Evaluation of Serum Copper and Iron Level among Lead Exposure Workers in Khartoum State

A dissertation submitted for partial fulfillment for the requirement of M.Sc Degree in Medical Laboratory science - Clinical chemistry

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بسم الله الرحمن الرحيم

قال تعالى:

قل لَوْ كَانَ الْبَحْرُ مِدَادًا لِكَلِمَاتِ رَبِّي لَنَفِدَ الْبَحْرُ قَبْلَ أَنْ تَنْفِدَ كَلِمَاتِ رَبِّيَّ وَلَوْ جَعَلْتُ نَمْثَلًا مِثْلَهُ مَدَادًا

صدق الله العظيم

سورة الكهف الآية (109)
Dedication

This research is lovingly dedicated to my respective parents who have been my constant source of inspiration. They have given me the drive and discipline to tackle any task with enthusiasm and determination. Without their love and support, this project would not have been made possible. Also, my dedication must go to my brothers—echo of my heart for their support and help.

Aya
Firstly, the great praise and thanks to God who gave me the ability to complete this work.

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Abstract

Background: Lead is a pervasive and persistent environmental pollutant which exists in almost all phases of environment and biological systems, although Lead causes neurological, hematological, gastrointestinal, reproductive, circulatory and immunological pathologies and interact with essential element, exposure to it is still unavoidable. Accordingly the study conducted to assess the effect of occupational lead exposure on blood level of iron and copper among factory workers.

Materials and Methods: Descriptive cross-sectional study was conducted during the period of February to March 2016. Eighty one subjects were enrolled in this study; they were classified into 40 subjects whom expose to lead as case and 41 whom not expose to lead as control, their age vary from 19 -60 years old, serum iron, copper and lead levels were measured using atomic absorption spectrophotometer.

Results: The mean concentration of copper was significantly increased among lead exposure subjects (0.312±0.273) in comparison with (0.073±0.024) in unexposed with p-value 0.000. In contrast the mean iron level showed insignificant difference in exposed subject (0.229±0.085) versus unexposed (0.223±0.078) with p-value 0.676. Also our results revealed insignificant difference in mean concentration of copper and iron in highly expose in comparison with low expose p value 0.808 and p-value 0.469 respectively. Person’s correlation showed, serum copper level is inversely correlated with serum iron and serum Lead concentration (r=-0.379, p-value 0.015) and (r=-0.394, p-value 0.011)

Conclusion: The study concluded that serum copper is higher among occupational lead exposure while iron is not changed.
المستخلاص

خلفية الدراسة: الرصاص من الملوثات البيئية الأكثر انتشار والتي توجد في جميع مراحل النظم البيولوجية والبيئة، وعلى الرغم من أن الرصاص يسبب العصبية، وأمراض الدم والجهاز الهضمي، وأمراض الجهاز التناسلي، وأمراض المناعة ويؤثر على الدورة الدموية ويعمل مع معظم العناصر الأساسية، إلا أنه لا يزال لا مفر من التعرض له ولذلك أجريت دراسة لتقييم مستوى الحديد والنحاس في الدم لدى العمال الذين ي تعرضون للرصاص في أماكن عملهم.

المواد والطرق: أجريت دراسة وصفية مستعرضة خلال الفترة من فبراير إلى مارس 2016. وشملت الدراسة 81 عامل تتراوح أعمارهم من 19-60 سنة، 41 منهم يتعرض للرصاص في أماكن عملهم في حين أن 40 لا يتعرضون للرصاص وتم قياس مستويات الرصاص، الحديد والنحاس باستخدام مطيافية الامتصاص الذري.

النتائج: أوضحت الدراسة أن هناك زيادة أحصانيه ذات دلاله في متوسط تركيز النحاس لدى الذين تعرضوا للرصاص (0.312 ± 0.273) مقارنة مع الذين لم يتعرضوا للرصاص (0.073 ± 0.24) القيمة الاحتمالية 0.000 في المقابل بينت الدراسة أنه ليس هناك تغير ذو دلاله إحصائي في مستوى الحديد لدى الذين تعرضوا للرصاص (0.229 ± 0.085) مقارنة بالذين لم يتعرضوا للرصاص (0.223 ± 0.078) القيمة الاحتمالية 0.676. كما كشفت الدراسة أنه لا يوجد تغير ذو دلاله إحصائي في متوسط مستوي الحديد و النحاس لدى العمال الأكثر عرضة للرصاص مقارنة بالعمال الأقل عرضة للرصاص القيم الإحتمالية = 0.808, 0.469 على التوالي.

كما بينت الدراسة وجود ارتباط عكسي بين مستوي النحاس في الدم ومستوي الرصاص وال الحديد في الدم (r=-0.394, p-value 0.011, r=-0.379, p-value 0.015) على التوالي.

الخلاصة: خلصت الدراسة إلى أن هناك زيادة في متوسط تركيز النحاس لدى العمال الذين تعرضوا للرصاص في حين لا يوجد تغير في متوسط تركيز الحديد.
Chapter One:

Introduction

&

Literature review
1. Introduction

1.1 Lead and lead Toxicity

Lead is a stable, silver-gray, ubiquitous heavy metal, has been used since ancient times. It is a pervasive and persistent environmental pollutant which exists in almost all phases of environment and biological systems. Lead is still being widely used in industry and life, as in electric storage batteries, lead solder, radiation shields, pipes, and sheaths for electric cable and hence it has indispensable properties like resistance to corrosion, malleability and low melting point. Unfortunately exposure to lead is unavoidable since it has many applications in the current life of human being from work to home and its accumulation in environment. Lead causes neurological, hematological, gastrointestinal, reproductive, circulatory and immunological pathologies depending upon the level and duration of exposure. Lead is a redox inactive metal however it interacts with a group of essential elements such as copper, zinc, selenium, chrome and iron (Bal et al., 2015).

1.2 Copper

Copper is an essential trace element for humans and animals. In the human organism, copper exists in two forms – the first and second oxidation form, as most of the copper in the human organism is in the second form (Angeloviet al., 2011).

1.2.1 Copper essentiality in human body

Copper plays an important role in our metabolism, largely because it allows many critical enzymes to function properly, copper is essential for
maintaining the strength of the skin, blood vessels, epithelial and connective tissue throughout the body. Copper plays role in the production of hemoglobin, myelin, melanin and it also keeps thyroid gland functioning normally. Copper can act as both an antioxidant and a pro-oxidant (Osredkar and Sustar, 2011).

1.2.2 Copper enzymes

Cytochrome C oxidase: is multisubunit complex containing copper and iron, it catalyze four electron reduction of molecular oxygen which necessary for ATP production (Brunet et al., 2006). Lysyl oxidase is cuproenzyme essential for stabilizing of extracellular matrix especially in cross-linking of collagen and elastin (Rucker et al., 1998). Superoxide dismutase (SOD) is abundant copper and zinc containing protein it primary functions as an antioxidant (Valentine et al., 2005). Ceruloplasmin-ferroxidases enzyme, is major copper-carrying protein in blood and play role in iron metabolism (Gaware et al., 2010). Tyrosinase: multi-functional oxidase that widely distribute in nature it key enzyme in melanin biosynthesis (Saghiae et al., 2013). Dopamine-beta-mono oxidase: is tetramerichomoprotein most likely with two copper atoms on each subunits it catalyze hydroxylation of dopamine to nor-epinephrine (Linder and Hazegh, 1996).

1.2.3 Copper Absorption

In mammals, copper is absorbed in the stomach and small intestine, Fractional absorption appears to be a function of the amount of copper in the diet and individual copper stores (Thus, it appears that the percent of copper absorbed decreases with increasing level of dietary copper) Factors that influence dietary copper absorption include competition by zinc, iron, molybdenum, lead, or cadmium. Fructose and other carbohydrates, dietary cellulose fiber, were found to reduce the bioavailability of copper (Ransom et al., 2006).
1.2.4 Copper Distribution
Copper is exported from the enterocytes into the blood by Cu-ATPase ATP7A, The majority of copper that emerges from the intestinal epithelium into the blood is delivered to the liver and less to kidney and other tissues, after entry into hepatocytes, copper is distributed to cytosol and mitochondria to utilize, also distributed to the secretary pathway. Distinct compartments of the secretary pathway, the trans-Golgi network (TGN), contain Cu-ATPases (ATP7B in hepatocytes), the ATPases then transfer copper across the membrane into the lumen of the trans-Golgi network in hepatocytes, where it incorporated into the copper-dependent ferroxidases ceruloplasmin (CP) which is subsequently secreted into the blood (Lutsenko et al., 2007). Uptake of copper from ceruloplasmin by various tissues involve: interaction with cell surface receptor (Linder and Hazegh, 1996).

1.2.5 Copper Excretion
Bile is the major pathway for the excretion of copper and is vitally important in the control of liver copper levels (Ransom et al., 2006; Turnlunl, 1998).

1.2.6 Copper deficiency
Copper deficiency is more commonly an acquired condition induced by the imbalance between need and dietary copper supply, also may a result of a rare inherited defect of copper transport (Uauy, 1998). The most common clinical manifestations of copper deficiency are anemia, neutropenia, and bone abnormalities, including fractures (Williams, 1983; Uauy, 1998).

1.2.6.1 Acquired copper deficiency
Acquired copper deficiency is mainly attributable to nutritional deficiency, and may be seen in malnourished low-birth-weight infants, newborns, and small infants, also after gastrointestinal surgery, intractable diarrhea, and prolonged parenteral or enteral nutrition (Aoki, 2003).

1.2.6.2 Genetic copper deficiency (Menkes disease)
Menkes disease is a rare X-linked, fatal disorder, resulting from a mutation in the gene encoding ATP7A. The mutant protein is no longer able to regulate the flux of copper resulting in a systemic deficiency of copper. Specifically, most of the Copper accumulates in intestinal epithelium and kidney (Krupanidhet al., 2008). Menkes disease is characterized by peculiar hair called kinky or steely and retardation of growth (Bishop et al., 2010).

1.2.7 Copper toxicity
Excessive copper intake can cause nausea, vomiting, abdominal pain and cramps, headache, dizziness, weakness, diarrhea, and metallic taste in the mouth. Chronic copper toxicity does not normally occur in humans because of transport systems that regulate absorption and excretion. Since excess copper is excreted through bile, copper toxicity is most likely to occur in individuals with liver disease or other medical conditions in which the excretion of bile is compromised (Osredkar et al., 2011).

1.2.7.1 Wilson disease
Wilson disease is an autosomal recessive disorder caused by mutations in the copper transport gene ATP7B (Desai and kaler 2008; Das and Ray 2006). Whose original function is to regulate the biliary excretion of excess copper, the result is the accumulation of copper in liver leading to cirrhosis and hemolysis. Advanced stages of the disorder are characterized by deposition of excess copper in brain and eyes in the form of Kayaer-Fleischer ring which serves as a diagnostic marker for Wilson’s disease (Krupanidhet al., 2008).

1.3 Iron
Iron plays a central role in oxygen transport and it an important part in energy metabolism. It forms part of the haem molecules of hemoglobin and myoglobin and is an important constituent of flavoproteins, cytochromes and most oxidases. Free iron is highly toxic and this probably related to inhibition of certain enzymes and initiation and catalyzing of free radical-mediated reactions (Koay and Walmsley, 1999).

1.3.1 Iron Absorption

Dietary iron is predominantly absorbed in the proximal small intestine, near the gastro-duodenal junction (Nadadur et al., 2008).

There are at least two separate mechanisms for the uptake of haem and non-haem iron into the enterocyte. The divalent metal transporter 1 (DMT1) transports inorganic iron, and is specific for ferrous iron. Non-haem iron uptake requires an acid pH, which is provided by gastric hydrochloric acid, to make it more soluble, duodenal cytochromes B reductase (DcytB), located on the luminal surface of the enterocytes, converts dietary ferric iron to the ferrous state (Jackson, 2010). In the intestinal cell, the iron may be stored by incorporation into ferritin in those individuals who have adequate plasma iron concentration or transported to a transport protein at the basolateral cell membrane and released into the circulation (Arora and Kapoor, 2012) specific protein Ferroportin (FPN1), has been identified in the Exportation of iron to circulation. Once exported by FPN1, iron needs to be transformed from the ferrous into the ferric form by ferroxidases such as Ceruloplasmin in order to bind iron to Transfrin (Abramowski et al., 2014).

Haem iron is absorbed into the enterocyte by a different, as yet unidentified, haem receptor. Once internalised in the enterocyte, iron is released from haem by haemoxygenase and then either stored or transported out of the enterocyte across the basolateral membrane via mechanisms similar to that of ionic iron (Siah et al., 2006).
1.3.2 Iron Transport

Iron is distributed systemically in the circulation as transferrin. Transferrin comprises a core carrier glycoprotein, apotransferrin, which can bind one or two atoms of ferric iron to form holotransferrin, which is usually called transferrin. The uptake of iron by cells is mediated by the binding of holotransferrin (Tf) to transferrin receptors (TfR) on cell membranes which is then internalized by endocytosis. The resulting endosome contains the Tf-TfR complex. Ferrous iron atoms are released and transferred out of the endosome to the cytoplasm by the local divalent metal transporter 1 (DMT1). The iron is then either stored as ferritin or used within the cell, e.g. hemoglobin synthesis in erythroid precursors. The apotransferrin and the transferrin receptors return to the cell surface and the apotransferrin are recycled into the plasma (Jackson, 2010).

1.3.3 Iron Storage

All cells have the ability to sequester iron either in the soluble complex ferritin or, as its insoluble derivative, haemosiderin. Ferritin is the major intracellular storage protein found in all cells with the highest concentrations in the liver, spleen, and bone marrow. Haemosiderin is produced by lysosomal denaturation of ferritin, in which the protein shells degrade and the iron cores aggregate. Haemosiderin iron is found in lysosomes and cytosol and, as it is less soluble than ferritin iron, it is less easily mobilized (Jackson, 2010).

1.3.4 Excretion

Iron is highly conserved and not readily lost from the body, there are some obligatory loss from the body that result from physiological exfoliation of cells from epithelial surface including skin, genitourinary tract and gastrointestinal tract (Abbaspour et al., 2014).

1.3.5 Regulation
Hepcidin is a 25–amino acid iron-regulatory hormone. Hepcidin binds to ferroportin, a cellular iron export channel, leading to its degradation and preventing iron efflux from iron-exporting tissues into plasma. Hepcidin synthesis is induced by iron loading and inflammation and suppressed by hypoxia and erythropoietic activity. By simultaneously regulating intestinal iron absorption and the release of iron from macrophages and hepatic stores, hepcidin can be viewed as a master regulator of systemic iron availability (Himmelfarb, 2007).

1.3.6 Iron deficiency
Iron deficiency refers to the reduction of iron stores that precedes overt iron deficiency anemia or persists without progression. Iron-deficiency anemia is more severe condition in which low levels of iron are associated with anemia and the presence of microcytic hypochromic red cells (Camaschella, 2015). Causes of Iron Deficiency either physiological as increased demand in infancy, rapid growth (adolescence), menstrual blood loss, pregnancy (second and third trimesters) and blood donation, or environmental as insufficient intake, resulting from poverty, malnutrition, pathological as decreased absorption (e.g. Gastrectomy, duodenal bypass, hookworm infestation), or genitourinary system, including heavy menses, menorrhagia (Camaschella, 2015).

1.3.7 Iron overload
The term ‘iron overload’ can be used to describe a condition resulting in increased total body iron stores, with or without organ dysfunction (Piperno, 1998). Which are broadly divided into two groups: Inherited or Primary iron overload and Secondary iron overload syndromes (Siddique and Kowdley, 2012).

1.3.7.1 Primary iron overload (Inherited)
**Type1 haemochromatosis:** is the classical and commonest of the primary iron overload syndrome. It is an autosomal recessive disorder resulting in iron overload and variable multi-organ dysfunction. A homozygous mutation in the hereditary haemochromatosis gene, *HFE* is responsible for type 1 primary haemochromatosis (Siahet *et al.*, 2006).

**Type2 Juvenile haemochromatosis (JH):** is an autosomal recessive disease characterized by massive hepatocellular iron deposition as well as iron deposition in endocrine glands. Depending on the gene involved, Juvenile haemochromatosis is divided into two subtypes, Type 2A is due to mutations in the *haemojuvelin (HJV)* gene encoding protein haemojuvelin, which is considered as an upstream regulator of hepcidin. The mutant haemojuvelin protein inhibits hepcidin expression. While Type 2B is due to mutation in the hepcidin gene (Siddique and Kowdley, 2012).

**HH type 3:** is a disorder resulting from mutations in the transferring receptor-2 gene (Roetto *et al.*, 2002).

**1.3.7.2 Secondary haemochromatosis**

This group includes iron overload either due to or associated with ineffective erythropoiesis, chronic liver diseases, parenteral administration or ingestion of excessive amounts of iron. Thalassemia major and sideroblastic anemia are the two best studied examples of iron overload secondary to blood transfusions and ineffective erythropoiesis (Piperno, 1998).

**1.4 Link between copper and iron metabolism**

The best characterized link between copper and iron is provided by ceruloplasmin, multi Copper binding protein that act as serum ferroxidases and is essential for mobilization of iron, so copper deficiency result in reduce ceruloplasmin production which reduce mobilization of iron and decrease plasma iron level (Sharp, 2004).

**1.5 Interaction of lead with copper and iron**
Lead interacts with some essential metals one of these metals is copper and iron. Copper is contain in ceruloplasmin, a a2-globulin having enzymatic properties, and is responsible for the oxidation of ferrous to ferric iron and catalyses the transport of iron to transferrin, which transfers bound ions to cells. Because Lead binds to both ceruloplasmin and transferrin, iron and copper metabolism in exposed individuals could be impaired (Leelakunakorns et al., 2005).

Researchers in previous study found that, the blood levels of copper in workers occupationally exposed to lead were significantly lower than control subjects, this may be related with either depression of Copper absorption or increased urinary excretion of copper, secondary to Lead induced tubular dysfunction (Balet al., 2015). Also in other study Copper plasma levels of workers expose to lead were significantly higher compared with the control group and correlated positively with lead concentrations, while no association between iron and blood lead levels (Kasperczyk et al., 2012). While another investigation revealed that there is no association between copper, and blood level of Lead (Mehdi et al., 2000; Chiba et al., 1996; Wasowicz et al., 2001).

Kim et al. (2003) reported a decrease in the serum iron level in lead-exposed workers, but a significantly lower dietary iron intake was observed concurrently. In another hand other investigations revealed that there is no association between serum iron, and blood level of Lead (Mehdi et al., 2000; Chiba et al., 1996; Lilis et al., 1978).

1.6 Objective
1.6.1 General objective:
To Study the effect of occupational Lead exposure on Copper and Iron level among workers

1.6.2 Specific objectives:

to measure copper, iron and lead in case and control groups.
To compare mean concentration of copper, iron and lead among exposure and non-exposure subjects.
To correlate between study parameters (copper, iron and lead) and study variables (age and duration of exposure)
1.7 Rationale
Despite years of intensive research, educational efforts, and remedial measures, Lead continues to receive as much attention as any modern environmental health risk therefore Lead is an important toxicant that can exert adverse effects in humans, given sufficient exposure and accumulation in the body. Systems known to be susceptible to adverse effects of high exposure includes: neurological, reproductive, renal, and hematological disorder (Juberg, 2000).

Lead is a redox inactive metal however it interacts with a group of essential elements such as copper, zinc, selenium, chrome and iron, their interactions are diverse and not clearly understood yet. Therefore the aim of this study was to determine the effect of occupational lead exposure on blood levels of copper and iron. Internationally two similar studies were done, in the Sudan no such study has been published yet. Benefit desired from this study is to inform workers with risk which around them and try to conduct rules to improve workers’ health and work environment and to improve awareness of workers with some nutrition that minimize adverse effect of lead toxicity.
Chapter Two:

Materials & Methods
2.1 Study Design
Descriptive cross-sectional study, conducted during the period of February to March 2016.

2.2 Study Area
This study was carried out in Saria industrial complex and Alshagaria industrial complex at Khartoum state.

2.3 Study Population
Eighty-one workers were enrolled in this study, and then classified based on exposure to Lead into two groups, group one not exposed to lead (41 workers) considered control, group two exposed to lead in their work (40 workers).

2.4 Inclusion criteria
Specimens were collected from healthy workers exposed to lead and non-exposed to Lead.

2.5 Exclusion criteria
Subjects with diabetes mellitus, renal diseases, hypertension and hypersensitivity have been excluded from the study.

2.6 Collection of Samples
Blood samples (5ml) were collected in plane containers under septic condition. Then left to clot at room temperature, serum obtained by centrifuged at 4000 rpm, and stored in -20° until use.

2.7 Ethical Considerations
Study was approved from ethical committee of the Sudan University of Science and Technology, verbal informed consent was obtained and all workers were informed by aims of the study.

2.8 Principle of atomic absorption spectrophotometer
Brief According to manufacture, electron of the atom promoted to higher orbital (excited state) for a short period of time by absorbing light energy of specific wavelength, as number of atoms in light path increases the amount of light absorbed also increases. By measuring the amount of light absorbed a quantitative determination of the amount of analyte can be made.
2.9 Method of iron estimation
Sample for serum iron is dilute a minimum of 1.0ml serum sample with an equal volume 20% (w/v) trichloroacetic acid(TCA) solution then heat in heating block at 90C for 15 minutes, cool and centrifuge, supernatant is aspirate and absorbance is measured at 248.3 nm by atomic absorbance spectrophotometer.

2.10 Method of copper estimation
Sample for serum copper is dilute with equal volume of deionized water, then dilute serum is aspirated and absorbance measured at wavelength 324.8 nm by atomic absorbance spectrophotometer.

2.11 Method of lead estimation
Sample for serum lead estimation is dilute 0.3 ml of serum with 2.7 ml of nitric acid(HNO3) then dilute serum is aspirate and absorbance measure at 283.3 nm by atomic absorbance spectrophotometer.

2.12 Statistical Analysis
The data was analyzed using statistical package of social science (SPSS computer program), frequencies, Means, SD, independent t-test and Pearson's correlation have been used to compare and correlate between parameters and study variables.
Chapter Three:

Results
3 Results

This study included 41 Lead exposure workers and 40 unexposures. The mean concentration of copper was significantly increased among lead exposure subjects (0.312 ± 0.273) in comparison with (0.073 ± 0.024) in unexposed with p-value 0.000 which presented in figure 3.1.

In contrast the mean iron level showed insignificant difference in exposed subject (0.229 ± 0.085) versus unexposed (0.223 ± 0.078) with p-value 0.676 which presented in figure 3.2. Also our results revealed insignificant difference in mean concentration of copper in highly expose (0.301 ± 0.263) in comparison with low expose (0.290 ± 0.322) with (p value = 0.808) is presented in figure 3.3.

Also our results showed insignificant difference in mean concentration of iron in highly exposed (0.219 ± 0.087) in comparison with low expose (0.238 ± 0.084) with p-value 0.469 which is presented in figure 3.4. Person’s correlation showed, serum copper level is inversely correlated with serum iron and serum Lead concentration (r = -0.379, p-value 0.015) and (r = -0.394, p-value 0.011) respectively, while no correlation observed when associate serum copper with age of workers and duration of exposure (r = -0.178, p-value 0.267) and (r = -0.242, p-value 0.128) respectively all are presented in table 3.1.

Serum iron level is not correlated with age of worker, duration of exposure and serum lead level (r = 0.155 p-value 0.332), (r = 0.063 p-value 0.698) and (r = 0.276 p-value 0.081) all are represented in table 3.2.
Figure 3-1: Mean copper level among lead exposure and unexposed

Results express as mean±SD, significant considered as p-value ≤ 0.05.
Figure 3.2: Mean iron level among lead expose and unexposed

Results express as mean ± SD, insignificant consider as $p$-value $\geq 0.05$. 

$p$-value = 0.767
Figure 3.3: Mean copper level among highly expose and low exposed

Results express as mean ±SD, insignificant consider as $p$-value ≥0.05.
Figure 3.4: Mean iron level among highly expose and low exposed

Results express as mean ±SD, insignificant consider as p-value ≥0.05.
Table 3.1: Correlation between copper and study variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>R-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.178</td>
<td>0.267</td>
</tr>
<tr>
<td>Duration</td>
<td>-0.242</td>
<td>0.128</td>
</tr>
<tr>
<td>Iron</td>
<td>-0.379</td>
<td>0.015</td>
</tr>
<tr>
<td>Lead</td>
<td>-0.394</td>
<td>0.011</td>
</tr>
</tbody>
</table>
Table 3.2: correlation between iron and study variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>R-Value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
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<tr>
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<td>0.063</td>
<td>0.698</td>
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<tr>
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<td>0.015</td>
</tr>
<tr>
<td>Lead</td>
<td>0.276</td>
<td>0.081</td>
</tr>
</tbody>
</table>
Chapter four:

Discussions &

Conclusion &

Recommendations
4.1 Discussions

Lead is a toxicant that can exert adverse effects in humans, causing neurological, hematological, gastrointestinal, reproductive, circulatory, and immunological pathologies depending upon the level and duration of exposure. It also markedly alters the function and metabolism of some micronutrients (Bal et al., 2015). Therefore, a descriptive cross-sectional study was carried out to evaluate the status of essential elements copper and iron in workers who are occupationally exposed to lead in Khartoum State. The present study revealed that there was an insignificant difference in mean concentration of iron in lead exposed compared to the control group with p-value 0.808. This finding indicates that serum iron is not affected by exposure to lead. Our finding was in agreement with previous reports who stated that there is no association between serum iron and blood level of lead (Mehdi et al., 2000; Chiba et al., 1996; Lilis et al., 1978; Kasperczyk et al., 2012). In contrast with other studies, our findings contradict those that serum iron level decreased in lead-exposed workers, but a significantly lower dietary iron intake was observed concurrently (Kim et al., 2003). Person’s correlation revealed no correlation between serum iron in occupational exposed and blood lead level was observed (r=0.276, p-value 0.81). This data is similar to data obtain by previous study which reveal that no correlation between serum iron and serum lead in occupational lead exposed worker (Lilis et al., 1978).

The results of the present study provide evidence that serum copper level was significantly increased in occupational exposed group in comparison with unexposed with p-value 0.000. This result indicates that exposure to lead...
increase blood level of copper, our data is similar to result obtain by previous study (Kasperczyk et al., 2012). Earlier study showed that Lead exposure is associated with an elevated activity of superoxide dismutase isoenzymes that contains Copper and Zinc (CuZn-SOD) in both serum and erythrocytes (Kasperczyk et al., 2004). Therefore, an increase in the Copper level, which was observed in the present study, may be caused by increased Cu-Zn-SOD activity. This enzyme is part of the antioxidant defensesystem and its activity may be elevated because of Lead induced oxidative stress (Kasperczyk et al., 2005) the increase in plasma Copper levels may also be caused by competitive displacement of the metal from tissues by lead ions. However our data is disagreeing with a pervious study which revealed no association between serum copper and lead exposure (Mehdi et al., 2000; Chiba et al., 1996; Wasowicz et al., 2001). Also our result is disagree with previous study which state that, blood levels of copper in workers occupationally exposed to lead were significantly lower than control subjects, The authors attributed the decrease in the Copper level to either depression of Copper absorption or increased urinary excretion of copper, secondary to lead induced tubular dysfunction (Bal et al., 2015).

This descriptive cross sectional study reveal that serum copper level is inversely correlated with serum lead concentration (r=-0.394, p-value 0.011) in contrast with pervious study (Kasperczyk et al., 2012) which reveal that serum copper is positively correlated with serum lead concentration. In fact that serum lead is not reflecting Lead toxicity which is correctly noticed by estimation of erythrocytes and or intracellular lead concentration, accordingly we recommend for further study to estimate erythrocyte and or intracellular Lead level.
4.2 Conclusion

The study was concluded that, serum copper is higher among occupational lead exposure workers while iron is not changed.

4.3 Recommendations

1. Estimation of lead in erythrocyte.

2. Provide workers with especial nutritional diet to counteract effect of lead exposure on their health.

3. Use Lead chelators for neutralization of excess Lead in the body.

4. Awareness the workers with the risk of Lead exposure and used of safety methods that reduce toxicity of Lead.
References
5 References:


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hepcidin is associate with severe juvenile hemochromatosis. Nature genetic. 33:21-22


Appendix (1)
Sudan University of Science and Technology
College of Graduate studies
1. العمر:
2. السكن:
3. المهنة:
4. عدد سنوات العمل:
5. هل تتبع نظام غذائي معين: أ- نعم ( ) ب- لا ( )
6. نوع النظام الغذائي الذي تتبعه:

7. هل تعاني من أي حساسية: أ- نعم ( ) ب- لا ( )
8. نوع الاعراض: