بسم الله الرحمن الرحيم

SUDAN UNIVERSITY OF SCIENCE AND TECNOLOGY
COLLEGE OF GRADUATE STUDIES

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

تقويم مستوي النحاس والحديد في مصل الدم لدي العمال الذين يتعرضون للرصاص في ولاية الخرطوم

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

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الآية

بسم الله الرحمن الرحيم

قال تعالى:

قُلْ لَوْ كَانَ الْبَحْرُ مِدَادًا لِكَلِمَاتِ رَبِّي لَنَفِدَ الْبَحْرُ قَبْلَ أَنْ تَنْفَدَ كَلِمَاتُ رَبِّي وَلَوْ جِئْنَا بِمِثْلِهِ مَدَدًا

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

Acknowledgment

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

I am gratefully acknowledging my supervisor **Dr. Amar Mohamed Ismail** for his support. This thesis would not have been possible unless his great support valuable advice and appreciated assistance.

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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 wasconducted during the period of February to Marsh 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 usingatomic 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 levelis inverselycorrelated with serum ironand 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.

المستخلص

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 المناعه ويؤثر علي الدورة الدموية ويتفاعل مع معظم العناصر الأساسيه ، الا أنه لا يزال لا مفر من التعرض له و لذلك أجرت دراسة لتقييم مستوى الحديد والنحاس في الدم لدي العمال الذين يتعرضون للرصاص في أماكن عملهم.

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

النتائج:أوضحت الدراسه أن هنالك زيادة أحصائيه ذات دلاله في متوسط تركيز النحاس لدي الذين تعرضوا للرصاص (0.312 ± 0.273) مقارنة مع الذين لم يتعرضوا للرصاص (0.073 ± 0.024)القيمه الأحتماليه 0.000 في المقابل بينت الدراسه أنه ليس هنالك تغير ذو دلاله أحصائيه في مستوى الحديد لدي الذين تعرضوا للرصاص(0.229 ± 0.085) مقارنه بالذين لم يتعرضوا للرصاص (0.223 ± 0.078) القيمة الاحتمالية 0.676. كما كشفت الدراسه أنه لايوجد تغيير ذو دلاله أحصائيه في متوسط مستوي الحديد و النحاس لدي العمال الأكثر عرضه للرصاص مقارنه بالعمال الأقل عرضه للرصاص القيم الاحتماليه = 0.469,0.808على التوالي.

كما بينت الدراسه وجود ارتباط عكسي بين مستوي النحاس في الدم ومستوي الرصاص والحديد في الدم (r=-0.379, *p*-value 0.015) و(r=-0.394, *p*-value 0.011) علي التوالي .

الخلاصة: خلصت الدراسة إلى أن هنالك زياده في متوسط تركيز النحاس لدي العمال الذين تعرضوا للرصاصفي حين لايوجد تغيير 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 electricstorage batteries, lead solder, radiation shields, pipes, and sheaths forelectric cable andhence 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 inenvironment. 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 forhumans and animals. In the human organism,copper exists in two forms – the first andsecond oxidation form, as most of the copperin the human organism is in the second form (Angelovi*et 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. Copperplays 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(Osredkarand 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 (Brunse*t al.,* 2006).Lysyl oxidase is cuproenzyme essential for stabilizing of extracellular matrix especially in cross-linking of collagen andelastin (Ruckere*tal.*,1998).Superoxide dismutase (SOD**)**is abundant copper and zinc containing protein it primary functions as an antioxidant(Valentine *et al.*,2005).Ceruloplasminisferroxidases enzyme,is major copper-carrying protein in blood and play role in iron metabolism (Gawaree*tal*., 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 CopperAbsorption

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 individualcopper 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 tocytosol and mitochondria to utilize, also distributeto the secretary pathway. Distinct compartments of the secretarypathway, the *trans*-Golgi network (TGN), containCu-ATPases (ATP7B in hepatocytes), the ATPases then transfer copper across the membrane into the lumen of the *trans*-Golgi networkin hepatocytes,where it incorporated into the copper-dependentferroxidasesceruloplasmin (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 CopperExcretion

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

1.2.6 Copper deficiency

Copper deficiency is more commonly an acquired condition induced by theimbalance 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

Acquiredcopper 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).

1.2.6.2Genetic 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 inintestinal epithelium and kidney(Krupanidh*et al.*,2008).Menkes disease is characterized by peculiar hair called kinky or steely and retardation of growth(Bishop *et al.*,2010).

1.2.7Copper toxicity

Excessive copper intake can cause nausea, vomiting, abdominalpain and cramps, headache, dizziness, weakness, diarrhea, and metallic taste in the mouth. Chronic copper toxicitydoes not normally occur in humans because of transport systems thatregulate absorption and excretion. Since excess copper is excretedthrough bile, copper toxicity is most likely to occur in individuals withliver disease or other medical conditions in which the excretion of bile is compromised (Osredkar*et al*.,2011).

1.2.7.1Wilson disease

Wilson disease is an autosomal recessive disorder caused by mutations in the copper transport gene*ATP7B*(Desai andkaler2008; Das and Ray 2006).Whose original function is to regulate the bilary excretion of excesscopper, theresult 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 diagnostic marker for Wilson's disease(Krupanidh*et al*.,2008).

1.3Iron

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 myoglobinand is an important constituent of flavoproteins, cytochromes and most oxidases. Free iron is highly toxic and this probably related to inhibition of certainenzymes and initiationand catalyzing of free radical-mediated reactions (Koay and Walmslely,1999).

1.3.1 IronAbsorption

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-haemiron 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 makeit more soluble,duodenal cytochromes B reductase (DcytB), located on theluminal 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 thoseindividuals 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 proteinFerroportin(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(Abramowsk*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 IronTransport

Iron is distributed systemically in the circulation as transferrin. Transferrin comprisesa 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 byendocytosis. The resulting endosome contains the Tf-TfRcomplex. Ferrous ironatoms are released and transferred out of the endosome to the cytoplasm by thelocal divalent metal transporter1 (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 apotransferrinare recycled into the plasma(Jackson, 2010).

1.3.3 IronStorage

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 storageprotein found in all cells with the highest concentrations in the liver, spleen andbone marrow, Haemosiderin is produced by lysosomaldenaturation of ferritin, in which the proteinshells degrade and the iron cores aggregate. Haemosiderin iron is found in lysosomesand 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 body ,there are some obligatory loss from 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 itsdegradation and preventing iron efflux from iron-exporting tissues into plasma. Hepcidin synthesis is induced by iron loading andinflammation and suppressed by hypoxia and erythropoieticactivity. By simultaneously regulating intestinal iron absorption and the release of iron from macrophages andhepatic stores, hepcidin can be viewed as a master regulator of systemic iron availability (Himmelfarb,2007).

1.3.6Iron 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 demandin Infancy, rapid growth (adolescence), menstrual blood loss, pregnancy (second and third trimesters)and blood donation, or Environmental as Insufficient intake, resulting from poverty, malnutrition, orpathological asdecreased absorption (e.g.Gastrectomy, duodenal bypass, hookworm infestation), or genitourinary system, including heavy menses, menorrhagia(Camaschella,2015).

1.3.7Iron 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).

1.3.7.1Primary iron over load (Inherited)

Type1 haemochromatosis:is the classical and commonestof the primary iron overload syndrome. It is an autosomal recessive disorder resulting in iron overload andvariable multi-organ dysfunction. A homozygous mutationin the hereditary haemochromatosis gene, *HFE* is responsible for type1primary haemochromatosis (Siah*et al.*, 2006).

Type2Juvenile haemochromatosis (JH): is an autosomal recessivedisease characterizedby massive hepatocellular irondeposition as well as iron deposition in endocrine glands.Depending on the gene involved, Juvenile haemochromatosisis divided into two subtypes, Type2A is due to mutations in the *haemojuvelin (HJV)* gene encoding protein haemojuvelinJV,whishconsidered as an upstream regulator of hepcidin. The mutant haemojuvelin protein inhibitshepcidinexpression. While Type2B is due to mutation in the hepcidin gene(Siddique and Kowdley, 2012).

HH type3: is a disorder resulting from mutations in the transferring receptor-2 gene (Roetto*et al*.,2002).

1.3.7.2Secondary haemochromatosis

This group includes iron overload either due to or associated with ineffective erythropoiesis, chronic liver diseases, parenteral administration or ingestion ofexcessive amounts of iron. Thalassemia major and sideroblastic anemia arethe 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 α2-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 (Bal*et al*.,2015).

Also in other study Copper plasma levels of workers expose to lead were significantly higher compared with the control group and correlatedpositively with lead concentrations,while no association between iron and blood lead levels (Kasperczyk*et al.*,2012). Whileanother 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 dietaryiron 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

1.6.2Specific 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 remedialmeasures, Lead continues to receive as much attention as any modernenvironmental 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 exposureincludes: 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 studieswere done, in the Sudan no such study has been published yet. Benefit desired from this study isto inform workerswith 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

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Methods

2.1 Study Design Descriptive cross-sectional study, conducted during the period of February to Marsh 2016.**2.2 StudyArea**Thisstudywas carriedout inSariaindustrial complex and Alshagaria industrial complex at Khartoum state.**2.3 Study Population**

Eighty one worker were enrolled in this study, and then classified based on exposure to Lead into two groups, group one not expose to lead (41 worker)considered control, group two expose to lead in their work(40worker).

2.4 Inclusion criteria Specimens were collected from healthy worker expose to lead and non-expose 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 obtain 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.

2.8Principle 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 lightenergy 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.

2.9Method 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 deionizedwater, 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.

2.12Statistical 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

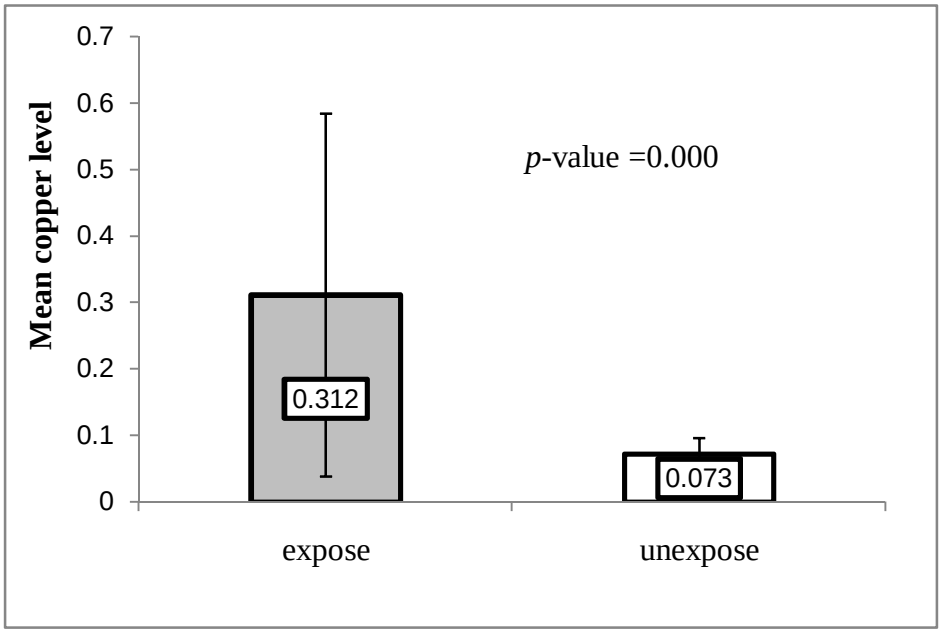
This study included 41 Lead exposure workers and 40unexposures.The mean concentration of copper was significantly increased among lead exposure subjects(0.312±0.273)in comparison with(0.073±0.024) in unexposed with p-value 0.000 whichpresented in figure 3.1.

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 whichpresented 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 figure3.3.

Also our resultsshowed 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*–value0.469 whichispresentedin figure 3.4. Person's correlation showed, serum copper levelis inverselycorrelated with serum ironand serum Lead concentration (r=-0.379, *p*-value 0.015) and (r=-0.394, *p*-value 0.011) respectively, whileno correlation observed when associate serum copperwith age of workers and duration of exposure(r -0.178, *p*-value0.267)and (r= -0.242,*p*-value 0.128) respectively all are presented in table 3.1.

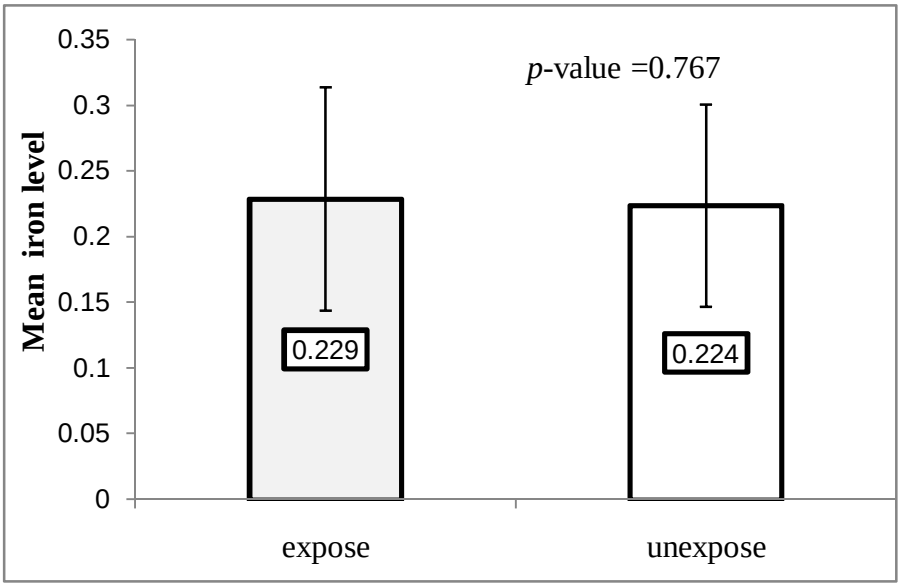
Serum iron level is not correlated with age of worker, duration of exposure and serum lead level(r= 0.155*p*-value 0.332), (r=0.063 *p*- value 0.698) and(r=0.276*p*-value0.081) all are represented in table 3.2.

Figure 3-1: Mean copper level among lead exposure and unexposed



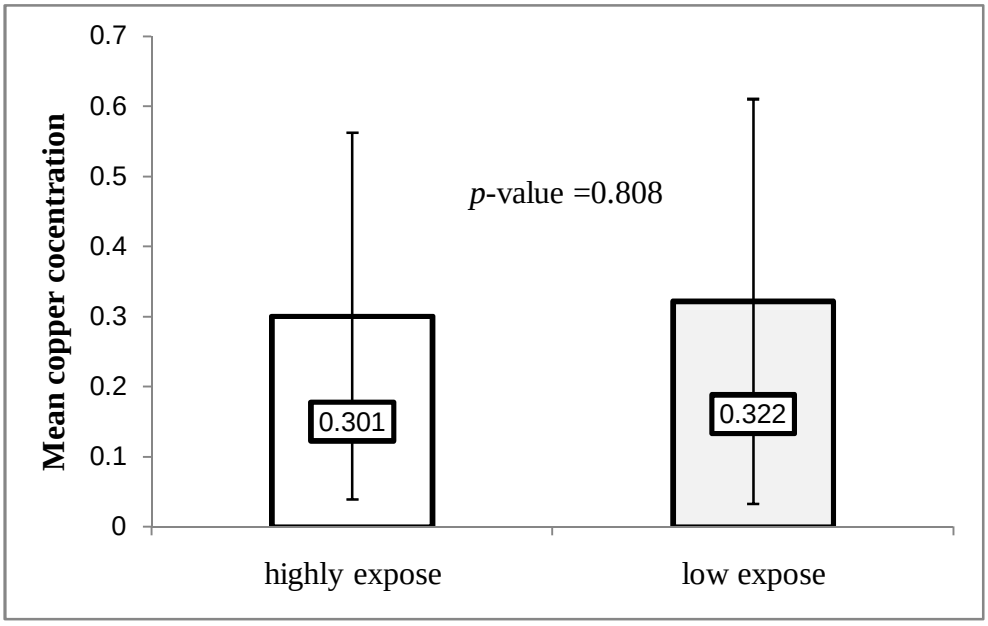
Results express as mean±SD,significant considered as p-value≤0.05.

Figure 3.2: Mean iron level among lead expose and unexposed



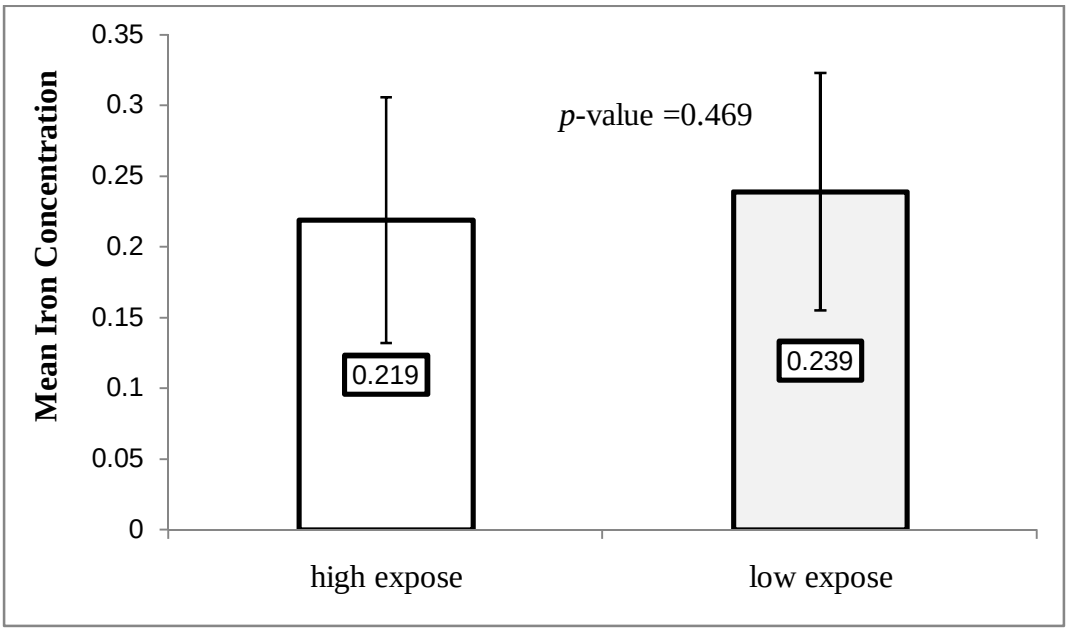
Results express as mean ±SD, insignificant consider as *p*- value ≥ 0.05.

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 3.1correlation between copper and study variables

Variable	R-value	*p*-value
Age	-0.178	0.267
Duration	-0.242	0.128
Iron	-0.379	0.015
Lead	-0.394	0.011

Table 3.2: correlation between iron and study variables

Variable	R-Value	*p*-value
Age	0.155	0.332
Duration	0.063	0.698
Copper	-0.379	0.015
Lead	0.276	0.081

Chapter four:

Discussions

&

Conclusion

&

Recommendations

4.1Discussions

Lead is toxicant that can exert adverse effects in humans, causes neurological, hematological, gastrointestinal, reproductive, circulatory and immunological pathologies depending upon the level and duration of exposure, it also markedly alter the function and metabolism of some micronutrients (Bal *et al*.,2015).Therefore descriptive cross-sectional study was carried out to evaluate status of essential elements copper and iron in workers whom occupationally expose to lead in Khartoum State.

The present study revealed that, there was insignificant difference in mean concentration of iron in lead exposed compare with control group with*p*-value0.808, this finding indicate 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 study reported contradict our finding that, serumiron 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*-value0.81)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 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 indicate 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 elevatedactivity of superoxide dismutase isoenzymes that containsCopper and Zinc (CuZn-SOD) in both serum and erythrocytes**(Kasperczyk*et al*., 2004)**. Therefore, an increase in the Copper level, which was observedin 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 Leadinducedoxidative stress**(Kasperczyk*et al*., 2005)**the increase in plasma Copperlevels 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 contrastwith perviousstudy **(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 workerswhile iron is not changed.

4.3Recommendations

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 chelatorsfor 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.

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Appendixs

Appendix (1)

Sudan University of Science and Technology

College of Graduate studies

M.SC of medical laboratory

Questionnaire

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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؟

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

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