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Original Research Article

Prevalence of glucose-6-phosphate dehydrogenase deficiency in newly diagnosed HIV patients: a hospital-based cross-sectional study

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ABSTRACT

Background: The prevalence of Glucose-6-phosphate dehydrogenase (G6PD) deficiency is 8.5% in India. G6PD deficient individual have different outcomes with certain drugs and result in unexpected events that could be even fatal. HIV affected individuals with G6PD deficient have inherently worse outcomes when they start on those drugs that precipitate the condition. We aimed to study the level of G6PD and its deficiency status among the newly diagnosed HIV patients.
Methods: A cross-sectional study among the newly diagnosed HIV patients was conducted at a tertiary hospital, Kolkata. All the eligible participants (n=100) were recruited consecutively after obtaining the consent. The details on socio-demography, clinical history and investigations were extracted from them. The data were analysed using the appropriate statistical methods.
Results: Out of 100 newly HIV diagnosed participants, the prevalence of G6PD deficiency was 12% (95% CI: 5.6-18.3%). Participants belonging to tribal population, with familial history of haemolytic disease, history of haemolysis, and increased LDH levels were significantly associated with the deficient G6PD levels among the study participants.
Conclusions: The prevalence of G6PD deficiency was high among the newly diagnosed HIV study population. Tribal population and familial history of haemolytic disorders had high number of deficiency and need to be screened for better clinical care.

Keywords: Human immuno-deficiency virus, Hospital, Tertiary care, Glucose-6-phosphate dehydrogenase deficiency

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is one of the most common inherited haemolytic disorders among humans affecting around 400 million people worldwide.[1] G6PD forms the only source of reduced nicotinamide adenine dinucleotide phosphate hydrogen (NADPH) in erythrocytes and catalyses the rate-limiting step in the pentose phosphate pathway. Erythrocyte antioxidant pathways require NADPH; those with low G6PD activity are unable to face oxidative stress causing intravascular and extravascular haemolysis. A common presentation of G6PD deficiency is acute haemolysis that is manifested by oxidative stressors, like fava beans, primaquine, sulfonamide, or infection.[2] Because of its X-linked inheritance pattern, male hemi zygotes and female homozygotes show more severe clinical phenotypes, whereas female heterozygotes show phenotypic variability due to random X inactivation.[3]

Screening of G6PD is being done among those who take prophylaxis of malaria.[4] The benefits of screening HIC infected patients are unclear. Since trimethoprim-sulfamethoxazole (TMP-SMX) and dapsone are commonly used in HIV-infected patients that can lead to

life-threatening haemolysis in case of G6PD deficient individuals. Interestingly, at one HIV clinic the prevalence of G6PD deficiency was around 10%; and among those receiving oxidative stress-inducing drugs, 10% developed severe haemolysis, indicating the potential danger of these drugs and need of G6PD screening in HIV infected patients [5.] HIV infected, G6PD deficient individuals may also have inherently worse outcomes i.e., oxidative stress, acute haemolysis, exacerbate HIV infection.[6-12] Thus, G6PD deficiency may play a role in the prognosis and treatment of HIV infected patients. This study was done to determine the prevalence of G6PD deficiency in set of newly diagnosed HIV infected individuals using a comprehensive testing approach.

METHODS

A cross-sectional study was done for 18 months from February 2018 to August 2019 at medical college and Hospital Kolkata. It was a tertiary hospital-based study among those patients with newly diagnosed HIV disease. The patients were identified either at OPD or at IPD of general medicine department and ART clinic. The newly diagnosed HIV patients who were yet to receive any treatment, aged between 18 and 60 years, and known case of G6PD deficiencies were included after getting written informed consent. If there were any female pregnant patients or known case of non-G6PD haemolytic anemia, then they were excluded. The prevalence of G6PD deficiency in India was 8% in general population.[13] By considering the caseload of G6PD deficiency based on medical records of the last 3-4 years at this institute, we arrived at the sample size of 100. The participants were enrolled consecutively based on the eligibility criteria. The basic demographic details, clinical history & examination, and certain investigations i.e., G6PD enzyme quantitative assay, CD4 count, haemoglobin level, and serum LDH were performed on the study participants. Venous sample was collected both clotted blood for serum LDH, and anticoagulated blood for G6PD activity, haemoglobin and CD4 count. G6PD level was determined in the laboratory by UV kinetic method for quantitative estimation of G6PD in erythrocytes. The enzyme G6PD present in the red blood cells is extracted by lysing the cells using a natural detergent. The extracted enzyme oxidizes G6PD to 6-phosphogluconate and simultaneously reduces co-enzyme NADP to NADPH giving increase in absorbance at 340nm. The initial absorbance is read and absorbance reading is repeated every 1, 2 and 3 minutes. The mean absorbance change per minute is then calculated.

Statistical analysis

Data were entered into a Microsoft Excel and then analysed by SPSS version 24.0. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate, $p \leq 0.05$ was considered as statistically significant.

RESULTS

A total of 100 newly diagnosed HIV patients were enrolled in the present study. Males (74%) formed the predominant population in the study. The mean (SD) age of the study participants was 38.2 (±8.3) in years. The minimum and maximum age of the study participants were 25, and 57 years respectively. Only few (35%) were above 40 years of age. Among the non-tribals and non-Muslim's, there were 67.1% participants (n=49) belonging to 14 different casts (Table 1).

Table 1: Socio-demographic details of the study participants (n=100).

Variables	N (%)
Age (years)	
≤30	21 (21.0)
31-40	44 (44.0)
41-50	25 (25.0)
51-60	10 (10.0)
Sex	
Male	74 (74.0)
Female	26 (26.0)
Religion	
Hindu	73 (73.0)
Muslim	27 (27.0)
Ethnicity	
Bengali	90 (90.0)
Non-Bengali	10 (10.0)
Community	
Tribal	27 (27.0)
Non-tribal	73 (73.0)

The prevalence of G6PD deficient was found in 12% (95% C.I.: 5.6-18.3%) of the newly diagnosed HIV patients. There were three levels of G6PD activity i.e. <6.4 U/gm of Hb in 12%, 6.4 to 10 U/gm of Hb 86%, and >10 U/gm of Hb 2.0% seen among the study participants. There was history of malaria among 54% of the study participants. One third of them found to be anemic (32%) and only 2% had increased LDH. The mean (SD) of the CD4 count, Hb in gm/dl, and serum LDH were 297.1 (±55.5), 12.5 (±1.5), and 270.7 (±72.8), respectively. There were no severe anemic participants, and the lowest and highest value of Hb (gm/dl) was 8.8, and 15.0, respectively. By logistic regression, it was found that tribals, patients with history of haemolysis, family history of haemolytic diseases, and increased LDH had higher odds of developing G6PD deficiency than those did not belong to that category. The odds of developing G6PD deficiency among HIV participants from non-tribal

population was 79% less compared to participants with normal G6PD activity in HIV participants (COR: 0.21 (95% CI: 0.06-0.73), p value: 0.01) and statistically significant. Familial history of haemolytic diseases had significant association with G6PD deficiency (COR: 0.04, 95% CI: 0.06-0.73, p value: 0.01). There was no significant association between age, sex, religion, history of malaria, or anaemia (Table 2).

Table 2: Association between G6PD activity and selected variables (n=100).

Variable	G6PD deficient (n=12) Frequency (%)	Normal (n=88) Frequency (%)	Total (n=100) Frequency (%)	COR (95% CI), p value	P value by Chi-Square	Chi-Square value
Age (years)						
≤40	7 (58.4)	58 (65.9)	65 (65.0)	0.72 (0.21-2.47), 0.60	0.50	0.90
>40	5 (41.6)	30 (34.1)	35 (35.0)			
Sex						
Male	10 (83.3)	64 (72.7)	74 (74.0)	1.87 (0.38-9.18), 0.43	0.66	0.18
Female	2 (16.7)	24 (27.3)	26 (26.0)			
Religion						
Hindu	10 (83.3)	63 (71.6)	73 (73.0)	1.98 (0.40-9.70), 0.39	0.60	0.26
Muslim	2 (16.7)	25 (28.4)	27 (27.0)			
Ethnicity						
Tribal	7 (58.3)	20 (22.7)	27 (27.0)	0.21 (0.06-0.73), 0.01	0.02	5.10
Non-Tribal	5 (41.7)	68 (77.3)	73 (73.0)			
History of malaria						
No	4 (33.3)	42 (47.7)	46 (46.0)	0.54 (0.15-1.95), 0.35	0.52	0.39
Yes	8 (66.7)	46 (52.3)	54 (54.0)			
History of haemolysis						
No	9 (75.0)	88 (100.0)	97 (97.0)	0.01 (0.0007-0.31), 0.007	0.000	14.9
Yes	3 (25.0)	0 (0.0)	3 (3.0)			
Family history of haemolytic diseases						
No	11 (91.7)	88 (88.9)	99 (99.0)	0.04 (0.001-1.12), 0.05	0.23	1.38
Present	1 (8.3)	0 (0.0)	1 (1.0)			
Anemia						
Absent	7 (58.3)	61 (69.3)	68 (68.0)	0.61 (0.18-2.12), 0.44	0.66	0.18
Present	5 (41.7)	27 (30.7)	32 (32.0)			
Increased LDH						
No	10 (83.3)	88 (89.8)	98 (98.0)	0.02 (0.001-0.52), 0.01	0.005	7.67
Yes	2 (16.7)	0 (0.0)	2 (2.0)			

COR- Crude odds ratio.

There was no significant mean difference between G6PD deficient and normal individuals with respect to age, CD4 counts and haemoglobin (Table 3).

DISCUSSION

The present study was done to measure the prevalence of G6PD deficiency among newly HIV diagnosed patients. There is no previous study on G6PD deficiency in newly diagnosed HIV positive patients in India and there are also a handful of studies which have been done worldwide. G6PD deficiency were not related to gender but males were predominant similar to other studies.[14,15] This could be due to more male participants tested positive for HIV. There was no religion or cast predominance among the G6PD deficient participants. But in tribal population, the prevalence of G6PD was high which could be attributed to their migration from their maternal place i.e. hilly forest malaria prone regions.

Age and religion were not related to G6PD deficiency in the present study similar to Aneke et al.[16]

Table 3: Mean difference between G6PD deficient and normal participants of selected variables (n=100).

Variable	G6PD Deficient (N=12) Mean (SD)	Normal (N=88) Mean (SD)	P value
Age (years)	39.0 (8.9)	38.1 (8.3)	0.74
CD4 count	299.5 (53.6)	296.7 (56.1)	0.87
Haemoglobin (gm/dl)	11.7 (2.1)	12.6 (1.4)	0.06

The prevalence of G6PD deficiency in present study was similar to another study by Mukherjee et al but it was lower in another meta-analysis by Kumar et al.[13,14] This finding of increased prevalence of G6PD deficiency in tribal people than non-tribal were similar to the findings of study done by Mukherjee et al.[17] In deficient G6PD group, 8 (66.7%) patients had H/O malaria. In normal G6PD group, 46 (52.3%) patients had H/O malaria. Association H/O malaria vs. G6PD deficiency was not statistically significant (p=0.52). There had been contrasting reports regarding the association of G6PD deficiency and protection against falciparum malaria as seen in study by Peters et al.[18]

Association of history of haemolysis vs. G6PD deficiency was statistically significant. This is similar to the findings by Julia et al where 57.1% deficient patients had h/o haemolysis.[15] Shanthala et al found that there was no significant mean difference between the individuals with G6PD deficient and normal population, alike to the present study.[19] In deficient G6PD patients, the mean CD4 count (mean±SD) of patients was 299.5±53.6.

In normal G6PD patients, the mean CD4 count (mean±SD) of patients was 296.7±56.1. Distribution of mean CD4 count vs. G6PD was not statistically significant (p=0.87). The present study was unique in Indian setting as there was no study on G6PD activity in HIV patients in India. The result could not be generalised due to its innate study design and setting. Our sample size was also less and molecular characterizations of the G6PD variants were not assessed.

CONCLUSION

The prevalence of glucose-6-phosphate dehydrogenase deficiency was relatively high among these newly diagnosed HIV patients with no severe clinical manifestations and significantly higher among tribal population. Considering the expenses incurred in diagnosis, the test to analyse G6PD level ought to be performed cautiously on the suspects.

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