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# Subclinical copper poisoning in asymptomatic people in residential area near copper smelting complex

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## ABSTRACT

**Objective:** During an outbreak of industrial chronic copper poisoning at least 10000 sheep died in Kerman, Iran in 2009. Therefore present study was carried out to evaluate the prevalence of subclinical copper toxicosis in asymptomatic people in residential area near copper smelting complex. **Methods:** A total of 120 serum samples were collected from randomly selected individuals during June to December, 2011. **Results:** The data obtained revealed that serum levels of AST, ALT and ALP were significantly increased in 7.50%, 4.16% and 5.84% of cases respectively. Results showed that serum levels of copper and ceruloplasmin were significantly increased in 4.16% and 5% of cases as well. **Conclusions:** Findings of the study revealed that health hazards increased with closeness to the copper mine and smelting complex.

## 1. Introduction

Copper is an essential trace element that is widely distributed in various tissues. It is component of a number of metalloenzymes such as catalase, peroxidases, and cytochrome oxidase, and is essential for the utilization of iron[1,2]. The necessity of copper for human health derives from its involvement in myriad biological processes, including iron metabolism, antioxidant defense, neuropeptide synthesis, and immune function[3,4]. Copper can be absorbed into the systemic circulation from the gastrointestinal tract, the lungs, and skin[5]. The gastrointestinal absorption of copper is influenced by a number of factors, including its chemical form: soluble copper compounds (oxides, hydroxides, citrates and sulfate) are readily absorbed, but water-insoluble compounds (sulfides) are poorly absorbed[6]. Absorbed copper binds to plasma albumin and amino acids in the portal blood and is transported to the liver where it is incorporated into ceruloplasmin and later released into the plasma[5]. Age,

sex, amount of dietary copper, and overall health determine the amount of copper distributed to the various tissues[5].

Chronic copper poisoning is the most common form of copper toxicity in animals. Its occurrence is associated with a long-term intake of copper compounds of different origin. Animals which are reared close to copper mine and smelting factories receive copper from industrial deposits through feed or from the air mostly together with other toxic elements throughout their entire lives[7]. As a result, animals under such conditions adapt to a certain degree to chronic intake of increased doses of copper and clinical and pathological manifestations of intoxication are not always characteristic.

Due to the factors mentioned, the prevention of industrial copper intoxication raises some problems and its effectiveness depends, in addition to the amount and the period of copper intake, also on the nutritional status[8].

## 2. Materials and methods

Shahrbabak County is a county in the west part of Kerman Province in Iran. The capital of the county is Shahrbabak. At the 2006 census, the county's population was 100 192 in 22 973 families.

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## 2.1. Samples collection and processing

A total of 120 serum samples were collected from randomly selected individuals during June to December 2011. Samples were collected aseptically using sterile 5 mL syringe. Serum was separated by centrifugation of blood at 3000 g for 10 minutes at room temperature, the sera were transferred into 1.5 mL sterile microtubes (Eppendorf) and were kept at  $-20^{\circ}\text{C}$  until required. These samples were submitted to Research Laboratory of Teaching and Research Hospital of School of Veterinary Medicine at Shahid Bahonar University of Kerman, Iran.

## 2.2. Biochemical parameters assays

The serum concentration of ceruloplasmin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) were determined by biochemical automatic analyser (Autolab, AMS Corporation; Rome, Italy), using commercial kits (Pars Azmoon, Esfahan, Iran). Serum copper was analyzed by an atomic absorption spectrometer (Buck Scientific Co., East Norwalk, CT, USA).

## 2.3. Statistical analysis

Means and their standard errors (SE) were calculated using the SPSS16 program. A value of  $P < 0.05$  was considered statistically significant.

## 3. Results

**Table 1**

Number and prevalence of cases with normal and elevated serum parameters among 120 people.

Biochemical parameters	Range	Number (%)
Serum copper ( $\mu\text{g/dL}$ )	Normal (50–150)	115 (95.84)
	Elevated ( $>150$ )	5 (4.16)
Ceruloplasmin (mg/dL)	Normal (15–60)	114 (95.00)
	Elevated ( $>60$ )	6 (5.00)
AST (IU/L)	Normal (6–40)	111 (92.50)
	Elevated ( $>40$ )	9 (7.50)
ALT (IU/L)	Normal (5–56)	115 (95.84)
	Elevated ( $>56$ )	5 (4.16)
ALP (IU/L)	Normal (38–140)	113 (94.16)
	Elevated ( $>140$ )	7 (5.84)

Results of enzymes levels and biochemical parameters were presented in Table 1. The data obtained revealed that serum levels of AST, ALT and ALP were significantly ( $P < 0.05$ ) increased in 7.50 (9 cases), 4.16 (5 cases) and 5.84 (7 cases) percent of cases respectively. Table 1 showed that serum levels of copper and ceruloplasmin were significantly ( $P < 0.05$ ) increased in 4.16 (5 cases) and 5 (6 cases) percent of cases, as well. Minimum, maximum and MSE of mentioned parameters had been presented in Table

2. Serum levels of ceruloplasmin, AST, ALT and ALP had been increased in all of 5 cases (4.16%) with elevated serum copper level significantly ( $P < 0.05$ ).

**Table 2**

Minimum, maximum and mean $\pm$ SE of serum parameters of 120 cases.

Biochemical parameters	Minimum	Maximum	Mean $\pm$ SE
Serum copper ( $\mu\text{g/dL}$ )	61	755	94.8 $\pm$ 11.1
Ceruloplasmin (mg/dL)	21	190	42.9 $\pm$ 5.6
AST (IU/L)	9	800	31.7 $\pm$ 6.1
ALT (IU/L)	8	400	47.6 $\pm$ 1.3
ALP (IU/L)	43	110	79.0 $\pm$ 7.8

The biochemical evaluation showed that serum levels of AST, ALT and ALP in 111 (92.50%), 115 (95.84%) and 113 (94.16%) Cases among 120 samples were in normal range, respectively. Results revealed that serum concentrations of copper and ceruloplasmin in 115 (95.84%) and 114 (95.00%) Cases among 120 sera were in normal range, respectively, as well.

## 4. Discussion

Sarcheshmeh and Miedook, the biggest copper mines in Iran, and Khatunabad copper smelting complex are located around Shahrbabak County. Mozaffari *et al* described an outbreak of industrial chronic copper poisoning in sheep in this county. Results of the previous study showed that at least 10000 out of 75000 sheep (13.3%) originating from 50 flocks died over a period of 3 years in the Khatunabad region. Toxicological analysis showed an exceeding of the permitted limit (150 mg/kg) of copper in liver samples by 7.97 times (1196.9 $\pm$ 20.6 mg/kg). In kidney samples the excess was by 9.14 times (137.20 $\pm$ 8.96 mg/kg). The copper concentrations in water (0.3 $\pm$ 0.02 ppm) and pasture plant samples (6208.00 $\pm$ 58.69 ppm) around the factory were very high, suggesting that water and pasture plants were the sources of intoxication[7].

Results of previous study demonstrated that copper smelting activities at Khatunabad copper smelting complex were having a direct influence on the biophysical environment, contaminating the soils, and the atmosphere. Atmospheric pollution due to release of particulate air matter was eminent at Khatunabad copper smelting complex. It was hence suspected that the inhabitants of the area probably inhale polluted air[7]. Meteorological conditions such as temperature, wind speed and wind direction aid in the transportation and deposition of particulate air matter. Therefore we decided to continue previous study and evaluate the prevalence of subclinical copper toxicosis in asymptomatic people in residential area near copper smelting complex.

Harvey *et al* suggested that serum copper and ceruloplasmin may be the most useful biomarker of copper status and appears to be effective in both replete and

depleted individuals. Results of present study show that serum copper and ceruloplasmin have increased in 4.16% of residents. Increased level of liver enzymes in mentioned cases confirm hepatotoxicosis due to copper poisoning<sup>[9]</sup>.

Gopinath *et al* showed that inhalation of fumes in the area by human and animals could also lead to chronic copper intoxication<sup>[10]</sup>. Copper accumulates in the tissues and progressive histological and histo-chemical changes occur in the liver<sup>[11,12]</sup>. Magdalena *et al* demonstrated some changes in serum enzyme levels that indicated that a functional disturbance of the liver can occur before the hemolytic crisis<sup>[13,14]</sup>. Ortolani *et al* concluded that increasing GGT followed by AST are the best enzymes to assess copper load in animal during the pre-hemolytic phase<sup>[15]</sup>. Severe liver damage in chronic copper poisoning could lead to an increase in AST, ALT and ALP activity as suggested by Maiorka *et al*<sup>[16]</sup>.

In present study increased level of serum ceruloplasmin may be attributed to an increase in copper concentration in the liver, which can be explained by the delivery of copper, accumulating in the non-metallothionein-bound form, to ceruloplasmin outside the Golgi apparatus of the liver.

This study focused on elucidating on the health status of residents of the study area based on the influence of mining and smelting activities. Findings of the study revealed that health hazards increased with closeness to the copper mine and smelting complex. In order to reduce the health hazards due to mining and smelting activities at Khatunabad, the residents should avoid staying outdoors as much as possible where the risk of exposure to contaminated air is quite high; and for those who are frail in health, they should consider relocation to other township areas away from the fumes. Residents should have regular check-ups of their health status. Government and related agencies, and the Mine Authorities should work as a team in monitoring pollution activities at Khatunabad. In collaboration with Health Service Providers, active Health Education Programs which focus on sanitation, and health and wellness of the inhabitants of the study area should be regularly conducted. Expansion of Khatunabad copper smelting complex should be regulated in such a way that the growing population is least exposed to the fumes.

### Conflict of interest statement

We declare that we have no conflict of interest.

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