Prevalence of Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency across Tribal, Non-Tribal, and Mixed Populations in Northeast India: A Review

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ABSTRACT

The paper aims to highlight the prevalence of G6PD deficiency among various populations in Northeast India. This region, including Nagaland, Assam, and Manipur, shows significant rates of G6PD deficiency. Populations such as the Angami Naga of Nagaland (27.06%), Muslims of Manipur (21.32%), Mizos of Mizoram (17.5%) and the Rabha and Mikir populations of Assam exhibit a high frequency of G6PD deficiency, exceeding 15%, with an overall regional prevalence of 6.56%. The overall frequency of G6PD deficiency is higher among the tribal populations (8.37%), while non-tribal populations show 4.40% and mixed populations 4.88%. These differences are statistically significant, as indicated by chi-square values of 27.4397 (p<0.00001) and 16.9447 (p=0.000038) respectively. The frequency trends reflect a complex interplay of genetic factor and environmental pressures, particularly malaria in the region.

Keywords: G6PD, prevalence, tribal, non- tribal, mixed population, Northeast India

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme that plays an essential role in cell metabolism. Its primary function is to neutralize oxidising substances and protect red blood cells from oxidative stress. Adequate levels of G6PD enzyme are therefore required to prevent such stress; otherwise oxidative stress can destroy red blood cells, leading to a condition called haemolytic anaemia. The G6PD gene is located in the long arm of X-chromosome and consists of 13 exon (Martini et al.1986). G6PD deficiency is one of the most common enzymatic disorders in humans, affecting more than 400 million people worldwide, and is characterised by considerable biochemical and molecular heterozygosity (Luzzatto et al. 1995). Allison (1960) and Motulsky (1960) reported that G6PD deficiency provides a selective advantage in the presence of malarial parasitaemia. The deficiency of the G6PD enzyme is highly polymorphic in the malaria endemic regions and represents an example of balanced polymorphism, in which the high mortality associated with the disorder is offset by the protection it offers against *plasmodium falciparum* malaria (Luzzatto et al. 1979).

Alleles of the G6PD gene that encode a deficient enzyme attain high frequencies in regions where malaria is or has been endemic (Nagel et al. 1989). It has also been reported that decreased parasitaemia is observed among patients with G6PD deficiency, and the malaria parasite does not grow well in G6PD deficient red cells compared to normal cells (Roth et al. 1988). However, this protective effect is reported to be stronger in hemizygous males than in homozygous females (Aldiouma et al. 2007).This disorder is believed to have been naturally selected in regions with endemic malaria. A correlation has been observed between the high prevalence of malaria caused by *plasmodium falciparum* and the incidence of G6PD deficiency (Mohnty et al. 2003). The paper presents a comprehensive review of the prevalence of glucose-6-phosphate dehydrogenase (G6PD) deficiency among tribal, non-tribal, and mixed populations in Northeast India. It examines existing studies to provide insights into population specific differences and the overall epidemiological patterns of G6PD deficiency in the region.

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MATERIALS AND METHOD

Secondary data were collected from libraries in the form of journals, reference books. Research papers and articles were also sourced from Elsevier, PubMed, Google Scholar, Research Gate for comparative analysis. The selected literature includes reports by Seth and Seth, 1971; Flatz et al. 1972; Das et al. 1982; Dash et al. 2005, Achoubi et al. 2010; Basumatary et al. 2021; and Parween et al. 2024, excluding hospital-based studies. A total of 6125 individuals from different states of Northeast india were included in the study (excludiding Sikkim due to unavailability of reports). The populations were grouped into tribal, non-tribal and mixed categories (the mixed category includes populations not specifically identified in the earlier reports). Among them, 3,152 belonged to tribal populations, 1,887 to non-tribal, and 1,086 to mixed populations. The chi-square test was employed to assess the significance.

RESULTS AND DISCUSSION

The state-wise distribution of G6PD deficiency among the North-eastern states of India is presented in Table 1. The Northeast region of India, particularly the state of Assam, is significant with regards to G6PD deficiency, as prevalence rates of 15% or higher has been reported among the Rabha and Mikir (Karbi) populations of Assam (Das et al. 1982). Das et al. (1982) also reported a G6PD deficiency rate of above 11% among the Garo and Rajbanshi populations of Assam. A G6PD deficiency rate of 5% or higher has been observed among the Ahom, Mishing, Khasi, and Dimasa populations of Assam (Flatz et al. 1972; Parween et al. 2024). In contrast, G6PD deficiency has not been detected in certain communities in Assam, such as the Chutia, Bodo, Brahmin, Bengali and Bihari (Parween et al. 2024). Among some caste populations, G6PD deficiency ranges from 0.8% in Kalitas to 4.32% in Assamese populations (Flatz et al. 1972; Parween et al. 2024). Intermediate frequencies are observed in Nepali (1.4%), Rajbongshi (1.4%), Muslim (1.5%), Tea Garden Labourers (1.8%), Kachari (20%), Kochari (2.1%), Ahom (2.4%), Deori (2.7%), Koibotter (3.4%), and Lalung with 3.7% (Flatz et al 1972; Parween et al. 2024). The frequency of G6PD deficiency is notably high among certain Mongoloid tribal populations of Assam and those with a close ethnic affinity to these groups (Das et al. 1982). The protective advantage of G6PD deficiency in malarial environments is a well-established concept, which helps explain the high prevalence of this trait among various populations in Northeast India (Das et al. 1982; Kar et al. 1995; Seth et al. 1971).

Table 1: Frequency distribution of G6PD enzyme deficiency in various populations of Northeast India

Population	Sample size	G6PD Normal %	G6PD Deficient %	Source
Assam				
Rabha	57	84.21	15.79	Das et al. 1982
Mikir	83	84.34	15.66	Das et al. 1982
Rajbanshi	103	88.35	11.65	Das et al. 1982
Garo	76	92.11	7.89	Das et al. 1982
Khasi	100	93.00	7.00	Flatz et al. 1972
Proto Australoid	1436	93.38	6.62	Basumatary et al. 2021
Ahom	130	94.62	5.38	Flatz et al. 1972
Mising	170	94.70	5.30	Parween et al. 2024
Assamese	185	95.68	4.32	Flatz et al. 1972

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Lalung	81	96.30	3.70	Das et al. 1982
Koibotter	88	96.60	3.40	Parween et al. 2024
Deori	74	97.30	2.70	Parween et al. 2024
Ahom	379	97.60	2.40	Parween et al. 2024
Kochari	93	97.90	2.10	Parween et al. 2024
Tea Garden Labour	279	98.20	1.80	Parween et al. 2024
Muslim	134	98.50	1.50	Parween et al. 2024
Nepali	71	98.60	1.40	Parween et al. 2024
Rajbongshi	69	98.60	1.40	Parween et al. 2024
Kalita	113	99.20	0.80	Parween et al. 2024
Bengali	109	100.00	0.00	Parween et al. 2024
Bihari	85	100.00	0.00	Parween et al. 2024
Bodo	72	100.00	0.00	Parween et al. 2024
Brahmin	85	100.00	0.00	Parween et al. 2024
Chutia	73	100.00	0.00	Parween et al. 2024
Others	71	100.00	0.00	Parween et al. 2024
Kachari	5	80.00	(1*) 20.00	Flatz et al. 1972
Nagaland				
Angami Naga	85	72.94	27.06	Seth and Seth, 1971
Meghalaya				
Tura	230	95.22	4.78	Bharti et al. 2019
Arunachal Pradesh				
Changlang	267	95.13	4.87	Bharti et al. 2019
Mizoram				
Mizo	490	82.5	17.5	Dash et al. 2005
Lunglei	214	94.86	5.14	Bharti et al. 2019
Tripura				
Gomti	304	94.08	5.92	Bharti et al. 2019
Manipur				

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Muslim	136	78.68	21.32	Achoubi et al. 2019
Brahmin	127	90.51	9.49	Achoubi et al. 2019
Kabui	51	94.12	5.88	Achoubi et al. 2019
Overall	**6125**	**93.44**	**6.56**	

* Total sample size of the reported Kachari population is only 5, and 1 individual is found to be G6PD deficient, which is 20%.

In Assam the prevalence the prevalence of G6PD varied from 0.00% to 20% (Flatz et al. 1972; Das et al. 1982; Basumatary et al. 2021; Parween et al. 2024). In Nagaland, the prevalence of G6PD was found to be 27.06% among the Angami Naga (Seth and Seth 1971). Bharti et al. 2019 reported G6PD deficiency prevalence in Meghalaya (4.78%), Arunachal Pradesh (4.87%), Mizoram (5.14%) and Tripura (5.92%). However, Dash et al. (2005) reported higher prevalence of 17.5% among the Mizo population of Mizoram. Similarly, Achoubi et al. (2010) reported G6PD deficiency frequencies in Manipur of 5.88% among the Kabui, 9.49% among the Brahmins, and 21.32% among Muslims.

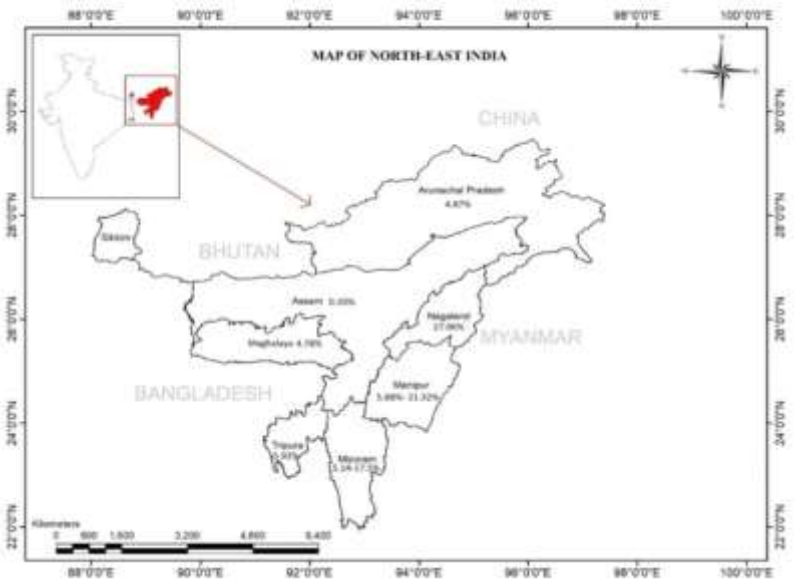

Fig.1 Prevalence of G6PD deficiency among the Northeast states of India

The distribution of G6PD enzyme deficiency across tribal, non-tribal, and mixed populations in Northeast India is presented for clearer interpretation (Table 2). Out of 6,125 individuals, 3,152 belong to tribal populations, 1887 to non-tribal populations, and 1,086 to mixed populations. The prevalence of G6PD deficiency ranged from 0 to 27.06%, with an overall prevalence of 6.56% in Northeast India. Mukerjee et al. (2015) reported an overall prevalence of 7.7% among different tribal groups in India. In Northeast India, prevalence varies across populations, being highest among tribal populations (8.37%) compared to mixed populations (4.88%) and non- tribal populations (4.40%).

Table 2: Frequency distribution of G6PD enzyme deficiency in Tribal, non-tribal and mixed populations of Northeast India

Population	**Sample size**	**G6PD Normal %**	**G6PD Deficient %**	**Reference**
Tribal population				
Angami Naga	85	72.94	27.06	Seth and Seth, 1972

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Kachari	5	80.00	20.00	Flatz et al. 1972
Mizo	490	82.5	17.5	Dash et al. 2005
Rabha	57	84.21	15.79	Das et al. 1982
Mikir	83	84.34	15.66	Das et al. 1982
Garo	76	92.11	7.89	Das et al. 1982
Khasi	100	93.00	7.00	Flatz et al. 1972
Proto Australoid	1436	93.38	6.62	Basumatary et al. 2021
Kabui	51	94.12	5.88	Achoubi et al. 2010
Mising	170	94.70	5.30	Parween et al. 2024
Lalung	81	96.30	3.70	Das et al. 1982
Deori	74	97.30	2.70	Parween et al. 2024
Kochari	93	97.90	2.10	Parween et al. 2024
Tea Garden Labour	279	98.20	1.80	Parween et al. 2024
Bodo	72	100.00	0.00	Parween et al. 2024
Overall	**3152**	**91.63**	**8.37**	
Non-tribal Population				
Muslim	136	78.68	21.32	Achoubi et al. 2010
Rajbanshi	103	88.35	11.65	Das et al. 1982
Brahmin	127	90.51	9.49	Achoubi et al. 2010
Ahom	130	94.62	5.38	Flatz et al. 1972
Assamese	185	95.68	4.32	Flatz et al. 1972
Koibotter	88	96.60	3.40	Parween et al. 2024
Ahom	379	97.60	2.40	Parween et al. 2024
Muslim	134	98.50	1.50	Parween et al. 2024
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Rajbongshi	69	98.60	1.40	Parween et al. 2024
Kalita	113	99.20	0.80	Parween et al. 2024
Bengali	109	100.00	0.00	Parween et al. 2024
Bihari	85	100.00	0.00	Parween et al. 2024

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Brahmin	85	100.00	0.00	Parween et al. 2024
Chutia	73	100.00	0.00	Parween et al. 2024
Overall	**1887**	**95.50**	**4.40**	
Mixed Population				
Gomti	304	94.08	5.92	Bharti et al. 2019
Lunglei	214	94.86	5.14	Bharti et al. 2019
Changlang	267	95.13	4.87	Bharti et al. 2019
Tura	230	95.22	4.78	Bharti et al. 2019
Others	71	100.00	0.00	Parween et al. 2024
Overall	**1086**	**95.12**	**4.88**	

*****Mixed Population - refers to reports whose specific ethnic groups were not clearly identified or mentioned, and therefore could not be classified as either Tribal or Non-Tribal.

Northeast India bears a significant malaria burden and is co-endemic for both *plasmodium falciparum* and *plasmodium vivax* malaria (Warji et al. 2016; Sharma et al. 2016). *Plasmodium vivax* malaria has been reported in almost all the states of Northeast India, accounting for 60-80% of all malaria cases in some states (Sharma et al. 2015). The northeastern region of India, particularly, Nagaland, Manipur, Mizoram, and Assam, demonstrates notable rates of G6PD deficiency. Certain groups, such as the Angami Naga (27.06%), Muslims of Manipur (21.32%), Mizos of Mizoram (17.5%) and the Rabha and Mikir populations, reports prevalence rates exceeding 15% (Seth and Seth, 1971; Das et al. 1982; Dash et al. 2005; Achoubi et al. 2010).

The prevalence of G6PD deficiency in the tribal population in the Northeast India is higher than national average (7.7%), with the highest prevalence reported among the Angami Naga (27.06%). Among non-tribal populations, a comparatively high prevalence rate is observed among the Brahmin population of Manipur (21.32%) (Achoubi et al. 2010). There is a considerable variability in the prevalence of G6PD deficiency across populations, ranging from 0.00-27.06% among the tribal populations, 0.00-21.32% among the non-tribal populations and 0.00-5.92% among the mixed populations. Overall, a wide range of variability in G6PD deficiency is observed across of populations in Northeast India.

The tribal population has the highest proportion of G6PD-deficient individuals, with 264 cases out of 3152 (approximately 8.37%). In contrast, the non-tribal population shows a lower deficiency rate, with 87 cases out of 1887 (about 4.40%). The chi-square value of 27.4397 and the extremely small *p*-value (< 0.00001) indicate that this difference is statistically significant. Similarly, the mix population also has a lower prevalence of G6PD deficiency (53 out of 1086, or approximately 4.88%) compared with the tribal group. The chi-square value of 16.9447 and *p*-value of 0.000038 further confirm that this difference is statistically significant. Overall, the results indicate a clear pattern in which G6PD deficiency is significantly more common in the tribal population compared with the other non-tribal and mixed groups (Table 3).

Table 3: Chi square comparison between Tribal, Non-Tribal and Mixed populations of Northeast India

Population	Sample size	G6PD Normal	G6PD Deficient	Chi-square	*p*-value
Tribal	3152	2888	264		
Non-Tribal	1887	1802	85	27.4397	< 0.00001

Mixed Population	1086	1033	53	16.9447	0.000038

CONCLUSION

The variation in the prevalence frequencies of G6PD deficiency among the Northeastern region highlight a complex interaction of genetic predisposition and environmental pressures, especially in relation to malaria and G6PD deficiency often follows a geographic distribution similar to that of *plasmodium falciparum* malaria. The prevalence ranges from 0.00-27.06% across populations, with an overall regional prevalence of 6.56%, indicating strong heterogeneity. G6PD deficiency often follows a geographic distribution similar to that of *plasmodium falciparum* malaria. The significance of G6PD deficiency in this region is considerable, with higher prevalence observed among the tribal populations (8.37%) compared to non-tribal (4.40%) and mixed populations (4.88%). These difference are statistically significant, as indicated by chi-square values of 27.4397 ($p > 0.00001$ and 16.9447 ($p = 0.000038$). the highest recorded prevalence is 27.06% among the Angami Naga population. Administration of antimalarial drugs and other oxidant medications can pose a risk of drug-induced haemolysis in G6PD deficient individuals, highlighting the need for screening strategies in at risk populations. Furthermore, addressing public health implications, particularly its relationship with malaria, is essential in developing targeted healthcare strategies in this region. Future research should prioritize large scale epidemiological studies, molecular characterization of variants, to support safer treatment strategies and more effective public health interventions in the region.

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