

## **DISORDERS OF SERUM COPPER CONCENTRATION IN CHRONIC RENAL FAILURE PATIENTS**

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### **ABSTRACT**

Copper is an essential nutrient for all forms of life, being the vital constituent of living cells. The essentiality of copper is by virtue of its ability of catalyse biological oxidation, whether the copper is in the protein bound or ionic forms, although it is likely that ionic copper is able to do this more efficiently than protein bound copper. It is a necessary component of the variety of metallo-enzymes. Abnormalities of copper metabolism in chronic renal failure have been of interest in the introduction of maintenance dialysis therapy for uremia. Hypercupremia in dialyzed patients has been attributed to active uptake of copper during dialysis from contaminated water supply or from certain types of artificial kidneys. The present study includes the study of serum copper levels of 200 patients (according to age group and sex) with chronic renal failure (CRF) before and after the process of treatment and it has been compared with 50 normal healthy individuals comprising the control group.

**Keywords:** *Hypercupremia, Chronic renal failure, Biochemical Studies, Copper Metabolism*

### **INTRODUCTION**

It has been observed that there are at least 29 different types of elements in our body. Organic compounds such as carbohydrates, proteins and lipids form about 90% of the solid matter and mainly consist of C, H, O and N.

Chronic renal failure affects metabolism of trace elements like any other infectious disease. Although it is more than a century since copper was first associated with living tissue, it was not until 1928 that it was conclusively shown to be an essential component of the diet of mammals. It is probable that Miessner was the earliest worker to show that copper is the constituent of plants.

During the next fifty years many investigations established the fact that copper is consistently present in plants and animal tissue. Copper occurs in varying concentrations in every tissue and organ of the body, but individual variability is too great to allow definite values to be assigned to particular organs. The endocrine glands pituitary, thyroid and thymus are examples of organs with very low copper content, whereas the liver, kidneys, heart, brain and the hairs have highest copper concentration. Chronic Renal Failure (CRF) is a disease of insidious onset and progressive course with gradual deterioration of renal function and of such severity that the kidneys are no longer be able to keep the internal environment normal.

Swelling in the hands, face or feet, Nausea or vomiting, Loss of appetite, Changes in urination, Itching of the skin, Headache and confusion, Fatigue and weakness etc are the signs which have been observed by Fiaccadori *et al.*, (2001).

Stenvinkel *et al.*, (2002) reported that chronic renal failure (CRF) is one of the most severe diseases worldwide. Lise *et al.*, (2009) studied that renal failure occurs when the kidneys cannot properly remove wastes that causes buildup of waste and fluid in the body. Brune *et al.*, (1966), Blomfield *et al.*, (1971), Mansouri *et al.*, (1970) and Barbour *et al.*, (1971) has reported an elevated copper concentration in dialyzed patients with chronic renal failure. Providing the proper physical therapy program for patients with chronic renal failure is often a challenge because of such complications as congestive heart failure and peripheral neuropathies studied by Paula *et al.*, (1982). Stevons *et al.*, (1970) reported approximately 50 persons per million populations suffer from chronic renal failure. Severity of renal failure is common feature now a day in India.

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### MATERIALS AND METHODS

The present study was carried out on 200 adult patients of chronic renal failure attended in the S.V.B.P. hospital attached to L.L.R.M. Medical College, Meerut and also 50 normal healthy individuals with age, sex matched who had no history of renal failure to serve as controls. All the known cases of chronic renal failure were included in this study on the basis of clinical and biochemical criteria. A known case of renal failure for more than three months' duration (Harrison XIII edition. Page 1284) and persons having blood urea more than 50 mg% were chosen for study. After confirmation of diagnosis on the above parameters, blood samples were drawn from these patients for the estimation of serum copper. All the chemicals and reagents used were of analytical grade: otherwise they were purified before use.

### Observations

**Table I: Showing Distribution of C.R.F. CASES According to Age Group and Sex**

Age Groups (Years)	Number of Cases		Total
	Males	Females	
10-30	5	2	7(3.5%)
31-50	50	25	75(37.5%)
51-70	63	40	103(51.5%)
71-above	10	5	15(7.5%)
Total	128(64.0%)	72(36.0%)	200(100.0%)

Out of 200 individuals, 128 (64%) controls were male's individuals and rest 72 (36%) were females. The maximum number of cases, 103 (51.5%), were observed in the age group of 51-70 years followed by 75 (37.5%) cases in the age group of 31-50 years, 15(7.5%) cases in the age group of above 70 years and 7 (3.5%) cases in the age group of 10-30 years.

**Table II: Showing Distribution of Control Cases According to Age Group and Sex**

Age Groups (Years)	Number of Cases		Total
	Males	Females	
10-30	4	1	5(10.0%)
31-50	12	6	18(36.0%)
51-70	18	9	27(54.0%)
Total	34	16	50(100.0%)

Out of 50 control cases, 34 (68.0%) cases were males and 16 (32.0%) were females. 54.0% were found in the age group 51-70 years, 36.0% were 31-50 years age group and 10.0% were 10-30 years age group.

**Table III: Distribution of C.R.F. Cases According to Duration of Illness**

Duration of Illness	No. of Cases	Percentage %
3 months-6 months	42	21.0%
6 months-1 year	114	57.0%
More than 1 year	44	22.0%
Total	200	100.0%

The majority of chronic renal failure cases were among more than 6 months- 1 year duration (114 cases, 57.0%) and then more than I year children (44 cases, 22.0%).

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**Table IV: Serum Copper Levels in Normal Healthy Control**

Age in Years	Male			Female			Total		
	No.	Range (µg/100 ml)	Mean=S.D.	No.	Range (µg/100 ml)	Mean=S.D.	No.	Range (µg/100 ml)	Mean=S.D.
10-30	4	95-115	110.00±11.18	1	76-100	99.20±10.97	5	76-115	107.84±10.89
31-50	12	82-150	121.29±20.62	6	77-148	125.23±24.16	18	77-150	122.61±21.94
51-70	18	102-148	125.22±13.47	9	86-140	109.00±17.1	27	86-148	119.81±16.64
Total	34	82-150	122.03±20.51	16	76-148	114.46±24.98	50	76-150	118.92±22.05

The level of serum copper in healthy subjects was 76-150 µg/100ml (mean 118.92±22.05 µg/100ml). In males, the range was 82--150 µg/100ml (mean 122.03±20.51 µg/100ml) and in females, the range was 75-148 µg/100ml (mean 114.46±24.98 µg/100ml). The highest serum copper level was observed in the age group of 31-50 years, ranged as 77-150 µg/100ml (mean 122.51±21.94 µg/100ml) followed by the age group of 51-70 years, ranged as 86-148 µg/100ml (mean 119.81±16.64 µg/100ml) and the age group of 10-30 years, ranged as 76-115 µg/100ml (mean 107.84±10.89 µg/100ml) respectively. No significant difference was seen among the serum zinc levels of different age groups and sexes.

**Table V: Serum Copper Levels Before and After Treatment in Total Cases of Chronic Renal Failure**

Interval	No. of Cases	Serum Sodium	
		Range (µg/100 ml)	Mean ± S.D.
Control	50	76-150	118.92±22.05
Before treatment	200	124-179	162.04±14.94***
15 days after treatment	186	120-167	151.48±11.99***
30 days after treatment	169	112-159	137.44±12.67***
60 days after treatment	145	96-152	122.16±16.18**
90 days after treatment	122	92-146	118.72±17.17

P- Significance, control vs treatment

\*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001.

In patients of chronic renal failure serum copper levels was significantly high before and after thirty days of treatment as compared to controls. The range of serum copper level before and after fifteen, thirty and sixty days of treatment were 124-179 µg/100 ml (mean 162.04±14.94 µg/100 ml), 120-167 µg/100 ml (mean 151.48±11.99 µg/100 ml), 112-159 µg/100 ml (mean 137.44±12.67 µg/100 ml) and 96-152 µg/100 ml (mean 122.16±16.18 µg/100 ml) respectively. Serum copper level ninety days of the treatment ranged as 92-146 µg/100 ml (mean 122.72±17.17 µg/100 ml). No significant difference was seen after ninety days of treatment in chronic renal failure patients as compared to controls.

**Discussion**

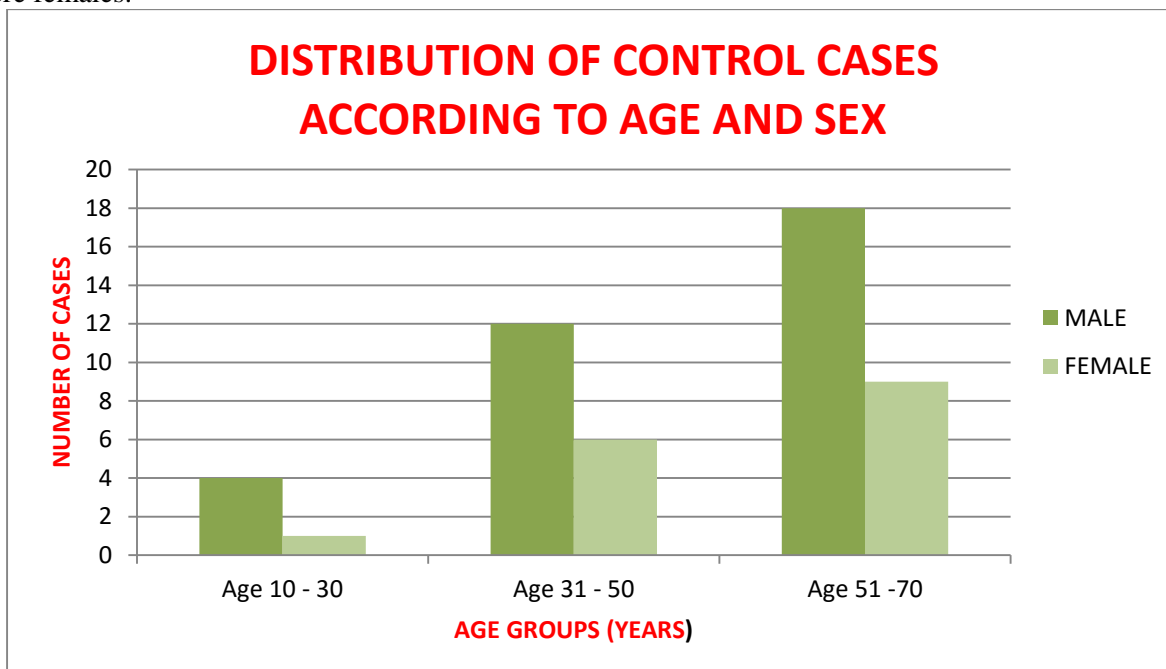
Chronic renal failure is the disease in which kidneys are no longer able to keep the internal environment normal. The alterations in biochemical and clinical signs and symptoms have become more and more questionable. In recent years with the advent of dialysis and renal transplantation, the profile of chronic renal failure has changed to a great extent. The longevity of patients of chronic renal failure has substantially increased with the treatment by dialysis and renal transplantation. The purpose of present study is to find out some biochemical procedure which may be helpful in making the diagnosis of chronic renal failure and monitoring the prognosis of disease and find out any biochemical abnormalities in the

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patients of chronic renal failure. The present study is conducted on a total of 250 individuals, out of which 50 are normal healthy individuals comprising the control group and rest 200 is of chronic renal failure.

#### Controls

All the 50 healthy controls were between the age group of 10-70 years. The majority being of the age group 51-70 years. Out of 50 healthy controls 34 (68%) controls were male individuals and rest 16 (32%) were females.



**Figure 1: Distribution of control cases according to age and sex**

Serum Copper level have been studied in control. In normal healthy controls serum copper ranged between 76-150  $\mu\text{g}/100\text{ml}$  (mean  $118.92 \pm 22.05 \mu\text{g}/100\text{ml}$ ). In males, it ranged from 82-150  $\mu\text{g}/100\text{ml}$  (mean  $122.03 \pm 20.51 \mu\text{g}/100\text{ml}$ ) and in females, 76-148  $\mu\text{g}/100\text{ml}$  (mean  $114.46 \pm 24.98 \mu\text{g}/100\text{ml}$ ). Highest serum copper level was observed in the age group of 31-50 years ( $122.61 \pm 21.94 \mu\text{g}/100\text{ml}$ ) followed by the age group of 51-70 years ( $119.81 \pm 16.64 \mu\text{g}/100\text{ml}$ ) and the age group of 10-30 years ( $107.84 \pm 10.89 \mu\text{g}/100\text{ml}$ ). No significant difference in respect of age and sex was noted in this study. Similar results have been obtained by Koch *et al.*, (1957), Legutko *et al.*, (1977) and Brieter *et al.*, (1978). Panvalkar *et al.*, (1961) found serum copper level  $122.00 \pm 22.00 \mu\text{g}/100\text{ml}$ . Vreman *et al.*, (1980) found serum copper level  $118.00 \pm 5.00 \mu\text{g}/100\text{ml}$ . However, Mahajan *et al.*, (1985) found serum copper level to be  $116.00 \pm 14.00 \mu\text{g}/100\text{ml}$  in normal healthy subjects.

#### Biochemical Studies

The levels of serum copper were studied in controls and in all cases of chronic renal failure. In normal healthy controls, total serum copper ranged between 76-150  $\mu\text{g}/100\text{ml}$  (mean  $118.92 \pm 22.05 \mu\text{g}/100\text{ml}$ ). In males, it ranged from 82-150  $\mu\text{g}/100\text{ml}$  (mean  $122.03 \pm 20.51 \mu\text{g}/100\text{ml}$ ) and in females, 76-148  $\mu\text{g}/100\text{ml}$  (mean  $114.46 \pm 24.98 \mu\text{g}/100\text{ml}$ ). No significant difference owing to age and sex was noted in this study. In cases of chronic renal failure, the level of serum copper was significantly elevated in 72% cases and before treatment, the level was  $162.04 \pm 14.94 \mu\text{g}/100 \text{ml}$  which was significantly high ( $p < 0.001$ ) as compared to that of controls ( $118.92 \pm 22.05 \mu\text{g}/100 \text{ml}$ ). Our findings also resemble those to Mahaletetal., & Blomfield *et al.*, (1971), Tuskamoto *et al.*, (1980), Fischer *et al.*, (1984), Festa *et al.*, (1985) and Hosokawa *et al.*, (1986) but Zumukley *et al.*, (1979), Armstorng *et al.*, (1980) and Thomson *et*

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al., (1983) described the normal serum copper level in chronic renal failure cases. Piechota *et al.*, (1983) found slightly low serum copper level. After 15 days of treatment, the level of serum copper decreased to  $151.48 \pm 11.99 \mu\text{g}/100\text{ml}$ . This was significantly high ( $p < 0.001$ ) as compared to controls. Thirty days after treatment, the level of serum copper declined to  $137.44 \pm 12.67 \mu\text{g}/100\text{ml}$  which was significantly elevated ( $p < 0.001$ ) as compared to that of controls. After 60 days of treatment, the level of serum copper returned to normal in 98 cases and the level was  $112.16 \pm 16.18 \mu\text{g}/100\text{ml}$ . This was significantly high ( $p < 0.001$ ) as compared to that of controls. Ninety days after treatment, the level of serum copper returned to normal in all cases of chronic renal failure. The level was  $118.72 \pm 17.17 \mu\text{g}/100\text{ml}$ . In the present study, only 122 cases out of 200 cases turned up for follow-up to the last. This figure was low, because most of the cases defaulted in treatment. The cases showing normal level of serum copper were also found to be clinically improved cases and thus, the serial estimation of serum copper level during follow-up is a useful tool for assessing the prognosis of the disease.

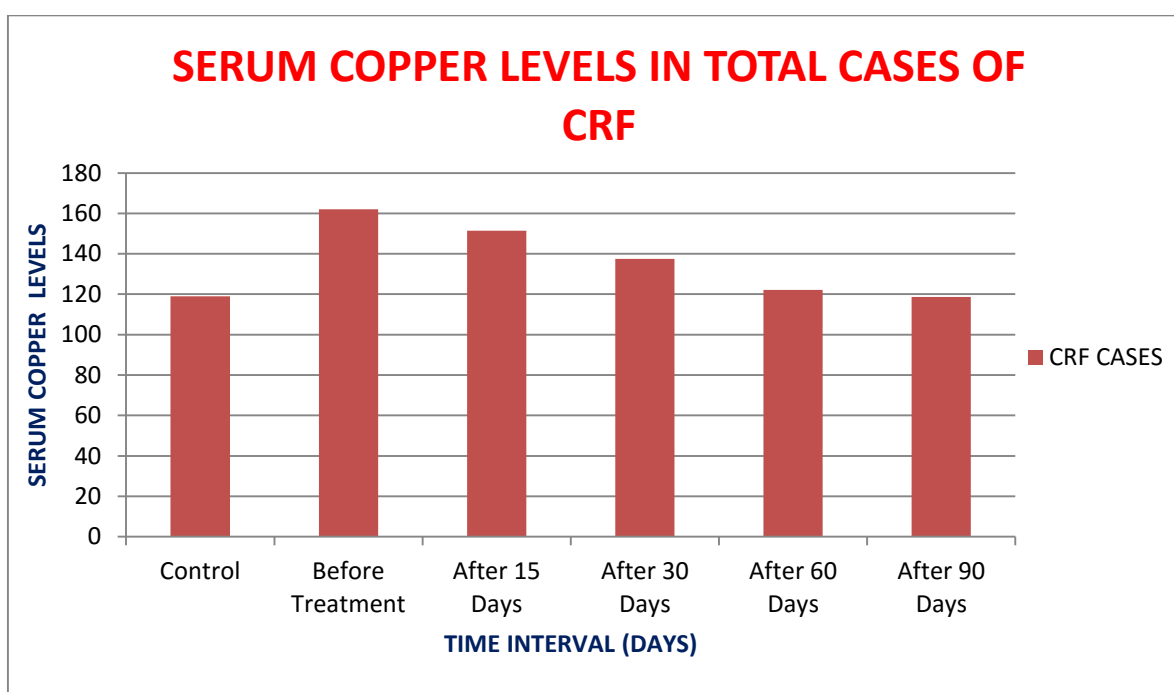


Figure 2: Serum Copper Levels in Total Cases of Chronic Renal Failure

### Conclusion

The present study was carried out on 200 patients of chronic renal failure, who came to the S.V.B.P. hospital attached to L.L.R.M. Medical College, Meerut. In this study 250 individuals were included. Out of these 200 patients were of chronic renal failure and 50 individuals were normal healthy controls.

The diagnosis of chronic renal failure was made on clinical, biochemical and radiological basis. 50 normal healthy individuals including 34 males and 18 females, between the age of 10 to 70 years, were studied as controls. Blood samples were collected and serum copper was estimated before treatment and after the treatment on 15<sup>th</sup>, 30<sup>th</sup>, 60<sup>th</sup> and 90<sup>th</sup> day in chronic renal failure patients.

The highest levels of serum copper were seen in chronic renal failure patients who were without treatment. The levels ranged between 124-179  $\mu\text{g}/100 \text{ ml}$  and (mean  $162.04 \pm 14.94 \mu\text{g}/100 \text{ ml}$ ). After sixty days of treatment, the levels of serum copper remained elevated. The levels of serum copper after fifteen, thirty and sixty days of treatment ranged between (120-167  $\mu\text{g}/100 \text{ ml}$ ), 112-159  $\mu\text{g}/100 \text{ ml}$  and 96-152  $\mu\text{g}/100 \text{ ml}$  and mean  $151.48 \pm 11.99 \mu\text{g}/100 \text{ ml}$ ,  $137.44 \pm 12.67 \mu\text{g}/100 \text{ ml}$  and  $122.16 \pm 16.18$

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µg/100 ml respectively. After ninety days of the treatment ranged between 92-146 µg/100 ml and mean 118.72±17.17 µg/100 ml.

In normal healthy controls serum copper ranged between 76-150 µg/100ml and mean 118.92±22.05 µg/100ml. In study group, the levels of serum copper was found highly increased, ranging between 124-179 µg/100ml and mean 162.04±14.94 µg/100ml. Highly significant difference (p< 0.001) was observed among the chronic renal failure patients and controls. Serum copper levels are related to the extent of disease.

The following conclusions are derived from this study:

- i. There was insignificant difference in the levels of all the above mentioned parameters as regards to age or sex of the healthy controls included in this study.
- ii. Maximum probabilities of serum copper level were found in the age group of 31-50 years (51.5%).
- iii. Minimum probabilities of serum copper level were found in the age group of 10-30 years (3.5%).
- iv. The levels of serum copper were found to be significantly elevated in cases of chronic renal failure as compared to that of controls.
- v. The fall in the levels of serum copper is related to the extent of the disease.
- vi. The levels shifted to normal range as the condition of patients improved clinically.

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