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Prevalence of Glucose-6-Phosphate Dehydrogenase Deficiency among Thalassemia Patients Attending Yemen Society for Thalassemia, Sana'a.

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Abstract:

***Background**: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzyme deficiency worldwide. Determining the prevalence of G6PD deficiency is an essential step toward evaluating its impact on the community health especially Thalassemia patients. **Aim**: To determine the prevalence of G6PD deficiency and classification of severity of G6PD deficiency among Thalassemia patients in Yemen Society for Thalassemia and Genetic Blood Disorders(YSTH). **Methods**: A cross-sectional study was conducted at YSTH. All Thalassemia patients who are registered in (YSTH), were enrolled in this study. 67 patients were selected using simple random sampling method. Data on demographic characteristics of patients and their parents was collected using a pre-designed questionnaire. G6PD deficiency was qualitatively detected and quantitative test of G6PD was performed on who deficient to assess the severity of deficiency. SPSS was used for statistical analysis. **Results** : Out of 67 screened Thalassemia patients (40 males and 27 females), 4 patients(3 male and 1 female patients) were G6PD-deficient, with an overall prevalence of 6.0 %. G6PD deficiency was not significantly associated with sex of patients. Results of the study showed that all patients who have G6PD deficiency have moderate deficiency. **Conclusion**: G6PD deficiency is prevalent among Thalassemia patients. It is more prevalent among males than females, and it was not statistically significantly associated with sex and consanguinity between the parents. All G6PD deficiency patients were on moderate class according to WHO classification.*

Keywords: Thalassemia; G6PD deficiency; Rapid diagnostic test; Sana'a

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Introduction

Glucose-6-phosphate dehydro-genase (G6PD) deficiency is a genetic metabolic abnormality caused by deficiency of the enzyme G6PD, the normal functioning of red blood cells depends on this enzyme. [1] G6PD deficiency comprises the most common enzyme deficiency worldwide, the enzyme glucose-6-phosphate dehydrogenase aids in the detoxification of free radicals, protecting cells from oxidative damage. [2]

Most of the time, those who are affected live without symptoms. [1] Following a specific triggers (food, drugs and infection) symptoms may develop.[1-3] World Health Organization (WHO) has classified variants on the basis of residual enzyme activity and of disease severity into five classes. [1-4] Thalassemia is an

inherited disease, blood disorder caused when the body doesn't make enough of a protein called hemoglobin, an important part of red blood cells that cause anemia condition. [5] There are two main types, alpha thalassemia and beta thalassemia. [6]

About 400 million people worldwide suffer from the disease, male are more likely to be affected than female. [3] G6PD deficiency resulted in 3,400 deaths in 1990, 4,100 deaths in 2013 and 33,000 death in 2015. [7-8] A total of 8.96 million were born with glucose-6-phosphate dehydrogenase deficiency in 2019. [9] In some countries, the disease has a prevalence of 25%. [10] Thalassemia affects approximately 280 million people in 2015, of whom approximately 439,000 have severe condition. [8]

Both thalassemia and G6PD deficiency are congenitally independent hemolytic diseases, the co-heredity of the two diseases has a greater influence on RBCs pathology than is usually seen in either disease alone, G6PD deficiency co-inherited with male thalassemia was resulted in worse RBC pathology than hereditary thalassemia alone. [11]

A study conducted in Yemen showed that G6PD deficiency was prevalent in about 5.0% of newborns at Sana'a city hospital. [12]

Another study in Yemen showed that the prevalence of thalassemia was 13%, (4.43%) features suggestive of beta-Thalassemia and features suggestive of alpha-thalassemia (8.6%) in Sana'a. [13]

However, no previous studies had been published on the prevalence of G6PD deficiency among Thalassemia patients in Yemen so far. Therefore, the present study aimed to determine the prevalence and classification of severity of G6PD deficiency among Thalassemia patients in Yemen Society for Thalassemia and Genetic Blood Disorders, Sana'a – Yemen.

Aim of the study: To determine the prevalence of Glucose-6-Phosphate dehydrogenase deficiency and the classification of severity of G6PD deficiency among Thalassemia patients in Yemen Society for Thalassemia and Genetic Blood Disorders.

Materials and Methods

A descriptive, cross-sectional study was conducted to assess prevalence of Glucose-6-Phosphate dehydrogenase deficiency among Thalassemia patients at The Yemen Society for Thalassemia and Genetic Blood Disorders (YSTH), Sana'a – Yemen. All Thalassemia patients who are registered in (YSTH), during the period from 15th Apr. 2000 till Oct 2021 were enrolled in this study.

The study protocol was approved by the Research Ethics Committee of the University of Al-Razi - Sana'a. Informed consent was obtained from the parents or guardians of the patients after explaining the purpose of the study.

A sample size was calculated based on an expected prevalence of G6PD deficiency of 5.0% [12] at a confidence level of 95.0% and an accepted marginal error of 5.0%. However, 67 Thalassemia patients were included in the present study.

67 patients were selected using simple random sampling method. A list of demographic characteristics of the patients were collected using a pre-designed, structured questionnaire through interviews. Fresh blood samples were collected from Thalassemia patients (40 males and 27 females).

Qualitative screening for G6PD deficiency was performed on fresh venous blood using CareStart™ G6PD rapid diagnostic tests (RDTs) (Access Bio, New Jersey, USA) according to the manufacturer's instructions [14], Briefly, two microliters of blood were added into the sample well and two drops of buffer into the buffer well. Test results were read visually after 10 minutes. Samples with normal G6PD activity produce a distinct purple color background in the result window while no color change was observed for samples with deficient G6PD activity. Samples with a pale purple color background were classified as normal.

Quantitative screening was done for patients who showed a deficiency results to detect the level of G6PD deficiency. The quantitative test calculates the G6PD activity in a sample of whole blood and provides a numerical result. Standard TM G6PD test kit (SD Biosensor, Inc, Korea) was used and the procedure in briefly, 10 microliters of blood were added into the extraction buffer, mix and transfer 10 microliters from

the extraction buffer into the test device, after 2 minutes of reaction time, the test results appeared.

According to WHO classification of G6PD [4]

Class I : Very Severe, level of G6PD <1%.
Class II : Severe, level of G6PD 1-10 %.
Class III : Moderate, (enzyme levels 10-60%).
Class IV : Normal activity (enzyme level 60 – 150 %).

Statistical Package for the Social Sciences (SPSS) version 20.0 was used for data entry and analysis. Descriptive statistics such as percentages and frequencies for categorical data were determined.

The categorical outcomes were analyzed using Chi-square test to show the significance of association, *P-value* < 0.05 was considered significance. The study protocol was approved by the Research Ethics Committee of the University of Al-Razi - Sana'a. Informed consent was obtained from the parents or guardians of the patients after explaining the purpose of the study.

Results

General characteristics of Thalassemia patients

Of 67 patients, 40 were males and 27 were female, with a male: female ratio of 1.4:1 with aged ranged from 1- 40 years. In the other hand, the majority of Thalassemia patients were from Hajjah governorate at percentage of 28.3%. More than half of Thalassemia patients were in basic school 56.7%, 84% had a poor income with only 7% had a good income (Table 1).

Of Thalassemia patients, 81% were born to consanguineous parents, nearly half of mothers were illiterate (52.2%). Among fathers, a third of them had a high school education (31.3%) (Table 2).

G6PD deficiency was detected among 6% of the Thalassemia patients (Figure 1), nearly half of the patients (50.7%) had relatives with a positive history of Thalassemia diseases (Figure 2)

Factors associated with G6PD deficiency

G6PD deficiency was 3-fold higher in males than females (7.5% vs. 3.7%, respectively) with a male: female ratio of 3:1, but the difference was not statistically significant (OR = 2.1; 95 % CI: 0.047–4.81, *p* = 0.467, also, consanguinity between parents was not significantly associated with G6PD deficiency (*p*=0.181) (Table 3).

Discussion

Up to the best of our knowledge, this study is assumed to be the first in Yemen that revealed the prevalence of Glucose-6-Phosphate Dehydrogenase deficiency among Thalassemia patients. The prevalence rate that found in this study may be the base for future studies in the same subject.

For the prevalence of Glucose-6-Phosphate Dehydrogenase deficiency among Thalassemia patients the current study showed that it was (6.0%). Several previous studies showed similar results to the current study, such that done by Al-Nood *et al., (*2012) in Yemen which found that the Glucose-6-Phosphate Dehydrogenase deficiency prevalence was (7.1%). [15] Another study done in Sana'a City has reported that (5.0%) of newborns in the hospitals of Sana'a city were Glucose-6-Phosphate Dehydrogenase deficient.[12]

Glucose-6-Phosphate Dehydrogenase deficiency was observed in South Western Region Nepal with (4.8%) of Thalassemia patients**.** [16] A study conducted in Thailand reported that Glucose-6-Phosphate Dehydrogenase deficiency with Thalassemia was present in (10%) of the participants, resulting in worsening of red blood Cell pathology compared with inheritance of Thalassemia alone. [17]

The result of the current study showed that male had the large percentage with (75%) from patients with both Glucose-6-Phosphate Dehydrogenase deficiency and Thalassemia. This study showed that gender had no significant association with Glucose-6-Phosphate Dehydrogenase deficiency. Several previous studies showed similar results to the result of the current study that most of the

Glucose-6-Phosphate Dehydrogenase deficiency patients were males.

For example, a study in Egypt reported that Glucose-6-Phosphate Dehydrogenase deficiency was significantly higher among male compared with female neonates in Egypt (6.2% vs. 2.1%, respectively) with a male: female ratio 3.2: 1. 18 The lack of statistically significant association the gender of thalassemia patients and G6PD deficiency in the present study is consistent with the findings results of a study in Yemen found that G6PD deficiency was more prevalent among males than females, with no statistically significant difference, 2.4-fold higher in males than females (6.5% vs. 2.8%, respectively) with a male: female ratio of 2.8:1. 12

Table 1. Demographic characteristics of Thalassemia patients (N =67)

Demographic characteristics	**F**	**%**
Sex		
• Male	40	59.7
• Female	27	40.3
Age range in year		
• ≤ 5	11	16.4
• 6-10	24	35.8
• 11-15	21	31.3
• 16-20	8	12.0
• > 21	3	4.5
Educational level		
• Illiterate	2	3.0
• Before school	23	34.3
• Basic education	38	56.7
• Secondary education	3	4.5
• Bachelor or above	1	1.5
Residency		
• Hajjah	19	28.3
• Sana'a	16	23.9
• Mahweet	8	11.9
• Dhamar	7	10.4
• Amran	6	9.0
• Al-Hudaydah	4	6.0
• Ibb	4	6.0
• Al-Jawf	1	1.5
• Raymah	1	1.5
• Taiz	1	1.5
Income		
• Poor	56	84
• Moderate	6	9
• Good	5	7

Table 2. Demographic characteristics of parents (N =67)

Demographic characteristics	F	%
Educational level (fathers)		
• Illiterate	19	28.3
• Literate	2	3
• Basic education	17	25.4
• Secondary education	21	31.3
• Bachelor or above	8	12
Educational level (mothers)		
• Illiterate	35	52.2
• Literate	2	3
• Basic education	22	32.8
• Secondary education	7	10.5
• Bachelor or above	1	1.5
Consanguinity between parents		
• Yes	54	81
• No	13	19

Table 3. Factors associated with G6PD deficiency among Thalassemia patients (n=67).

Variable		Total	Deficient		*p*-value
		N	*n*	(%)	
Sex	Male	40	3	7.5	0.467
	Female	27	1	3.7	
Consanguinity between parents	Yes	54	4	7.4	0.181
	No	13	0	0	

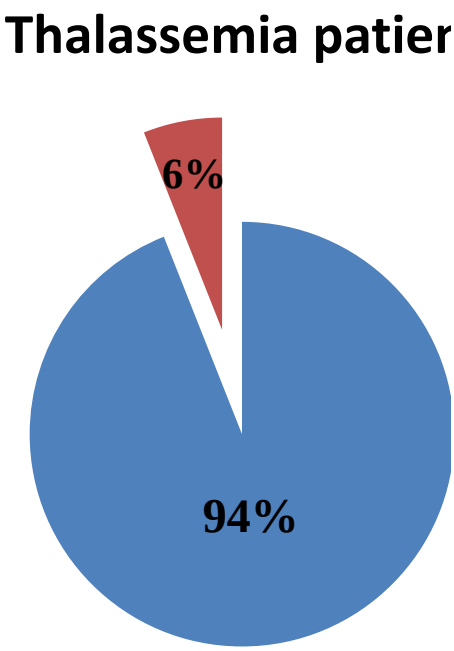

Figure 1 : Prevalence of Glucose-6-Phosphate Dehydrogenase Deficiency among Thalassemia Patients

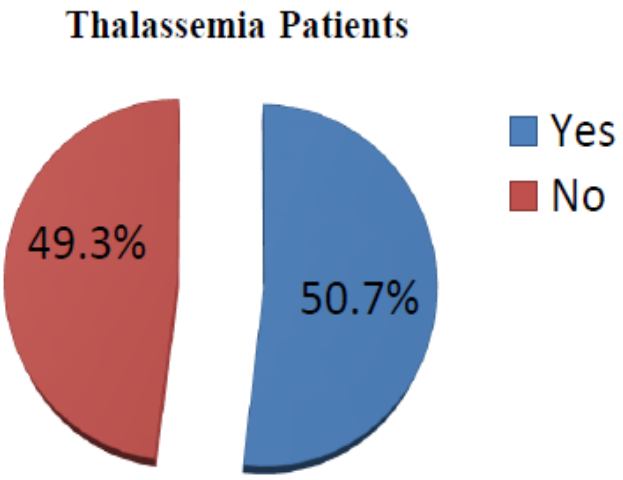

Figure 2 : Distribution of thalassemia patients according to family history of thalassemia disease

In **Nigeria** a study done in **2017** the results showed that the prevalence of Glucose-6- Phosphate Dehydrogenase deficiency was concentrated predominantly among male subjects (22%). While (2.4%) among females. [19]

The higher G6PD deficiency rate among males is because that the disorder is recessively X-linked, leading to its greater expression in males as they have only one X-chromosome with no ability to suppress the expression of the defective gene. However, the heterozygous females having one defective gene and one normal gene may express as normal or mild deficient and may not be detected by usual screening tests or even enzyme assays. [20-21]

Because G6PD deficiency is a hereditary disease, the result of the current study showed that there was a consanguinity between all parents of Thalassemia patients who had Glucose-6-Phosphate Dehydrogenase deficiency.

A study in Yemen reported that among newborns with Glucose-6-Phosphate Dehydrogenase deficiency in Sana'a city, Yemen (57.9%) had consanguinity between parents while (42.1%) had no consanguinity between parents. [12] Another study between Egyptian neonates showed that family history of Glucose-6-Phosphate Dehydrogenase deficiency and consanguinity were reported among (67.3%). [22] In contrast, a study done in Pakistan has revealed that consanguinity was present in around (41.6%) of the neonates who had Glucose-6-Phosphate Dehydrogenase deficiency. [23]

Conclusion

G6PD deficiency is prevalent among Thalassemia patients (6%). It is more prevalent among males than females, and it was not statistically significantly associated with sex, consanguinity between the parents and income. All G6PD deficiency patients were on moderate class according to WHO classification.

References

1. *NORD (National Organization for Rare Disorders) 2017.* "Glucose-6-Phosphate Dehydrogenase Deficiency". Author is Ilan Youngster Retrieved from https://rarediseases.org/rare-diseases/glucose-6-phosphate-dehydrogenase-deficiency (Accessed at: 11 May 2022).
2. Monteiro, W. M., Val, F. F., Siqueira, A. M., Franca, G. P., Sampaio, V. S., Melo, G. C., ... & Marcus Vinícius G, L. (2014). G6PD deficiency in Latin America: systematic review on prevalence and variants. Memórias do Instituto Oswaldo Cruz, 109, 553-568.
3. *Genetics Home Reference* "Glucose-6-phosphate dehydrogenase deficiency". . MedlinePlus is the New Home of Genetics Home Reference. National Library of Medicine . Last updated May 1, 2017 accessed at *6 June 2022*.
4. World Health Organization (WHO). Glucose-6-phosphate dehydrogenase deficiency. Working Group. Bull World Health Organ. 1989;67(6):601-611
5. CDC Centers for Disease Control and Prevention, 2021, Thalassemia Homepage, What is Thalassemia? Retrieved from https://www.cdc.gov/ncbddd/Thalassemia /facts.html (accessed at 15 July 2022).
6. National Heart, Lung, and Blood Institute (NHLBI) NIH, Thalassemia Causes, "What Are Thalassemias?". . Last updated on June 01, 2022, Retrieved from : https://www.nhlbi.nih.gov/health/Thalassemia/causes , Accessed at 3 July 2022.
7. Global Burden of Disease (GBD) 2013 Mortality and Causes of Death, Collaborators. "Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013". Lancet. 385 (9963): 117–71.
8. Global Burden of Disease (GBD) 2015 Mortality and Causes of Death, Collaborators. "Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for

the Global Burden of Disease Study 2015". Lancet. 388 (10053): 1459–1544.
9. IHME (The Institute for Health Metrics and Evaluation) 2019 G6PD deficiency — Level 4 cause Retrieved from : http://www.healthdata.org/results/gbd_summaries /2019/g6pd-deficiency-level-4-cause (Accessed at : 3 April 2022)
10. LaRue N, Kann M, Murray M, Leader BT, Bansil P, McGray S, et al. Comparison of quantitative and qualitative tests for glucose-6-phosphate deficiency. Am J Trop Med Hyg. 2014;91:854–61.
11. Pengon, J., Svasti, S., Kamchonwongpaisan, S., & Vattanaviboon, P. (2018). Hematological parameters and red blood Cell morphological abnormality of Glucose-6-Phosphate dehydrogenase deficiency co-inherited with Thalassemia. Hematology/oncology and stem Cell therapy, 11(1), 18-24.
12. Nassar, M., Hudna, A., Alhaj, A., Alqubaty, A., Alqahtani, T. Glucose-6-Phosphate Dehydrogenase Deficiency among Newborns in Sana'a City, Yemen. Zagazig University Medical Journal, 2020; (806-813): -. doi: 10.21608/zumj.2020.32403.1876 .
13. Al-Nood H. Thalassemia trait in outpatient clinics of Sana'a City, Yemen. Hemoglobin. 2009;33:242–246.
14. Access Bio, 2020 , CareStart™, G6PD rapid diagnostic tests (RDTs) Retrieved from:https://accessbio.net/products/rapid-diagnostic-tests/carestart-g6pd-rdt - accessed at 11 July 2022.
15. Al-Nood, H. A., Bazara, Fakiha A., Al-Absi Rashad & Habori Molham (2012). Glucose-6-Phosphate Dehydrogenase deficiency among male blood donors in Sana'a city, Yemen. Oman medical journal, 27(1), 46.
16. Gautam, N., Gaire, B., Manandhar, T., Marasini, B. P., Parajuli, N., Lekhak, S. P., & Nepal, M. (2019). Glucose 6 phosphate dehydrogenase deficiency and hemoglobinopathy in South Western Region Nepal: a boon or burden. BMC Research Notes, 12(1), 1-6.
17. Pengon, J., Svasti, S., Kamchonwongpaisan, S., & Vattanaviboon, P. (2018). Hematological parameters and red blood Cell morphological abnormality of Glucose-6-Phosphate dehydrogenase deficiency co-inherited with Thalassemia. Hematology/oncology and stem Cell therapy, 11(1), 18-24.
18. Elella, S. A., Tawfik, M., Barseem, N., & Moustafa, W. (2017). Prevalence of glucose-6-phosphate dehydrogenase deficiency in neonates in Egypt. Annals of Saudi medicine, 37(5), 362-365.
19. Jidda, M., Ibrahim, K., Aiki, G., Ngaski, A., Blessing, J., Asiya, U., & Nwachukwu, C. (2017). The Prevalence of Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency in Students of Sultan Abdurrahaman School of Health Technology Gwadabawa, Sokoto, North-Western Nigeria. International Blood Research & Reviews, 7(4), 1-6.
20. Behjati-Ardakani S, Sedaghat ANM: The association between G6PD deficiency and total serum bilirubin level in icteric neonates. Acta Med Iran 2007; 233-5.
21. Weng YH, Chiu YW: Spectrum and outcome analysis of marked neonatal hyperbilirubinemia with blood group incompatibility. Chang Gung Med J 2009; 32(4): 400-8.
22. Kasemy, Z. A., Bahbah, W. A., El Hefnawy, S. M., & Alkalash, S. H. (2020). Prevalence of and mothers' knowledge, attitude and practice towards glucose-6-phosphate dehydrogenase deficiency among neonates with jaundice: a cross-sectional study. BMJ open, 10(2).
23 Shahzeen, A. A. J., Kayani, A., Zubair, A., Noreen, R., & Fatima, S. (2022). Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency in Neonates Presenting with Indirect Hyperbilirubinemia in Neonatal Intensive Care Unit of Tertiary Health Care Center of Pakistan: Is the Trend Changing with Change in Consanguineous Marriages?. Fortune Journal of Health Sciences, 5(3), 510-516.

انتشار عوز إنزيم سداسي فوسفات الجلوكوز النازع للهيدروجين بين مرضى الثلاسيميا المترددين على الجمعية اليمنية لمرضى الثلاسيميا – صنعاء.

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الخلاصة

الخلفية: يعتبر أنيميا عوز إنزيم سداسي فوسفات الجلوكوز النازع للهيدروجين أكثر أنواع نقص الإنزيم شيوعًا في جميع أنحاء العالم. يعد تحديد مدى انتشار عوز إنزيم سداسي فوسفات الجلوكوز النازع للهيدروجين خطوة أساسية نحو تقييم تأثيره في صحة المجتمع وخاصة على مرضى الثلاسيميا **الهدف:** تحديد مدى انتشار أنيميا عوز إنزيم سداسي فوسفات الجلوكوز النازع للهيدروجين وتصنيف شدة نقص الإنزيم بين مرضى الثلاسيميا في الجمعية اليمنية للثلاسيميا واضطرابات الدم الوراثية. **الطرق:** تم إجراء دراسة وصفية مقطعية لتقييم انتشار أنيميا عو ز إنزيم سداسي فوسفات الجلوكوز النازع للهيدروجين بين المرضى المترددين على الجمعية اليمنية لمرضى الثلاسيميا والدم الوراثي صنعاء– اليمن .جميع مرضى الثلاسيميا المسجلين في الجمعية هم مجتمع هذه الدراسة. تم اختيار ٦٧ مريضا باستخدام طريقة أخذ العينات العشوائية البسيطة. تم جمع البيانات عن الخصائص الديموغرافية للمرضى وأولياء أمورهم باستخدام استبيان مصمم مسبقًا. تم الكشف عن نقص الإنزيم نوعيًا وتم إجراء اختبار كمي للإنزيم لمن يعاني من النقص لتقييم شدة النقص. وتم استخدام برنامج SPSS للتحليل الإحصائي. **النتائج:** من بين ٦٧ مريضاً بالثلاسيميا تم فحصهم (٤٠ ذكراً و٢٧ أنثى)، كان ٤ مرضى (٣ ذكور ومريضة واحدة) يعانون من أنيميا عوز إنزيم سداسي فوسفات الجلوكوز النازع للهيدروجين ، مع معدل انتشار إجمالي قدره ٦,٠٪. لم يرتبط نقص الإنزيم بشكل كبير بجنس المرضى. أظهرت نتائج الدراسة أن جميع المرضى الذين يعانون من أنيميا عوز إنزيم سداسي فوسفات الجلوكوز النازع للهيدروجين لديهم نقص متوسط. **الاستنتاج:** أنيميا عوز إنزيم سداسي فوسفات الجلوكوز النازع للهيدروجين منتشر بين مرضى الثلاسيميا. وهو أكثر انتشارا بين الذكور منه بين الإناث، ولم يكن له ارتباط ذو دلالة إحصائية بالجنس أو صلة القرابة بين الوالدين. جميع مرضى أنيميا عوز إنزيم سداسي فوسفات الجلوكوز النازع للهيدروجين يعانون من نقص متوسط حسب تصنيف منظمة الصحة العالمية.