CHAPTER - 4

Summary
The present study was undertaken to systematically investigate the changes in red cell function and metabolism in patients afflicted with fluorosis from an endemic village of this region 'Ralla Anantapuram'. The present study included a preliminary survey of the population of this village with a view to identify the population affected by fluorosis and to choose the subjects for the study.

A preliminary survey of the total population of the village consisting of 91 males and 78 females has revealed that the incidence of dental and skeletal fluorosis is high with 95.6% males and 86.5% females and 74.7% males and 78.2% females respectively, with varied degree of severity. Most of the afflicted population have been residing in the village since birth consuming water having high fluoride content (7.2 - 10.7 ppm). While the incidence of symptoms of mild form of skeletal fluorosis like joint pains and back pain were almost similar in both sexes, the severe manifestations like stiffness of back, difficulty in rising, crippling and knock-knees were more in males. Based on the preliminary survey, 10 male members of the age group 22-35 years with severe manifestations of skeletal fluorosis of the village, who volunteered to donate blood were chosen for
further investigations. Healthy males of same age group residing in neighbouring villages with permissible water fluoride content (0.5-1.0 ppm) were investigated for comparison and the data analysed statistically.

The data obtained from the present study revealed the toxic effects of chronic consumption of toxic dose of fluoride by human beings on red cell metabolism. The hemoglobin, red blood cell count, PCV, MCV and MCH showed significant decrease in fluorotic patients with no change in MCHC. These results indicated the presence of hypochromic microcytic anemia in these patients. The deficiency of iron as a cause for the development of anemia has been ruled out since the level of serum iron and iron-binding capacity did not show any change in fluorotic patients compared to controls.

The altered red cell membrane lipid and protein composition, lipid peroxidation and ATPases are suggestive of functional impairment of red cell membrane by fluorosis. The rise in GSH status and the glutathione metabolising enzymes indicates a form of adaptation on the part of the system to counteract the oxidative stress in the erythrocytes of fluorotic patients. However, the protection provided by GSH, and the scavenging enzymes viz. GSH-Px and catalase appear to be
insufficient to counteract the cellular damage as the protection system is unable to prevent increased lipid peroxidation under this toxic condition.

The reduction of $H_2O_2$ or lipid peroxides in erythrocytes in the presence of GSH is coupled with oxidation of glucose via HMP shunt, which provides NADPH for the reduction of GSSG by GR. The increase in activity of GSH-Px and GR in erythrocytes of fluorotic patients is suggestive of increased utilisation and generation of GSH.

HMP shunt activity and the activity of G-6-PDH were found to be significantly increased in RBCs of these subjects, indicating increased utilisation of glucose through HMP shunt for meeting the enhanced requirement of NADPH by erythrocytes of fluorotic patients. A similar stimulation of HMP shunt activity was also observed by in vitro addition of fluoride (10 mM) to erythrocytes from normal healthy adult males.

The inhibition of glycolysis is probably related either to direct effect of fluoride or due to altered composition or both in red cells of patients. The increase in the activity of NADH-dependent methemoglobin reductase in the erythrocytes of fluorotic patients is
suggestive of a part of adaptation necessary for the reduction of methemoglobin whose generation might have been increased by autooxidation of hemoglobin in these erythrocytes. However, the inhibition of glycolysis in the erythrocytes of these patients may not provide sufficient NADH for methemoglobin reduction.
CHAPTER 4

Bibliography


The Lancet, 2: 877.


