THE STUDY OF HEPATO-RENAL PROFILE ASSOCIATED WITH LEAD TOXICITY IN SPRAY PAINTERS
S. Chuhitha¹, R. Viswa Kumar², V. Chandra Mohan³, K. Madhavi⁴, P. Prabhakar Rao⁵

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ABSTRACT: Lead is a soft, dense, ductile, blue-grey metal. Lead is very stable and resistant to corrosion. It does not conduct electricity. Lead is effective shield against radiation. Lead present in natural deposits as ores, has been exploited extensively for commercial purposes because of its useful physiochemical profile. With years of knowledge on toxic effects of lead, it is used extensively in various products of common use found in and around our homes posing threat to humans. Occupational exposure to lead is entirely unregulated in many developing countries. The present study was carried out in spray painters to assess the magnitude of lead toxicity and also to highlight the subclinical toxicity with emphasis on renal and hepatic function. We have done a comparative study of blood lead levels, renal function parameters like serum creatinine, BUN, uric acid and liver function parameters like serum proteins, Albumin, Bilirubin AST, ALT in spray painters and non-painters. In our present study the blood levels (p<0.001) were significantly increased as compared to the control group. Serum creatinine (p<0.001), BUN (p<0.001) and serum uric acid levels (p<0.004) were significantly increased in spray painters as compared to controls. Even though the mean values of liver function parameters were altered in spray painters as compared to controls, the range of values were within the acceptable limits for assay methods used. Currently there are some early and sensitive biochemical markers for detection of toxic effects of lead but they are still under epidemiological validation. The measured blood lead levels would be a good reference for monitoring the current status of lead toxicity, for evaluating the risk of progressive renal insufficiency and to apply possible lead chelating therapy early in clinical practice.


INTRODUCTION: Lead paint is actually paint containing lead pigment in various co-ordinated states. Most common type of lead paints used are Lead chromate and Lead carbonate. Lead speeds up paint drying, increases durability and resists moisture that causes corrosion. Global Alliance defined “Lead paint” as any paint with lead concentration >90 ppm.¹

In India 10% of total lead metal is utilized in manufacture of paints. Tests by centre for science and environment -2008 found that the paint products of many leading companies have shocking amount of lead i.e., 180 times the voluntary standard code of 1000 ppm.² Approximately 30-40% of inhaled lead is absorbed into the blood stream. Most of the adult exposure is occupational.

Lead is unique as toxicant and called as “The Silent epidemic”. There is an agreement among CDC, ATSDR, EPA that is there no toxic threshold for lead.³

The present study attempts to assess the magnitude of lead exposure in an occupational setting i.e., spray painters by measuring blood lead levels (BLL) and its impact on the renal and hepatic function, compared with non-painters.
Chronic high levels of lead results in irreversible changes in kidney. Individuals with blood lead levels > 60 µ g/dl are at definite risk of developing renal failure. More recently it has become evident that blood lead levels as low as 10 µ g/dl previously considered to be safe may also be associated with renal function abnormalities. Lead nephropathy manifests as proximal tubular damage, glomerular sclerosis and interstitial fibrosis. Histological changes include eosinophilic intranuclear inclusions in proximal tubular cell consisting of lead-protein complexes and mitochondrial swelling. Kim et al study found a positive correlation between BLL and Serum creatinine concentrations. The Normative Aging study of low level lead exposure & Impairment of renal function shows that blood lead concentrations was positively and significantly associated with concurrent concentrations of serum creatinine. A 10 fold increase in Blood lead levels predicted an increase of 0.08mg/dl (7µmol/L) in serum creatinine which is roughly equivalent to the increase predicted by 20 years of aging and creatinine clearance reduction of 10-13 ml/min.

Gout was found in half of the patients with chronic lead nephropathy Known as Saturnine gout. Enhanced formation of reactive oxygen species (ROS) i.e., superoxide radical, hydroxyl radical, Hydrogen peroxide, and peroxy nitrite has been suggested to play a role in liver disease process.

Hepatic Cytochrome p450 inhibition by lead at the level of transcription, decreased synthesis of heme and heme saturation of the Cytochrome p 450. However the mode of cell death and intracellular signaling mechanism induced by ROS in hepatocytes remain controversial.

MATERIALS AND METHODS:

**Subjects:** This is a case- control study involving 30 male workers engaged in spray painting as the study group. Female workers were excluded from the study due to reasons like lack of co-operation and unwillingness towards collection of blood samples.

All the cases were in the range of 20-40 years of age. Non-smokers, non-alcoholics who were in spray painting for more than 6 hrs/day with duration of exposure from 5-20 years were selected for the study. None of them had a past history of major illness. Most of the workers had major complaints of anorexia, myalgia, headache, abdominal colic, insomnia, arthralgia.

The study objectives were explained, both ethical clearance and patients consent were obtained from the Institutional Ethical Committee and the patients before commencement of the study. 15 normal healthy subjects of similar age group who were non-painters served as non-exposed controls. Due to this stringent criteria the sample size was limited to 45 only.

Random venous samples were collected from both the groups. 3-4ml collected in heparin coated vacutainers for blood lead estimation.

2 ml of blood sample collected in plain vacutainers for serum separation.

Biochemical parameters included total proteins, albumin, alanine transaminase, aspartate transaminase, serum total bilirubin, creatinine, BUN, uric acid were measured by using standard kit methods on the same day of collection. Blood lead levels were measured by atomic absorption spectrophotometer in small batches within a week after sample collection. Instruments used Erba chem. Semi autoanalyser, Atomic absorption spectrophotometer.

Estimation of Lead levels-200 µl of whole blood sample is taken in precleaned centrifuge tube. To this add 1200 µl of matrix modifier solution (0.2% Nitric acid +0.5% Ammonium dihydrogen
phosphate + 0.4% Triton X). Samples are left for 5 mins. Centrifuge at 3000 rpm for 6 mins. This sample is injected into the precoated graphite tube of atomic absorption spectrophotometer.

The furnace is programmed to achieve the temperature in a sequenced manner. Record the absorbance peak area generated by each specimen. Compare the absorbance peak areas derived from each specimen against calibration curve to determine the concentration of lead.\(^\text{19}\)

Determination of Creatinine by Jaffes method\(^\text{20}\), BUN-Urea in mg% X 0.467, Determination of Urea by Berthelot method\(^\text{21}\) and Uric acid by Uricase method.\(^\text{22}\) Determination of total proteins by Biuret method,\(^\text{23}\) Albumin by BCG dye method.\(^\text{24}\)

Bilirubin by Diazo method,\(^\text{25}\) AST and ALT by enzymatic methods.\(^\text{26}\)

**Statistical Analysis:** Data was expressed as Mean ± SD. Student’s t test used to compare normally distributed variables between groups. A p value of < 0.05 was considered statistically significant. Pearson correlation test was used to identify associations between the parameters. All statistical tests were done employing SPSS program version 16.

**RESULTS:** The observations of this study indicate that occupational lead exposure still remains a concern in developing countries. In our present study the blood lead levels (p <0.001) were significantly increased as compared to the control group. Serum creatinine (p <0.001), BUN (p <0.001) and serum uric acid (p <0.004) levels were significantly increased in spray painters as compared to controls. Serum proteins and albumin levels were marginally low in spray painters as compared to controls.

Table no.3 indicates the correlations between Lead levels and renal parameters. The table depicts that there were significant positive correlations between lead levels and serum creatinine (r=0.615) and uric acid (r=0.469) BUN (r= 0.205).

Table no. 4 indicates the correlations between Lead levels and Liver parameters. The table depicts that there were no significant (p>0.05) correlations between lead levels and all liver parameters.

Serum bilirubin levels were marginally high in spray painters. But the changes in serum proteins, albumin, bilirubin were not significantly altered in spray painters as compared to controls. The serum ALT and AST levels were marginally increased in spray painters as compared to controls. The present study which revealed the BLL in the spray painters ranging from 15-22µg/dl confirms the existence of lead toxicity:

- Renal functions in the spray painters were affected at the observed range of BLL.
- Liver function parameters were within the acceptable limits of assay methods used suggesting that the synthetic and hepatocellular functions were conserved at the observed range of BLL.

**CONCLUSION:** The present study is carried out to high-light the subclinical toxicity with emphasis on renal and hepatic function. The study shows that spray painters must be considered as risky group. Estimation of blood lead levels (BLL) would be a Good reference for monitoring current status of lead toxicity, for evaluating the risk of progressive renal insufficiency, to apply possible lead chelating therapy early in clinical practice.

Early screening and regular monitoring of spray painters is urgently needed to reduce the long term adverse effects of lead exposure.
ORIGINAL ARTICLE

ABBREVIATIONS:
- CDC- Centre for disease control.
- ATSDR- Agency for toxic substances and disease registry.
- EPA- Environment protection agency.
- AAS- Atomic absorption spectrophotometer.
- BLL- Blood lead levels.
- ROS- Reactive oxygen species.

REFERENCES:

Table 1:

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<thead>
<tr>
<th>PARAMETERS</th>
<th>CASES</th>
<th>CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>27.1 ± 6.32</td>
<td>29.4 ± 6.26</td>
</tr>
<tr>
<td>DURATION OF EXPOSURE</td>
<td>8.8 ± 2.73</td>
<td>--</td>
</tr>
</tbody>
</table>

Table 2:

<table>
<thead>
<tr>
<th>SL</th>
<th>PARAMETERS</th>
<th>CONTROLS</th>
<th>CASES</th>
<th>P VALUE</th>
<th>REMARKS</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>BLOOD LEAD</td>
<td>2.38±1.33</td>
<td>17.75±1.89</td>
<td>&lt;0.001</td>
<td>SIGNIFICANT</td>
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<tr>
<td>2</td>
<td>SERUM CREATININE</td>
<td>0.87±0.17</td>
<td>1.73±  0.26</td>
<td>&lt;0.001</td>
<td>SIGNIFICANT</td>
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<tr>
<td>3</td>
<td>BUN</td>
<td>9.36±1.06</td>
<td>21.37± 5.81</td>
<td>&lt;0.001</td>
<td>SIGNIFICANT</td>
</tr>
<tr>
<td>4</td>
<td>SERUM URICACID</td>
<td>4.75±1.26</td>
<td>6.50±  0.73</td>
<td>0.0004</td>
<td>SIGNIFICANT</td>
</tr>
<tr>
<td>5</td>
<td>TOTAL PROTEINS</td>
<td>6.76± 0.54</td>
<td>6.35± 0.68</td>
<td>0.06</td>
<td>NON-SIGNIFICANT</td>
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<tr>
<td>6</td>
<td>SERUM ALBUMIN</td>
<td>4.55± 0.39</td>
<td>4.25±  0.50</td>
<td>0.06</td>
<td>NON-SIGNIFICANT</td>
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<tr>
<td>7</td>
<td>SERUM BILIRUBIN</td>
<td>0.820±0.21</td>
<td>0.04±0.22</td>
<td>0.79</td>
<td>NON-SIGNIFICANT</td>
</tr>
<tr>
<td>8</td>
<td>SERUM ALT</td>
<td>18.75±2.00</td>
<td>21.25± 4.14</td>
<td>0.02</td>
<td>SIGNIFICANT</td>
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<tr>
<td>9</td>
<td>SERUM AST</td>
<td>20.35±1.96</td>
<td>23.45± 4.70</td>
<td>0.008</td>
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Table 3: correlations of different renal parameters in cases

<table>
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<tr>
<th>LEAD LEVELS (µg/dl)</th>
<th>LEAD LEVELS (µg/dl)</th>
<th>Serum creatinine (mg/dl)</th>
<th>BUN (mg/dl)</th>
<th>Uric acid (mg/dl)</th>
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<tbody>
<tr>
<td>Pearson Correlation</td>
<td>1</td>
<td>.615**</td>
<td>.205</td>
<td>.469**</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>N</td>
<td>30</td>
<td>30</td>
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</tbody>
</table>

The above table depicts that there were significant positive correlations between lead levels and serum creatinine (r=0.615) and uric acid (r=0.469) BUN (r= 0.205).

Table 4: correlations of different liver parameters in cases

<table>
<thead>
<tr>
<th>LEAD LEVELS (µg/dl)</th>
<th>LEAD LEVELS (µg/dl)</th>
<th>Total protein (gm/dl)</th>
<th>ALBUMIN (gm/dl)</th>
<th>Serum bilirubin (mg/dl)</th>
<th>ALT (IU/l)</th>
<th>AST (IU/l)</th>
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</thead>
<tbody>
<tr>
<td>Pearson Correlation</td>
<td>1</td>
<td>-.122</td>
<td>-.079</td>
<td>-.072</td>
<td>-.055</td>
<td>-.086</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>N</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

The above table depicts that there were no significant (p>0.05) correlations between lead levels and all liver parameters.

Figure 1
AUTHORS:
1. S. Chuhitha
2. R. Viswa Kumar
3. V. Chandra Mohan
4. K. Madhavi
5. P. Prabhakar Rao

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Biochemistry, Rajiv Gandhi Institute of Medical Sciences, Ongole.
2. Professor, Department of Biochemistry, Rajiv Gandhi Institute of Medical Sciences, Ongole.
3. Associate Professor, Department of Biochemistry, Rajiv Gandhi Institute of Medical Sciences, Ongole.
4. Professor, Department of Biochemistry, Sri Venkateswara Medical College, Tirupathi.
5. Associate Professor, Department of Biochemistry, Sri Venkateswara Medical College, Tirupathi.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Chuhitha,
Assistant Professor,
Department of Biochemistry,
RIMS Medical College,
Ongole.
Email: drsch2k6@rediffmail.com

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