IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 13, Issue 1 Ver. IX. (Feb. 2014), PP 83-88
www.iosrjournals.org

Association of Lead with Heamoglubin damage in males (car painters) of Lahore.

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Abstract: *Lead is a poisonous metal and is widely used in daily life for its good chemical properties. Increased use of lead in industry, its excessive inhalation and ingestion can adversely affect major biological functions in the human body.*

The study was carried out in Seventy car painter working in Lahore and. Cases were selected according to inclusion and exclusion criteria through stratified random sampling using proportional allocation.

Blood samples were drawn after informed consent. Blood lead concentrations was determined by atomic absorption spectrometer.

Correlation between lead level and Hb was observed by the data obtained. Data analysis was done by SPSS version 18.

Key Words: *ROS ,Reactive Oxygen Species (ROS), Lead, Heamoglubin (Hb)*

I. Introduction

Lead is one of the most useful metals having its applications worldwide, yet is among the most toxic ones (1). Lead is well known for its deleterious occupational and environmental hazards and is considered to be a ubiquitous global environmental pollutant. Humans have been using lead since decades and some of its toxic effects have been recognized for centuries. Lead is consumed widely in industry and daily life for its good mechanical and electrochemical properties including its high malleability, resistance to corrosion, low melting point, low cost and easy handling. The quantity of lead consumption in the 20th century is far more than the total consumption in all previous eras, mainly because of its industrial applications (2).

The heavy use of lead in industries has caused high levels in water and urban polluted air causing global contamination of air, water and soil. Multiple researchers have found that lead can cause neurological, hematological, gastrointestinal, reproductive, circulatory and immunological pathologies (3). Lead can elicit positive response in vast majority of biomolecular and biochemical tests, including enzyme inhibition, DNA damage, mutation, chromosomal aberrations, cancer and birth defects (4).

Chronic lead exposure over months or years produces adverse effects on calcium homeostasis, affects ATP inhibitors and mitochondrial oxidative phosphorylation process, thus interfering with normal growth of cell. Lead disturbs the pathway for Hb synthesis, coherence of cell membranes and breakdown of steroids. It also results in damage to motor axons and interferes with myelin formation and integrity of blood brain barrier. Anemia develops because of the inactivation of enzymes involved in heme synthesis which gives rise to basophilic stippling of red cells and appearance of lead lines in gums that are particular of lead chronicity. There is reduced sperm count affecting the male reproductive system. Renal failure and encephalopathy are other problems. Prolong lead exposure also leads to delayed motor and sensory nerve conduction causing significant hearing loss. A high body lead level results in decreased excretion of urinary urate and is connected with clinical gout (5).

Levels of lead should be zero in the body but it is not practically possible in the urbanized areas because of increased industrialization for the past few decades. In 1971, the minimum safety level for lead was decreased to 40 µg/dl, to 30 µg/dl in 1975 and to 25 µg/dl in 1985. It has been shown in later surveys that even below these levels some toxic manifestations may occur, mainly due to recent exposure (6).

Some of the lead compounds are used extensively in paints because of being colorful. Nevertheless, most of the lead found in food, paint and majority of lead containing consumer products is inorganic in nature. It is absorbed via skin in minimal amounts. Lead exposure occurs mainly through the respiratory and gastrointestinal (GI) tracts by inhalation or ingestion of lead respectively. Bloodstream absorbs roughly 30-40% of inhaled lead. The particle size of airborne lead is mostly too large to be inhaled in community environments.

For this reason, inhalation of airborne lead is a major source of exposure for occupationally exposed adults but not for children (7).

It has been shown in numerous studies that lead causes anemia by inhibiting heme and globin synthesis (8)**.** Lead related pathology mainly results from inhibition of heme sythesis and succeeding decreased body pool of heme.

II. Review Of Literature

Generation of reacting oxygen species induced by δ-ALAD

Hemoglobin gets oxidized after long term exposure to lead, which can also cause red blood cell hemolysis. This occurs because of inhibition of δ-ALAD. This enzyme is very sensitive to the toxic effects of lead and results in decreased heme formation. As a consequence, subjects exposed to lead have increased level of ALA (substrate for the enzyme δ-ALAD) in their blood and urine. The increased level of ALA generate H_2O_2 and O_2, and also interact with oxyhemoglobin, resulting in generation of OH°, the most reactive of free radicals. OH° is a potential genotoxic compound and is a probable cause of metal dependent DNA carcinogenicity of lead. Production of OH° in proximity to DNA causes it to react with DNA bases or the deoxyribosyl backbone of DNA producing damaged bases or strand breaks (9).

Oxygen radicals produced may induce generation of mutagens by inducing base alterations. However, DNA base modifications can be repaired by specific and general repair mechanism (10). ROS reacts with the biological molecules and interrupt the repair of DNA and its synthesis. The mechanism associated with this disruption is possibly inactivation of antioxidant key proteins and DNA repair enzymes induced by ROS-damage to these biomolecules (11).

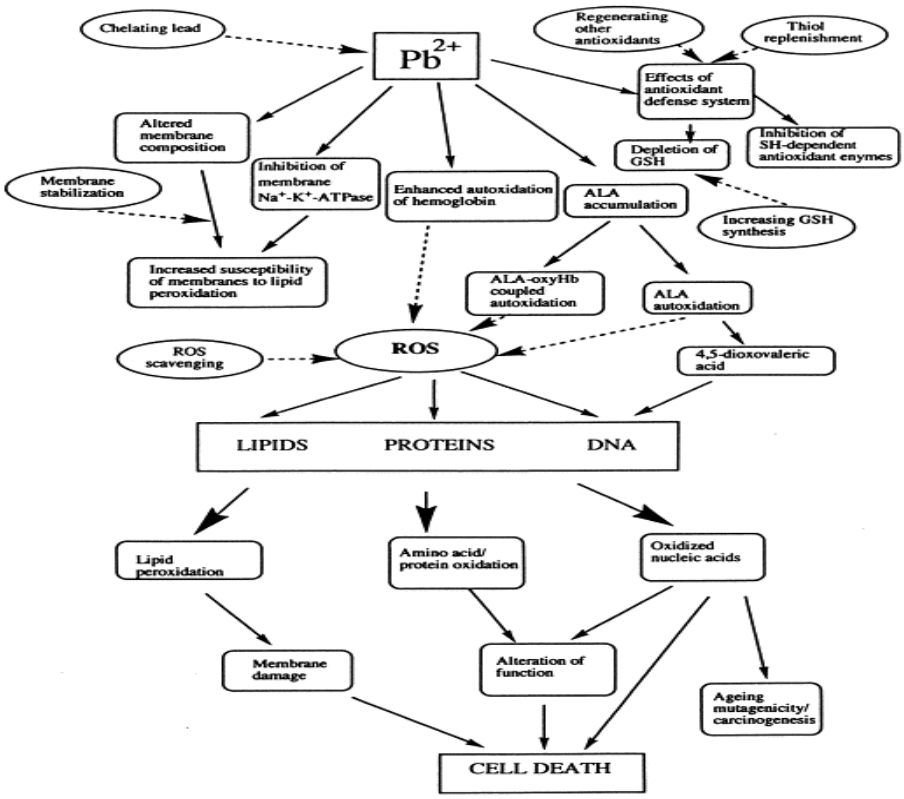
Hb lead interactions

Heavy metals like lead interact with oxygen forming oxyHb, methaemoglobin and other ferric and ferrous complex which is important source of superoxide radical formatiom in RBCs (12). Ferrochelatase is an enzyme that incorporates iron into protoporphyrin ring. Inhibition of this enzyme by lead results in binding of zinc to protoporphyrin and formation of Zinc Protoporphyrin. The presence of ZPP can also be used as a biomarker of lead toxicity (13).

Cells have different antioxidant defense systems against free radical attack. GSH plays an important role in protecting the cell against oxidative stress (13). It is formed in the interior part of lymphocyte and is a cysteine-based molecule. A major part of non-tissue sulfur in the human body is found in the form of tripeptide glutathione. It acts as an important antioxidant for sequestering free radicals, and also has many other important functions to perform. Glutathione has a sulfhydryl complex that binds directly to toxic metals having high affinity for it. Such binding efficiently inactivates glutathione, rendering it unavailable as an antioxidant and increasing the production of free radicals in the body. These toxic metals include lead, arsenic and mercury. It has been reported that glutathione concentration in the blood of lead-exposed animals, children and adults was considerably lower than the controls (Patrick, 2006). Zinc serves as cofactor for many enzymes in the body. Lead can replace Zn in these enzymes, resulting in their inactivation. It has been reported that antioxidant defense system can be altered by lead. This system includes enzymes such as GPx, glutathione-S-transferase, SOD, CAT, and nonenzymatic molecule like glutathione, which normally protect against free radical toxicity,in animals and humans (14,15). It is reported that heme synthesis is inhibited by lead, therefore the activity of CAT (heme containing enzyme) also decreases in the presence of lead. Copper and Zinc are essential for the activity of SOD. Copper ions undergo alternate oxidation playing a functional role. On the other hand zinc ions are thought to stabilize the enzyme. Lead replaces both these ions, decreasing the activity of SOD (16).

Overall, these inhibitory effects of lead on various enzymes would probably result in depletion of antioxidant defenses by cells and render cells more susceptible to oxidative attack through generation of highly reactive oxygen species. Formation of reactive oxygen intermediates beyond the scavenging capacity of these antioxidant defense mechanisms results in accumulation of harmful free radicals and likelihood of oxidative damage to critical biomolecules, such as enzymes, proteins, DNA and membrane lipids (17,18).

Lead is widely used in various paints because of its anticorrosive properties and ability to hold pigments together. Painters are continuously exposed to lead-containing paints as well as to an extensive variety of hazardous substances like organic solvents and residual plastic monomers (19).



AIMS / OBJECTIVES

Correlated the serum lead levels with various hematologic indices in car painters of Lahore.

III. Material And Methods

Study Design

It was a correlational study.

Settings

The study was conducted in the Department of Biochemistry, University of Health Sciences Lahore.

Duration

The study was completed in 6 months after the approval of synopsis.

Sampling Technique

Convenient sampling was done from Lahore. Blood samples of 70 car painters from Lahore were taken after an informed consent. The total sample size was 70 car painters that fulfilled the inclusion and exclusion criteria.

Sample selection

Inclusion criteria

1. Car painters from Lahore.
2. Age ranging between 25 – 50 years.
3. Car painters working for at least 5 years in the same industry.

Exclusion criteria

1. Car painter with prolonged history of infections/illness.

IV. Methodology

After an informed consent, blood samples were collected from 70 car painters fulfilling the inclusion and exclusion criteria. All the blood samples were drawn under aseptic conditions from the median cubital vein from anterior aspect of forearm. Five ml was obtained and divided into two tubes. Two mL of blood was transferred in a vaccutainer containing EDTA K3 anticoagulant for hematologic indices determination and three ml was collected in serum vaccutainers for lead determination. The sample was transported to University of Health Sciences in a cool box containing ice bags.

Hematologic indices were determined by an automated analyzer (Sysmex XT 1800i) on the same day.

STATISTICAL ANALYSIS

- The data were entered and analyzed using SPSS 20.
- Mean ± S.D was given for quantitative variables (Lead level, hematological indices and age).
- Distribution of variables was checked using the Shapiro-Wilk test. Because of non-normal distribution of parameters, the differences between mean values were tested with nonparametric tests the, Mann-Whitney U test.
- Spearmans rho correlation was applied to observe correlation between quantitative variables (Blood indices and lead level).
- Correlation coefficient (r) was determined and p value of ≤ 0.05 was considered as statistically significant.

V. Results

In the present study 70 Car painters were taken from Lahore which fulfilled the inclusion and exclusion criteria. On the basis of occupational exposure they were divided into two groups. One with an experience of 10 years or less and other with experience of more than ten years.

The age range of car painters was from 25 to 45 years with a mean of 30.41 ± 4.99. The experience in years ranged from a lowest of 5 years to 20 years with mean 10.32 ± 4.72. The subjects were divided into two groups based on experience. Group 1 contained car painters with experience ≤ 10 years. Group 2 contained car painters with experience > 10 years.

Hb of car painters ranged from a minimum value of 9.0 g/dL to a maximum of 17.40 g/dL with mean 14.34±1.13. The difference in means of the two groups was more than 0.05 and thus statistically insignificant (p value 0.187).

Parameters	N	Mean	Std. Deviation	Mean
Age in years	70	30.41	± 4.988	30.00
Experience in years	70	10.321	± 4.725	9.00
Serum lead levels in µg/dL	70	15.342	± 3.440	15.00
Hemoglobin in g/dL	70	14.340	± 1.125	14.40

Table 1: Mean ± SD and median values of variables

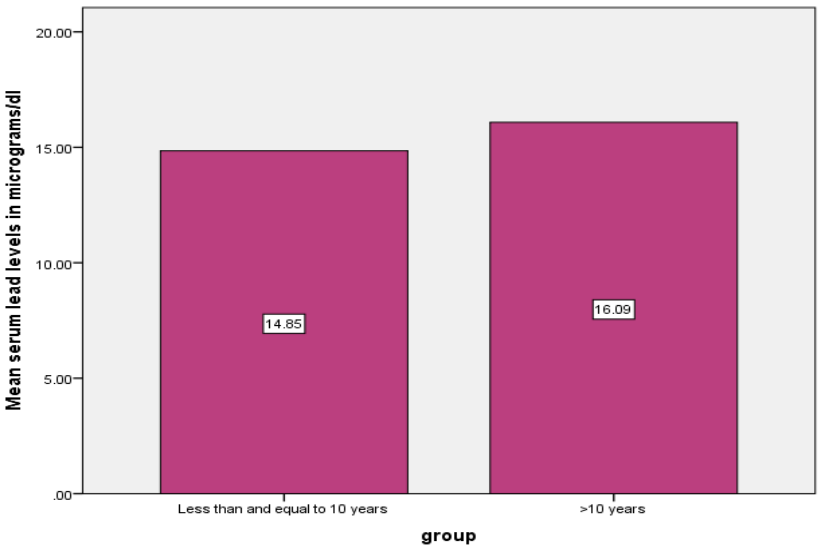


Figure 1: Mean serum lead level in two groups

Parameter	Group	N	Mean value	Mann-Whitney test (P-value)
Hemoglobin in grams /deciliter	Less than or equal to 10 years	42	14.21	0.187
	More than 10 years	28	14.52	

Table 2: Mean Hb in two groups

The mean values of hemoglobin of the group with an exposure for less than and equal to ten years was 14.21 and that with an exposure or more than 10 years was 14.52 but it was statistically insignificant with a p value of 0.187. A P value of $\leq$ 0 .05 is considered to be statistically significant.

Parameter	Group	N	Mean value	Mann-Whitney test (P-value)
Serum lead level in micrograms /deciliter	Less than or equal to 10 years	42	14.84	0.259
	More than 10 years	28	16.08	

Table 3: Mean serum lead level in two groups

The mean values of serum lead levels among the two groups were 14.84 and 16.08 respectively with a p value of 0.259 that was statistically insignificant. A P value of ≤ 0.05 is considered to be statistically significant.

Parameters	Correlation(p value)	Correlation coefficient(r)
Lead µg/dl	0.685	-0.049
Hb g/dl		

Table 4: Correlation of lead with Hb

VI. Discussion

Lead has been a known poisonous metal for thousands of years, and it remains a persistent environmental health threat. Exposure to lead can result in significant adverse health effects to multiple organ systems including the nervous, hematologic, renal, and reproductive systems. The different sources of lead and its unknown threshold of subclinical toxicity continue to make lead a matter of public health concern. Occupational exposure to lead is most often faced at battery manufacturing facilities and lead smelters, as well as in renovating houses in which workers inhale and ingest lead-contaminated fumes and dust from lead-based paint. Blood lead level (µg/dl) is most often used by health care providers as an indicator of recent lead exposure (20).

In Pakistan work regarding the lead levels in occupationally exposed individuals has not been done to a great extent particularly in commercial painters. However few researches in other occupationally exposed lead workers has been done like the traffic constables of Karachi and Islamabad .The mean age range of our subjects was from 25 - 40 years 30.41 ± 4.988. The mean age range in traffic constables of Islamabad and Karachi was 21-45 and 20-55 years respectively, not comparable with our study. The duration of service /exposure in our subjects ranged from minimum of 5 years to a maximum of 20 years whereas in their study it ranged from 3 months to 18 years, not as in our study. In their study blood lead levels, Hb, copper and manganese levels were determined. The blood lead levels ranged from 7.6 -108.8 µg/dl with a mean value 27.27 ± 4.04 µg/dl. 46% constables had lead level upto 20 µg/dl, 19% had lead level ranging from 20-25 µg/dl, 21 % had levels above 25 µg/dl and 13% above safety limit 40 µg/dl. Controls had a low mead blood lead level as compared to cases but there were no controls in our study. No significant difference was found in mean lead level at various age groups in the constables of Islamabad, however the levels were significantly high ($p < 0.0001$) at all age groups in traffic constables of Karachi. There was no correlation between Bpb and length of service as compared to our study but in our study the painters hematocrit mean was 41.06 in the group with less than 10 year exposure and 42.74 in the group with more than 10 years exposure, with a P value of 0.003***** that was statistically significant. Hb in their study was found to be normal in all age groups as compared to our study (21). Muhammad et al in another study reported oxidative stress parameters and lead levels in painters of Lucknow, India in which 35 painters aged 25 - 50 years were selected as in our study. The mean BLL < 400 micrograms were selected from 56 male painters that were initially screened for blood lead. Controls were also taken. Association was made between low level lead exposure and antioxidant status. It was found that BLL in painters were 219.2 ± 61.9 µg/dl, approximately seven times higher than controls (30.6 ± 10.1) µg/dl. The painters exhibited a significant decrease in antioxidant enzyme catalase (56.77 ± 11.11) versus controls (230.30 ± 42.55) and SOD (0.64 ± 0.19) compared to controls (2.68 ± 0.62). Painters duration of exposure was from 5 to 10 years and in our study from 5 to 20 years but in our study lead levels were below safety limits and not significantly high as in their study. This may indicate that the paint used in India is more hazardous than the one used in Pakistan but still the quantity of white lead in lead based paints made in our industries should be measured for the better health assurance of paint users (19).

VII. Conclusion

The following conclusions were drawn from our study

1. Serum lead levels were below the safety limits of 40 micogram/dl in all subjects.
2. Hb is negative correlated with serum Lead levels

Recommendations:

The improper use of aerosol removing respirator, lack of an isolated spraying room and poor personal hygiene habits, not wearing of protective masks may cause the failure to prevent heavy metal intoxication among the painters in workshops or commercial painters. Further efforts are needed to determine the true incidence of lead exposure and to educate employers, workers, and health care professionals about this ongoing problem and the importance of primary prevention of lead poisoning which is a significant constituent of several disease outcomes such as peripheral artery disease, renal diseases,hypertension and cognitive impairment.

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