STUDY ON GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) VARIANTS AND ITS ASSOCIATION WITH HAEMOGLOBINOPATHIES AMONG THE TRIBAL POPULATION OF MALARIA ENDEMIC INDO-BHUTAN BORDER DISTRICTS OF BTR, ASSAM, INDIA.

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SUMMARY AND CONCLUSION

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Over 400 million people are affected by G6PD deficiency worldwide. The prevalence of the deficiency varies from 0 to 30% in India with respect to the population group concerned. In India, the frequency of G6PD deficiency is higher in scheduled tribes and scheduled caste groups. Limited numbers of studies are conducted on the prevalence of G6PD deficiency and identification of the causative mutations among the population of Northeast India. The present study illustrated the prevalence of G6PD deficiency among two groups of tribal population: Proto-Australoids (tea tribes) and Mongoloids (Bodo, Rabha and Garo) from four districts of BTR, Northeast India. The G6PD deficiency prevalence observed among the studied population is 6.2%.

Northeast India is considered a hotspot for different forms of haemoglobinopathies as well as thalassaemia. High prevalence of these disorders is reported from the region. An overall prevalence of 42.7% of haemoglobinopathies was found in the present study. HbS was observed in the Proto-Australoids, and HbE in the Mongoloids. Four cases of HbE were found in Proto-Australoids. Two rare occurrences of co-occurrence of HbS and HbE were also identified. Earlier studies have varied opinion on the association of G6PD deficiency and haemoglobinopathies. In the study, only one case was detected with both G6PD deficiency and Hb E haemoglobinopathy, out of 2310 subjects, indicating the co-occurrence of the two disorders as a rare condition. Presence of high HbF values in HbE and HbS disease cases were recorded. Analysis of haematological parameters showed that the RBC parameters, viz., Hb, RBC count and MCHC showed significant positive co-relation with G6PD.

In Indian population, G6PD Mediterranean is the most commonly encountered variant followed by the variants Orissa and Kalyan-Kerala. However, these variants were not reported earlier from the Northeast Indian tribal population. The present study revealed the presence of these mutations in the study population. Instead of G6PD Mediterranean as

the most common variant in main land India, the study found G6PD Orissa as the predominant mutation, and was observed exclusively among the Proto-Australoids.

Even though the discovery of G6PD deficiency dates back to more than 60 years, no treatment has been developed yet to overcome the challenges associated with the deficiency. Naturally available antioxidants were studied as a potential therapeutic agent for G6PD deficient patients in the present study, attributing to their ability to reduce oxidative stress. Most of the antioxidants showed good binding affinities, have drug-likeness properties and are non-toxic or have minimal toxicity. Based on these properties, four complexes were selected one each for the four variants- Orissa-Myricetin, Kalyan-Kerala-Apigenin, Mahidol-Catechin and A^{+}-Diadzen. G6PD Mediterannean was excluded from the *in-silico* analysis since it is a class II variant and *in-silico* studies on the variant were available. Among these complexes, Kalyan-Kerala-Apigenin showed an improved stability compared to the mutant.

People with G6PD deficiency are generally asymptomatic, unless they are exposed to certain factors that trigger haemolysis in the G6PD deficient patients. These haemolytic triggers include medications such as Primaquine, Quinine, etc., and food items such as fava beans. Upon exposure to haemolytic triggers, the G6PD deficient people exhibit symptoms like episodes of acute haemolysis, persistent non-spherocytic haemolytic anaemia. In many parts of Northeast India including the study area, malaria is an endemic. Prior to starting primaquine medication, which may promote haemolysis, it is suggested to ascertain the G6PD status since individuals with G6PD deficiency typically do not exhibit any symptoms. Both the dose of primaquine and the degree of the deficiency determine the severity of haemolysis in the patient. To understand the severity of the deficiency, it is necessary to identify the causative mutation. Thus, identifying the mutation will recognize the severity of the deficiency and facilitate in appropriate prescription or development of customized antimalarial treatment regimes for G6PD deficient patients.