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COPPER AND ASCORBIC ACID STATUS IN CHILDREN SUFFERING FROM LEPROSY

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ABSTRACT
The abnormal pigment metabolism usually associated with leprosy led us to the study the biochemical role of ascorbic acid and vis-a-vis copper in this communicable disease. The subjects were all children aged between five to twelve years and chosen as no data are available in childhood leprosy of recent origin. Plasma dehydroascorbic acid, total copper, albumin bound copper, globulin bound copper, cerruloplasmin and serum γ - globulin were found to be increased with decreased level of plasma ascorbic acid and serum albumin in twenty two children suffering from lepromatous leprosy when compared with the data from twenty one normal child served as controls. The overall increases of copper content in all the compartments seems to be due to the lower level of ascorbic acid. It is suggested that a increased dehydroascorbic acid in leprosy could be related to its involvement in free radical metabolism.

KEYWORDS: Ascorbic acid, dehydroascorbic acid, ceruloplasmin, leprosy, protein electrophoresis.

INTRODUCTION
Leprosy is still an important communicable disease in India. Although some of its epidemiological and immunological aspects have been explored successfully, the actual mode of transmission as well as the biochemical mechanism of action in this disease is far from clear. Already some biochemical changes in leprosy have been reported.[1] A decrease in serum protein, hypoferrimia, hypolipidemia, a decrease in glucose tolerance as well as increased serum copper and beta-glucuronidase with over mobilisation of free fatty acids in cases of different forms of leprosy have been observed.[2, 3] However their correlation with the disease processes could not be ascertained as yet. Further these biochemical changes could be the superimposed effect of malnutrition usually associated with the disease.[4]

Copper is an important constituent of several enzymes, some of which are associated with the abnormal pigment metabolism found in leprosy. Similarly ascorbic acid, which has been associated with free radical metabolism, has been found to inhibit the growth of mycobacterium leprae bacillus noncompetitively required for the metabolism of hyaluronic acid.[4] Thus the close association between ascorbic acid and copper metabolism led us to investigate their role in the pathophysiology of leprosy. Ascorbic acid, dehydroascorbic acid, total copper and its fractions and total proteins along with its fractions were analysed in the plasma/ serum of normal controls and leprosy patients. The subjects chosen were all children as no data are available for them.

MATERIALS AND METHODS
Twenty two children suffering from leprosy were selected from the out patients department of North Bengal Medical College and Hospital, Hathighisa Leprosy Clinic and Jeshu Ashram, a leprosy clinic run by the Missionaries. All these collection centres are situated in the Darjeeling District of West Bengal, India. Twenty one normal controls were also selected from the same socioeconomic status residing in the adjoining areas. A thorough baseline clinical and laboratory examinations were carried out to establish the diagnosis of leprosy. They were of lepromatous variety. The subjects who were associated with any major or minor ailments were excluded from the leprosy group and from the control group. The children of both the groups were aged between five to twelve years with average height and weight. The project was explained to the children as well as to their guardians to which they gave their consent. The project was approved by the ethical committee of the institution which was partly financed by the Indian Council of Medical Research (ICMR), New Delhi. The

subjects were asked not to take any medicine for three days prior to the withdrawal of blood samples from them after an overnight fasting for ten to twelve hours. The plasma/ serum of all the subjects were analysed for total copper, albumin bound copper, globulin bound copper and ceruloplasmin[5], plasma ascorbic acid and dehydroascorbic acid[6], and serum total proteins with its functions by electrophoresis technique.[7]

RESULTS

An increase in total copper, albumin bound copper, globulin bound copper, ceruloplasmin, dehydroascorbic acid and gamma-globulin were observed in the children suffering from leprosy when compared with the normal controls ($p < 0.001$). A decrease in albumin and ascorbic acid in leprosy patients as compared to normal controls were also noted ($p < 0.001$). The results are tabulated in Table 1.

Table 1: Biochemical Parameters in Normal Children Control and in Children Suffering from Leprosy.

Parameters	Unit	Normal Children Control	Children Suffering from Leprosy
Plasma Ascorbic Acid	mg/dl	0.90 ± 0.20	0.62 ± 0.10
Plasma Dehydroascorbic Acid	mg/dl	0.09 ± 0.01	0.32 ± 0.02
Plasma Albumin bound Copper	µg/dl	35 ± 7	60 ± 9
Plasma Globulin bound Copper	µg/dl	115 ± 10	139 ± 10
Plasma Total Copper	µg/dl	150 ± 18	199 ± 13
Plasma Ceruloplasmin	mg/dl	24 ± 5	41 ± 6
Serum Total Protein	gm/dl	7.6 ± 2.2	8.0 ± 3.0
Serum Albumin	% of Total Protein	54 ± 4	36 ± 5
Serum α - globulin (1)	% of Total Protein	6 ± 2	8 ± 3
Serum α – globulin (2)	% of Total Protein	8 ± 2	10 ± 3
Serum β - globulin	% of Total Protein	12 ± 4	13 ± 5
Serum γ - globulin	% of Total Protein	20 ± 4	33 ± 6

Values are Mean ± SD

DISCUSSION

It has been reported that increased plasma copper is not a reflection of copper absorption from the gut. High intake of dietary copper hardly increases its plasma level. By binding ionic copper, metallothionein, a copper - protein complex, protects the cell from the possible damaging effects of the metal. Metallothionein regulates the passages of copper in the body and releases copper very quickly in the general circulation where it is loosely bound to plasma albumin and subsequently transported to liver where it is finally incorporated into ceruloplasmin, another major vehicle for copper transport.[8] Thus the higher level of plasma copper found in leprosy could be associated with acute phase reductions or a sudden out flow of copper from the liver as a consequence of decreased biliary excretion of the metal. It has been emphasised that the release of copper from liver as such represents merely the terminal stage of the disease; considerable liver damage occurs before the point is reached. One of the effects of excess copper, being a good catalyst for oxidation, is the peroxidation and hence the destruction of lysosomal membrane leading to destruction of cell.[9] As an endogenous modulator of the inflammatory response ceruloplasmin increased two to three folds in response to inflammation leading to its hepatic synthesis.[10] In leprosy, the increased copper content in both the albumin and globulin fractions indicate relatively the normal functioning of the liver where high availability of albumin – copper complex could lead to high ceruloplasmin content which subsequently incorporated into globulin. This typical picture in leprosy differentiates it from Wilsons' disease where an abnormal metabolism of copper with a low ceruloplasmin content exists. The serum total protein in both the groups did not differ much indicating their identical nutritional status; increased level of globulin in leprosy thus could be attributed to hypergammaglobinemia due to immunogenic response to infectious disease.

Ascorbic acid has been found to decrease the binding of copper by metallothionein and thereby interferes with copper absorption from the gut.[11] It is not very unlikely that the decreased level of ascorbic acid in leprosy could lead to increased absorption of copper from the gut leading to increased copper – albumin complex. Ceruloplasmin possesses an ascorbic acid oxidase activity. The oxidation of ascorbic acid via ceruloplasmin catalysis produces one mol of H_2O_2 per mol of dehydroascorbic acid.[12] So more ceruloplasmin will lead to more dehydroascorbic acid accumulation which is very toxic to the biological system.[13] With an intake of only 45 mg of ascorbic acid per day, a plasma ascorbate level of approximately 0.6 mg/dl could be expected.[14] In the present study, the plasma ascorbate level in leprosy was not below this level thereby ruling out the possible effect of low dietary ascorbic acid on the copper metabolism. Dehydroascorbic acid seems to be independent of ascorbic acid status in an individual. Even excessive intake of ascorbic acid could not produce much fluctuation in the level of dehydroascorbic acid.[15] Thus dehydroascorbic acid seems to be intimately related with some redox state in pathological processes leading to free radical metabolism in various disorders including leprosy.

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Conflict of Interest
The authors declare no conflict of interest in the present study.

Ethical Approval
All procedures performed in the studies involving human participants were in accordance with the ethical standards of the Institutional research committee.

Informed Consent
Informed consent was obtained from all the participants individually who were included in the study.

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