caregivers' awareness of and access to local resources [21,22]. Extracting key information regarding a patient's social situation is a sensitive process for clinicians, and some may prefer to focus on medical treatment and lifestyle counseling [23]. However, the importance of assessing social situations is evident in this case. Because of the continued and evolving support by the clinical team, the family was linked to various resources. This tailored support enabled the family to achieve metabolic control for their son despite setbacks and adversity.

The intermixing of psychosocial hardships and health inequity erects formidable barriers within the narrative of IEMs. To improve our health care system and make progress toward health equity, it is important for clinicians to have a working understanding of the diverse patients and communities that they may serve now or in the future. However, there are not enough published case reports documenting details of long-term management in the context of health equity barriers and how these challenges may be addressed. Overworked and burdened clinicians often desire to help address health inequities but lack tools or understanding in how to do so. In this supplement, we highlight the powerful narratives of patients with IEMs whose management was negatively impacted by SDOH. We identify shortcomings in the management of these patients and potential solutions to illustrate ways to increase health equity across patients with diverse backgrounds. We hope that by bringing greater attention to these complex facets of patient care, improvements can be made in patient-centric approaches that recognize the intricate interplay between SDOH and the management of UCDs and PKU.

Funding

Amgen Inc. funded manuscript editorial support, including editorial review, author coordination, and manuscript submission. No authors received compensation for the preparation of this manuscript outside of normal employment obligations.

CRediT authorship contribution statement

Amarilis Sanchez-Valle: Writing – original draft. **Corey Hicks:** Writing – original draft.

Declaration of competing interest

ASV has served as the primary investigator for multicenter clinical trials sponsored by Alexion, Amicus, Biomarin, Homology, Jnana, Recordati, and Ultragenyx. She has participated in advisory boards and/or received honoraria from Acer, Amgen Inc., Applied Therapeutics, Biomarin, Jnana, and Ultragenyx. CH is an employee of Amgen Inc.

Data availability

No data was used for the research described in the article.

Acknowledgments

Editorial support and medical writing, under the guidance of the authors, were provided by Azadeh Kia, PhD, at The Lockwood Group (Stamford, CT, USA) in accordance with Good Publication Practice (GPP3) guidelines.

References

[1] E.M. Tejada-Ortigosa, K. Flores-Rojas, L. Moreno-Quintana, M.C. Muñoz-Villanueva, J.L. Pérez-Navero, M. Gil-Campos, Health and socio-educational needs of the families and children with rare metabolic diseases: qualitative study in a tertiary hospital, An. Pediatr. (Engl. Ed.) 90 (2019) 42–50, https://doi.org/10.1016/j.anpede.2018.03.005.

[2] S.A. Fleary, R. Ettienne, Social disparities in health literacy in the United States, Health Lit. Res. Pract. 3 (2019) 47–52, https://doi.org/10.3928/24748307-20190131-01.

[3] S.S. Coughlin, M. Vernon, C. Hatzigeorgiou, V. George, Health literacy, social determinants of health, and disease prevention and control, J. Environ. Health Sci. 6 (2020) 3061. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7889072.

[4] M. Van Ryn, J. Burke, The effect of patient race and socio-economic status on physicians' perceptions of patients, Soc. Sci. Med. 50 (2000) 813–828, https://doi.org/10.1016/S0277-9536(99)00338-X.

[5] J.A. Cederbaum, C. LeMons, M. Rosen, M. Ahrens, S. Vonachen, S.D. Cederbaum, Psychosocial issues and coping strategies in families affected by urea cycle disorders, J. Pediatr. 138 (2001) S72–S80, https://doi.org/10.1067/mpd.2001.111839.

[6] M.H. Wojcik, M. Bresnahan, M.C. del Rosario, M.M. Ojeda, A. Kritzer, Y.S. Fraiman, Rare diseases, common barriers: disparities in pediatric clinical genetics outcomes, Pediatr. Res. 93 (2023) 110–117, https://doi.org/10.1038/s41390-022-02240-3.

[7] C.K. Gutman, K.C. Lion, C.L. Fisher, P.L. Aronson, M. Patterson, R. Fernandez, Breaking through barriers: the need for effective research to promote language-concordant communication as a facilitator of equitable emergency care, J. Am. Coll. Emerg. Physicians Open 3 (2022) e12639, https://doi.org/10.1002/emp2.12639.

[8] K.E. Coakley, S. Porter-Bolton, M.L. Salvatore, R.B. Blair, R.H. Singh, Food insecurity in females with phenylketonuria, JIMD Rep. 53 (2020) 103–110, https://doi.org/10.1002/jmd2.12115.

[9] S.A. Berry, M.K. Kenney, K.B. Harris, R.H. Singh, C.A. Cameron, J.N. Kraszewski, J. Levy-Fisch, J.F. Shuger, C.L. Greene, M.A. Lloyd-Puryear, C.A. Boyle, Insurance coverage of medical foods for treatment of inherited metabolic disorders, Genet. Med. 15 (2013) 978–982, https://doi.org/10.1038/gim.2013.46.

[10] A.M. Rose, S.D. Grosse, S.P. Garcia, J. Bach, M. Kleyn, N.-J.E. Simon, L.A. Prosser, The financial and time burden associated with phenylketonuria treatment in the United States, Mol. Genet. Metab. Rep. 21 (2019) 100523, https://doi.org/10.1016/j.ymgmr.2019.100523.

[11] Health Resource and Service Administration, Baby's First Test, Available from, https://www.babysfirsttest.org/newborn-screening/states, 2022.

[12] N.Ah. Mew, K.L. Simpson, A.L. Gropman, B.C. Lanpher, K.A. Chapman, M. L. Summar, Urea cycle disorders overview, in: M.P. Adam, H.H. Ardinger, R. A. Pagon, S.E. Wallace (Eds.), GeneReviews® [Internet], University of Washington, Seattle, Seattle (WA), 2003. Apr 29 [Updated 2017 Jun 22]. 1993–2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1217/.

[13] M.K. Wolfe, N.C. McDonald, G.M. Holmes, Transportation barriers to health care in the United States: findings from the National Health Interview Survey, 1997–2017, Am. J. Public Health 110 (2020) 815–822, https://doi.org/10.2105/AJPH.2020.305579.

[14] D.B. Cutts, A.F. Meyers, M.M. Black, P.H. Casey, M. Chilton, J.T. Cook, J. Geppert, S.E. De Cuba, T. Heeren, S. Coleman, R. Rose-Jacobs, D.A. Frank, US housing insecurity and the health of very young children, Am. J. Public Health 101 (2011) 1508–1514, https://doi.org/10.2105/AJPH.2011.300139.

[15] J.K.H. Woo, Effect of patient socioeconomic status on perceptions of first- and second-year medical students, Can. Med. Assoc. J. 170 (2004) 1915–1919, https://doi.org/10.1503/cmaj.1031474.
[16] N.C. Arpey, A.H. Gaglioti, M.E. Rosenbaum, How socioeconomic status affects patient perceptions of health care: a qualitative study, J. Prim. Care Community Health 8 (2017) 169–175, https://doi.org/10.1177/2150131917697439.
[17] S.M. Bernheim, J.S. Ross, H.M. Krumholz, E.H. Bradley, Influence of patients' socioeconomic status on clinical management decisions: a qualitative study, Ann. Fam. Med. 6 (2008) 53–59, https://doi.org/10.1370/afm.749.
[18] M. Winokur, A. Holtan, K.E. Batchelder, Kinship care for the safety, permanency, and well-being of children removed from the home for maltreatment, Cochrane Database Syst. Rev. (2014), https://doi.org/10.1002/14651858.CD006546.pub3. CD006546.
[19] G. Yeowell, D.S. Burns, F. Fatoye, The burden of pharmacological treatment on health-related quality of life in people with a urea cycle disorder: a qualitative study, J. Patient Rep. Outcomes 5 (2021) 110, https://doi.org/10.1186/s41687-021-00387-x.
[20] J.K. Stoller, The challenge of rare diseases, Chest 153 (2018) 1309–1314, https://doi.org/10.1016/j.chest.2017.12.018.
[21] G. Flores, The impact of medical interpreter services on the quality of health care: a systematic review, Med. Care Res. Rev. 62 (2005) 255–299, https://doi.org/10.1177/1077558705275416.
[22] C.D. Chang, Social determinants of health and health disparities among immigrants and their children, Curr. Probl. Pediatr. Adolesc. Health Care 49 (2019) 23–30, https://doi.org/10.1016/j.cppeds.2018.11.009.
[23] A. Andermann, CLEAR collaboration, taking action on the social determinants of health in clinical practice: a framework for health professionals, Can. Med. Assoc. J. 188 (2016) E474–E483, https://doi.org/10.1503/cmaj.160177.

Amarilis Sanchez-Valle[a,*], Corey Hicks[b]
[a] *Department of Pediatrics, Division of Genetics and Metabolism, University of South Florida, 2 Tampa General Cir 5th Floor, Tampa, FL 33606, USA*
[b] *Ultra-Rare Medicines, Amgen, One Amgen Center Dr, Thousand Oaks, CA 91320, USA*

[*] Corresponding author at: 2 Tampa General Cir 5th Floor, Tampa, FL 33606, USA.
E-mail address: Asanche6@usf.edu (A. Sanchez-Valle).