

Serum Copper Levels in Various Diseases: A Local Experience at Aga Khan University Hospital, Karachi

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Objective: To evaluate the possible alteration of serum copper levels in various clinical disorders using the method of Atomic Absorption.

Design: Descriptive analysis

Setting: The Aga Khan University Hospital (AKUH) Clinical Laboratories Karachi, Pakistan (January 2000 to July 2001).

Patients and Methods: 120 in-patients of AKUH were chosen through convenient sampling and their complete medical records obtained from Health Information & Management System (HIMS). Their serum copper was then measured by Flame Atomic Absorption method (Shimadzu AA 6500). Patients were categorised as having infectious (36), GI and hepatic (14), cardiovascular (20), renal (10), pulmonary (15), malignant (7) and haematological (18) disorders. Test results were sorted into high, low or normal serum copper levels for each clinical category, frequencies calculated for each group, and the overall percentage of normal, altered, high and low values determined.

Results: Statistically significant ($p < 0.05$) associations were seen between altered copper levels and infectious, GI & hepatic, renal, malignant and haematological disorders. Cardiovascular and pulmonary diseases also showed a high frequency of abnormal results, but not significantly. Overall, 50% patients had serum copper levels greater than the normal mean + 2SD (115 $\mu\text{g/dl}$), while 27.5% had low serum Cu levels suggestive of Cu depletion whereas 22.5% showed normal values even with various clinical disorders.

Conclusion: Alterations in Serum Copper, whether low or high, can give significant insight in disease process and should be further studied as a reasonable marker of patient health.

Key words: Serum Copper, Trace elements, Systemic disorders, Pakistan.

Introduction

Copper is an essential trace element, an important catalyst for heme synthesis and iron absorption. Following zinc and iron, copper is the third most abundant trace element in the body. Its role as a cofactor component of cytochrome oxidases, superoxide dismutase, tyrosinase, uricase, dopamine β -hydroxylase, lysyl oxidase and ceruloplasmin make it a key micronutrient for our oxidative pathways¹. The bioavailability of copper from the diet is about 65-70% depending on a variety of factors including chemical form, interaction with other metals, and dietary components. The biological half-life of copper from the diet is 13-33 days with biliary excretion being the major route of elimination.

Chronic copper toxicity is rare and primarily affects the liver. Wilson's disease and Indian childhood cirrhosis are examples of severe chronic liver disease that results from the genetic predisposition to the hepatic accumulation of copper. Serum, urinary and

liver copper levels have traditionally been used to diagnose Wilson's disease, Menkes Syndrome and Indian Childhood Cirrhosis. Several studies have been published that relate serum copper levels with the presence of certain systemic diseases other than those mentioned above²⁻¹⁷. At this juncture, there is a need to find out whether a clear-cut association exists between Serum Copper levels and the presence of different clinical disorders, and if this relationship is also seen in Pakistan.

Methodology

In all, 120 in-patients whose complete medical history and records were available with the Health Information and Management System (HIMS) of AKUH were chosen through convenient sampling.

From each patient 6 ml blood was collected in vacutainer tube and all samples were analyzed for serum copper levels through Flame Atomic

Absorption method on Shimadzu AA 6500, after performing recommended calibration (with a value of $r^2 = 0.9995 - 1.0000$). Controls of all three levels that were low, medium and high were run with each batch. Any abnormal results were rechecked to confirm them, the normal range of Serum Copper being 20-70 $\mu\text{g/dL}$ (infants), 80-190 $\mu\text{g/dL}$ (children), 70-140 $\mu\text{g/dL}$ (adult males) and 80-150 $\mu\text{g/dL}$ (adult females).

The results were sorted and analysed to give frequencies of normal, altered, high and low copper levels for each disease category. P-values were computed for these results using SPSS.

Results

The patients belonged to all age groups, 70 of them were male while 50 female.

Patients counted according to their main clinical diseases: Pulmonary (n = 15), renal (n=10), infectious diseases (n=36), malignant (n=7), cardiovascular (n=20), GI & hepatic including Wilson's disease (n=14) and haematological disorders (n=18).

Of the total 120 patients, 93 (77.5%) had altered serum copper levels, 60 (50%) high and 33 (27.5%) low and only 27 (22.5%) had normal serum copper levels.

A large percentage of infectious disease patients showed normal copper levels (52%) while none of GI and hepatic, renal, and malignant disease patients had them within normal range. Amongst altered serum copper, the tendency was on the higher side for all except infectious disease where low copper levels were the more common abnormality seen.

Table 1: Test Results: Rates of Copper Levels in Different Clinical Disorders and Their Statistical Significance

Clinical Disorder	Total	Altered Serum Cu Values	High	Low	Normal Values
Infectious diseases	36	17 (47%) (p-value 0.00)	5 (14%)	12 (34%)	19 (52%)
GI & Hepatic including Wilson's Disease	14	14 (100%) (p-value 0.00)	12 (86%)	2 (14%)	0 (significant)
Cardiovascular	20	17 (85%) (p-value 0.08)	11 (55%)	6 (30%)	3 (15%)
Renal	10	10 (100%) (p-value 0.025)	9 (90%)	1 (10%)	0 (significant)
Pulmonary Infection	15	11 (73%) (p-value 0.71)	8 (54%)	3 (20%)	4 (26%)
Malignant	07	07 (100%) (p-value 0.05)	5 (72%)	02 (28%)	0 (significant)

Haematological disorders	18	17(95%)	10(56%)	7(39%)	01(5%)
		(p-value 0.00)			

The results of the study are shown in Table 1 and represented for better comparison as a bar chart in Figure 1.

Discussion

According to our results, serum copper can be a good indicator of disease processes going on in the body as there were a high percentage of altered copper levels in the presence of a diverse group of diseases. The overall high rates of altered copper levels (77.5%) suggest Serum Copper as a good index of patient health. This is corroborated by Songchitsomboon et al² where serum copper/zinc ratios were assessed in pulmonary, renal, cardiovascular, infectious, malignant and haematological diseases amongst Thai patients and found to be higher than normal subjects. Serum copper has also been found to be altered in epilepsy¹⁶, eating disorders⁹, obesity¹⁰, Insulin-dependant Diabetics¹⁷ multiple sclerosis, acute and chronic liver diseases, infections, myocardial infarcts and schizophrenia⁴.

Contrary to expectations, infectious diseases did not show as high an association with altered copper concentrations (47%) as seen in other studies that related increased copper levels with giardiasis¹¹, measles¹², typhoid fever¹³ and tuberculosis¹⁵. The rise in copper levels in inflammations has been related to C-reactive protein and erythrocyte sedimentation rate⁴ and this could be explained by the requirement of

copper as cofactor of various oxidases in the body¹.

As predicted, copper concentrations were all deranged in the gastrointestinal and hepatic disease group which included Wilson’s disease. The high percentage of above normal levels (86%) support the findings obtained by Verma et al for Chronic cholelithiasis⁸, in acute and chronic hepatic disease⁴ and the accepted diagnostic feature of Wilson’s disease¹. However, the small number (14%) of low copper levels did not comply with the expectations from GI disorders that removal or disease of the gut generally leads to low serum copper levels due to malabsorption. GI symptoms are seen in copper toxicity¹ and our results may be explained by this reversal of cause-effect relationship.

Renal disease, malignancies and haematological disorders all depicted a very high percentage of abnormal copper levels (100%, 100% and 95% respectively), and of these, renal and malignant portrayed a tendency for high copper levels, as is well supported by several studies^{4-7, 14}. Malignancies of blood^{4, 6} as well as other organs^{4, 7} have shown a strong propensity for high copper levels in the past, copper levels changing with successful treatments⁴⁻⁶ and even used for prognosis⁵. Haematological disorders were found to be associated with both high (56%) and low (39%) serum copper which may be due to the presence of primary blood disorder or the result of copper deficiency that can lead to anaemia.

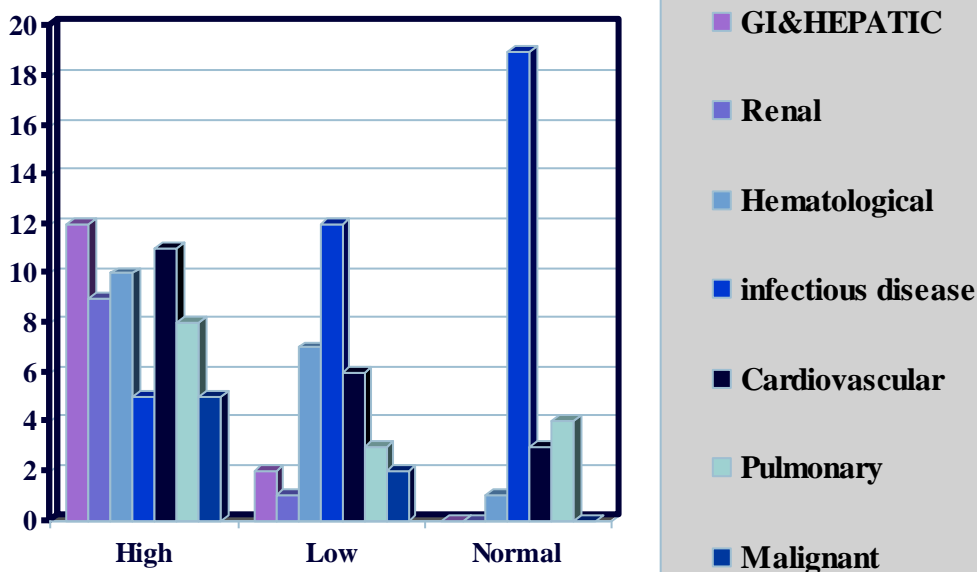


Figure 1: Frequencies of High, Low and Normal Copper Levels in Different Clinical Disorders

Cardiovascular disease and pulmonary infections groups did not show a significant ($p < 0.08$, $p < 0.71$ respectively) link with high copper levels, though there was a high rate of altered copper levels seen in each group (85%, 73%). Our results for both are backed by several studies that have found copper to be affected in cardiovascular disorders^{2, 3, 5}, even used to predict mortality rates, and in different pulmonary infections¹⁵.

Overall, high copper levels dominated the results, about 50% of all results and 65% of altered copper levels. These figures could have been higher if it hadn't been for the infectious disease group where there is a need to determine which infections cause a rise, fall or no change in serum copper concentrations.

Conclusion

It was revealed in this study that Serum Copper can become altered in a variety of disease processes. In the future, copper levels may be explored as a potential marker of disease process in the body.

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