RED CELL GLUCOSE 6-PHOSPHATE DEHYDROGENASE ACTIVITY IN SUBJECTS WITH CHRONIC KIDNEY DISEASE OF UNKNOWN AETIOLOGY IN NORTH CENTRAL AND UVA PROVINCES

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Introduction

Chronic kidney disease (CKD) is a growing worldwide health problem. In recent years investigators in Sri Lanka have noticed a very worrying increase in the number of patients with CKD in North Central (NCP) and Uva (UP) provinces of the country. Studies performed so far suggest a common, although yet unknown aetiology, leading to marked tubulointestitial fibrosis of the kidneys that finally causes kidney failure.

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest enzymopathy in the world. G6PD catalyzes the entry step of G6P into the Pentose Phosphate Shunt. In the red cells, this alternate anaerobic pathway for glucose metabolism is the only source for NADPH, which is required to maintain an effective redox potential protecting cell membrane against oxidative stress and injury. The literature shows that G6PD deficiency is so far related only to acute renal failure (Sarkar *et al.*, 1993; Luzzatto *et al.*, 1969; Copper *et al.*, 1972) and no association with chronic renal failure was found. The objectives of the study were to (1) assess the prevalence of G6PD deficiency among the CKD patients with unknown aetiology (2) ascertain whether G6PD could be used as a marker for CKD of unknown aetiology.

Methods and Materials

We selected 70 cases of biopsy proven CKD of unknown aetiology from different locations; 50 from Medawachchiya (NCP), 20 from Giradurukotte (UP) known to be having higher prevalence of CKD of unknown aetiology. The Medawachchiya population has been there for several generations with heavy exposure to malaria while Girandurukotte is a resettlement area in 1980s, with exposure to malaria. The renal failure patients included in the study sample and control group had creatinine levels between 100-300 □mol/l. We selected four control

groups to compare with the study samples from,

1. Unaffected age matched brother or sister from the same family from Medawachchiya which is a high prevalence area of CKD (n=20),

2. A group of known diabetic nephropathy patients attending the nephrology clinic at General Hospital Kandy (n=22) an area unaffected by CKD,

3. A group of normal healthy individuals from North Central province with a low prevalence of renal failure (low prevalence area in NCP, Huruluwewa) (n=24) and this population is among those resettled in this area in 1940-1950 from non malarial areas of the country,

4. A group of normal healthy individuals from Kandy (CKD unaffected area) (n=20).

The G6PD activity was estimated by measuring the absorbance change at 340 nm due to the reduction of $NADP^+$ by peripheral blood samples.

Results

There was no significant difference in G6PD activity between Medawachchiya patients and the controls from the same family ($p>0.362$). Medawachchiya patients with CKD had significantly low levels of G6PD ($158mU/10^9RBC$) than the Giranduruotte ($199mU/10^9RBC$) group (Table 1). Medawachchiya patients and controls had significantly low levels of G6PD than control groups from unaffected areas such as Kandy ($p<0.001$) and Huruluwewa ($p<0.001$). In patients with renal failure due to diabetic nephropathy, G6PD concentrations were significantly higher than in patients with CKD of unknown aetiology from Medawachchiya ($p<0.001$) and Girandurukotte ($p<0.001$). The history of malaria was highest in Medawachchiya, then Girandurukotte, Huruluwewa and least in Kandy.

Discussion

We observed that in patients from areas with higher prevalence of renal disease the red cell G6PD was significantly lower, irrespective of the location of the village (whether it is in the North Central province or Uva). Medawachchiya patients and controls had the lowest level of G6PD, probably because they were exposed to malaria for generations and had survival advantage due to malaria. Patients from Girandurukotte

Table 1. G6PD activity in cases and controls

Cases/ controls	Number	G6PD activity (mu/10^9 RBC)	History of Malaria in cases/controls
Madawachchiya	50 (cases)	158 ±42	78% (n=106)
Girandurukotte	20 (cases)	199±36	42% (n=53)
Madawachchiya	20 (control siblings)	170±52	60% (n=26)
Huruluwewa	24	228±30	20% (n=32)
Kandy	12 (healthy subjects)	226±28	none
Diabetic nephropathy	22	241±27	none

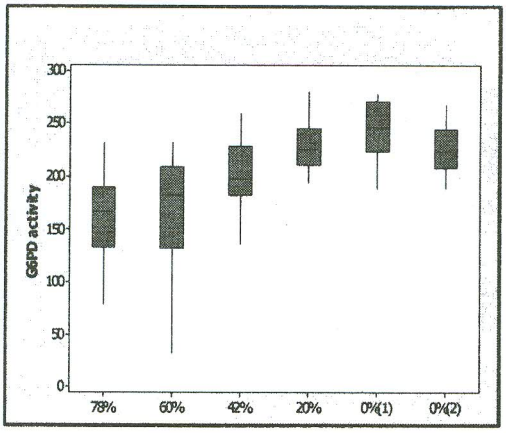

Fig 1. G6PD activity and prevalence of history of malaria

had significantly lower levels of G6PD probably they migrated 28 years ago and had moderate exposure to malaria. The control group from Huruluwewa although migrated 68 years ago were less exposed to malaria than Girandurukotte subjects.

The diabetic nephropathy patients with renal failure from Kandy showed no significant difference in G6PD activity between either the control groups from CKD unaffected area (Kandy) or from low CKD prevalence area (Huruluwewa). The comparison between the Medawachchiya patients and controls from the same families showed no significant difference in the G6PD concentrations. The reasons could be that

a. CKD of uncertain aetiology has no effect on G6PD concentration,

b. G6PD enzyme is not sensitive enough to detect the deficiency as the red cell survival is low in CKD and the cells don't live enough to get low levels,

c. the criterion for selection for the renal biopsy was by testing urine for proteinuria. It is possible that the individuals in the control group can be in the early stages of renal disease without developing proteinuria.

In view of these findings, future studies should be aimed at (1) identifying early and better markers of renal disease and (a) carrying out genetic study for detecting G6PD mutations instead of enzyme assay.

References

Sarkar, S., Prakash, D., Marwaha, R,K., Garewal, G., Kumar, L., Singhi, S. and Walia, B.N. (1993). Acute intravascular haemolysis in glucose-6-phosphate dehydrogenase deficiency. Annals of Tropical Paediatrics, 13(4):391-4.

Luzzatto, L., Usanga, E.A. and Reddy, S. (1969). Glucose-6-phosphate dehydrogenase deficient red cells. Resistance to infection by malarial parasites. Science, 164:839-42.

Cooper, M.R., De Chatelet, L.R., McCall, C.E., La Via, M.F., Spurr, C.L. and Baehner, R.L. (1972). Complete deficiency of leukocyte glucose-6-phosphate dehydrogenase with defective bactericidal activity. Journal of Clinical Investigation, 51:769-78.