

## Original Article

### A Study of Clinical Presentations of Chronic Lead Poisoning In Adult

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**Background** : Lead, an important industrial heavy metal, is known to cause toxicity to human beings. Being indispensable in modern industry based civilization, lead continues to cause toxicity to persons handling it. It can damage major organ systems in human body resulting in permanent dysfunction. With proper screening program this disease can be prevented or treated at an early stage. Presentation of chronic lead toxicity varies depending on the predominant organ involvement. There is scarcity of data in recent literature on clinical presentations of lead toxicity in this part of the world. Our study aims to fill this gap.

**Objective** : To describe various clinical presentations of chronic lead toxicity in adult patients so that they can be detected early in patients by serum lead level estimation and other relevant testing and timely intervention including prevention of further exposure and appropriate treatment may be instituted.

**Methods** : Adult patients (>18 years) presented to OPD or admitted in IPD of our tertiary care level hospital with clinical feature compatible with chronic lead toxicity and elevated serum lead level (> 10 mcg/dl) were recruited in this study. Patients having co morbidity like Diabetes were excluded from study. Thorough history taking and clinical examination were performed on each patient. Laboratory tests like Complete hemogram, Renal function tests, urine routine tests were performed in all patients and Nerve conduction studies, Imaging were performed whenever indicated. Data were recorded in a pre-specified Case record form (CRF).

**Result** : 14 patients were recruited in our study. Mean age at presentation of participants in our study was 39.6 years. Main source of lead exposure was battery industry. Most common presenting symptom was motor neuropathy (50%), while most commonly involved system was hematopoietic (78.5%). Renal involvement was found in 28.5% patients. Blood lead level was in higher range in participants with considerable interpersonal variation. So called hallmark features of chronic lead toxicity like blue line in gum or basophilic stippling of RBCs in peripheral blood film were seen much less frequently.

**Conclusion** : In our study lead toxicity is shown to affect middle aged industrial workers. A lower threshold of clinical suspicion is required to diagnose the condition in patients from appropriate occupational background so that early diagnosis and appropriate interventional measures can be taken to halt the progression of this silent killer. The most common system involved in this study was hematopoietic, most common presenting complaint was neurological. Blue lines of gum and basophilic stippling did not appear to be very sensitive clinical features. More studies with larger population are required to achieve deeper insights into this preventable disease.

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**Key words** : Lead, motor neuropathy, lead line, nephropathy.

Lead is one of commonest heavy metals known to cause toxicity in human beings. Lead is widely used in certain industries like mining, battery manufacturing and painting. In literature Ayurvedic products have also been reported to be source of lead<sup>1</sup>. Prevalence of Lead exposure and toxicity in developing countries is not very well documented, more so in recent years.

Lead is absorbed in human body through GI tract

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#### Editor's Comment :

- High degree of suspicion is required to diagnose chronic lead toxicity as manifestations can be as subtle as anaemia or mild nephropathy.
- Thorough occupational history is important as there is consistent history of exposure.
- Peripheral neuropathy is the most common complaint that brings patient to health care system.
- Lead line in gum or basophilic stippling in peripheral blood smear are less commonly found, hence should not be relied upon as important clinical diagnostic criteria.

and Lungs. Rate of absorption depends on various factors including particle size, route, state of feeding, age of subject etc<sup>2</sup>. Organic lead is absorbed more readily. Once it enters blood stream it is distributed to all tissues including mineralized tissues like bones and teeth where it is stored in vast amount and ultimately contribute to largest lead store burden of

the body. It is also deposited in soft tissues like lung, liver, heart. Half life of lead in blood is 28-36 days. Lead is excreted through kidney and bile.

Toxic effects of lead accumulation are manifested in different organ systems. Most commonly affected ones are kidneys, hematopoietic and peripheral nervous system. Anaemia, one of the commonest manifestations, is caused by inhibition of the enzymes delta-Aminolaevulinic Acid Dehydratase (ALAD) and Ferro chelatase which are involved in heme synthesis and results in formation of zinc protoporphyrin, which is a laboratory marker of lead toxicity. Renal involvement ranges from Acute Kidney Injury to Chronic Kidney Disease and is due to injury to Proximal Convoluted Tubule which may result in fanconi syndrome. Lead is deposited in motor nerves and in brain resulting in pure motor neuropathy and myriads of higher function abnormalities respectively. Children are more prone to CNS involvement. Lead exposure is also shown to affect production of spermatozoa<sup>3</sup>.

#### MATERIALS AND METHODS

This observational study was performed over 1 year period (October 2018 to September 2019) at General Medicine OPD and IPD of our Institution. The study protocol followed the principles expressed in the declaration of Helsinki. The study population included patients of either sex aged above 18 years attending General Medicine OPD or admitted in IPD in our Institution and being diagnosed with chronic lead toxicity by demonstration of elevated blood lead level (>10 mcg/dl). We excluded all patients having co morbidity like diabetes.

We used non probability convenient sampling method for this study. All patients satisfying inclusion and exclusion criteria were recruited. We could recruit 14 patients during the study period.

Thorough history taking and clinical examination were performed with special focus on occupation, extent and duration of exposure, symptomatology, functional status and special clinical features like looking for Anaemia, blue line in gum. Involvement of different organ systems susceptible to lead toxicity was evaluated. Involvement of kidney was evaluated by Renal function test, urine routine test, anaemia by Hb level & basophilic stippling, peripheral neuropathy by NCS. Data were recorded in a case report form (CRF) specifically designed for this purpose. The data from CRF was transcribed into an excel database. Data was summarized with routine descriptive statistics.

#### RESULTS

The study population included 14 patients recruited

from Medicine OPD and IPD of ESI-PGIMSR & ESIC Medical College, Joka, West Bengal, India.

#### Demographic Characteristics :

Analysis of Demographic Characteristics shows (Table 1) Mean age at presentation is around 40 years (39.6 +/- 12.0). 11 of 14 patients were male. All were from lower socio economic class (monthly family income <Rs 21,000 as per ESI norm). Table 2 shows majority of patients worked at Battery industry. Average weekly working time is around 45 hours.

| Parameter                  | Mean (standard deviation) N=13 |
|----------------------------|--------------------------------|
| Age (years)                | 39.6 (12.0)                    |
| Duration of exposure (yrs) | 6 (2.7)                        |
| Weekly working hours       | 44.8 (4.1)                     |

#### Clinical Characteristics :

Most common symptom which prompted medical consultation in our participants was motor neuropathy

| Source of Lead   | No of patients |
|------------------|----------------|
| Battery Factory  | 7              |
| Painting         | 3              |
| Smelting         | 2              |
| Wire Factory     | 1              |
| Chemical Factory | 1              |

followed by pain abdomen. Fig 1 shows presenting complaints. Most common organ system involvement in this study is hematopoietic system in the form of anaemia. Renal involvement is scarcest among 3 commonly involved systems. Fig 2 shows frequency of organ system involvement. It also depicts multiple organ system involvement in single individual (total frequency of organ system involvement is 23 in 14 participants).

Blue line in gums, the so called lead line, was present in only 3 out of 14 patients. 1 patient complained of hematuria. Another patient presented with convulsion. NCCT brain revealed cortical calcification (Figs 3 & 4).

#### Laboratory Characteristics :

There was wide variation in blood lead level at

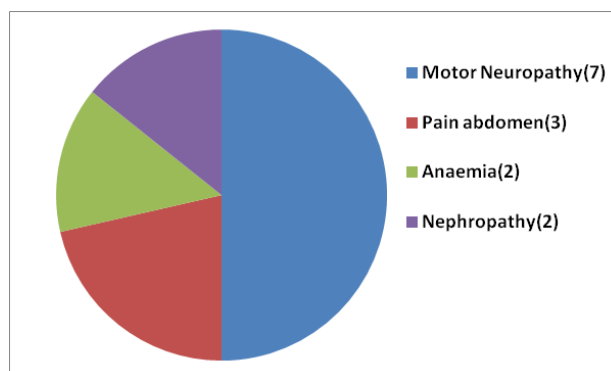


Fig 1 — Frequency of presenting symptom

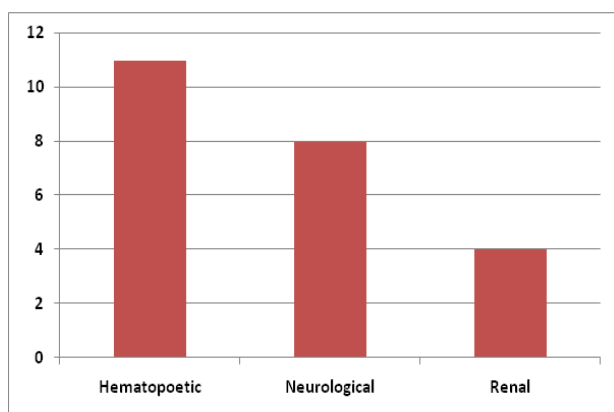


Fig 2 — Frequency of Organ systems involvement



Fig 3 — Wrist drop in a patient of chronic lead poisoning

presentation, highest being 130 mcg/dl and lowest being 50.11 mcg/dl. Mean Hb level in patients having anaemia was 9.1 gm/dl. Basophilic stippling was observed in 2 out of 11 patients suffering from anaemia (Fig 5).

Mean Creatinine value in patients suffering from nephropathy was 1.8 mg/dl. NCS of all patients suffering from neuropathy showed predominantly motor neuropathy with degree of reduction in CMAP being more in upper limbs than in lower limbs. High level of Urinary porphobilinogen was detected in 1 patient. The classic metaphyseal line in X-ray of knee joint were found in 3 patients who presented with bone pain and arthralgia. Non contrast CT scan of a patient revealed Cortical calcification (Fig 6).

#### DISCUSSION

Chronic lead toxicity is one of the commonest occupational diseases encountered now a days in industrialized countries. It accounts for 0.6% of global burden of all toxic environmental diseases. Lead toxicity has resulted in chronic ill health, decreased economic output, lower life expectancy. In India, Institute for Health Metrics and Evaluation (IHME) found 4.6 million



Fig 4 — Blue line in gum in a patient of chronic lead poisoning lead-attributable DALYs and nearly 165,000 deaths (The 2016 Global Burden of Disease, Injuries and Risk Factors Study).

Occupational exposure is the main route in adults-battery workers, plumbers, paint and construction workers, lead mining, smelters, firing range instructors, rubber industry workers are most vulnerable population. Deteriorating lead paints and lead containing household dust are the main causes of chronic lead poisoning<sup>4</sup>. In our study battery factory workers constituted 50% of patient population followed by paint industry workers. Mean age of patients in our study was 40 years and mean duration of lead exposure before becoming symptomatic was 6 years.

GI tract (10-15% of adults), inhalational routes, skin are the routes of entry in adults. 99% of ingested or inhaled lead remains in the blood stream with a half life of 40 days and redistribute in brain and long bones. Kidney and liver take part in metabolism.

Lead acts by tilting the oxidant-antioxidant balance by decreasing antioxidant level. (Reduced level of glutathione, ALAD, Glutathione peroxidase and increase aminolaevulinic acid and reactive oxygen species in cell).

Serum level varies considerably among exposed individuals. It is determined by degree of absorption, rate of absorption and redistribution from bones and brain. In our study serum lead level varied considerably within participants. However even the lowest value in our study (50.11 mcg/dL) was much higher above safety level (5 mcg/dL).

Most of the clinical feature of chronic lead poisoning in adults are non specific. Chronic lead poisoning can present with number of signs and symptoms<sup>4,5</sup> including abdominal pain (lead colic), constipation, anorexia, headache, irritability, decreased libido, difficulty concentrating and deficits in short term memory, nephropathy (Fanconi type syndrome), a lead line (bluish pigmentation seen at the gum

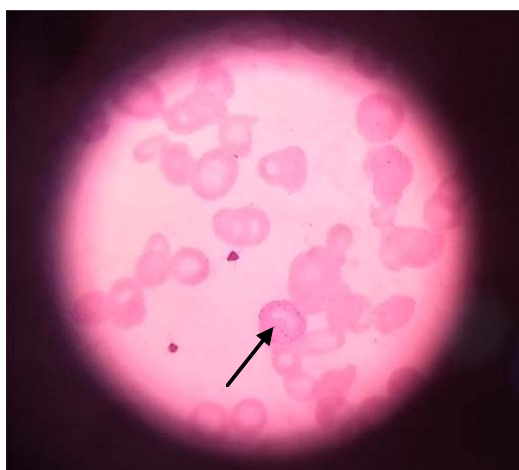


Fig 5 — Basophilic stippling in chronic lead poisoning (Arrow)

tooth junction), anaemia, basophilic stippling on blood smear, a peripheral neuropathy manifesting as extensor weakness due to wrist/ankle drop due to axonal degeneration affecting motor nerves<sup>6</sup>. The blue line, wrist drop, basophilic stippling of RBCs in peripheral blood film are classic findings but they are not always present. Hypertension, coronary artery disease are the main cardiovascular manifestation. In our study anaemia (78.57%) was most common clinical manifestation while most common presenting complaint was motor neuropathy (50%) followed by lead colic (21.4%).

Anaemia is a common manifestation of chronic lead toxicity. In our study anaemia was the most common clinical feature. Although this finding is partially offset by high prevalence of anaemia in Indian population, especially in females. Chronic lead exposure has been shown to induce dysplastic changes in erythroid precursors<sup>17</sup>. Basophilic stippling is not so common in lead poisoning as is usually described. In our study only 2 out of 11 patients with anaemia had basophilic stippling.

Chronic lead exposure has been associated with neuropsychiatric effects in the form of decline in neurocognitive function<sup>5</sup>, distal sensory and motor neuropathies<sup>6</sup>, conduction delay in ECG<sup>6</sup>. One study found that cumulative lead exposure may increase the risk Parkinson's disease<sup>7</sup>. In our study neurological involvement was quite common (57.14%). 7 out of 14 patients suffered from motor neuropathy and presented with either wrist drop or weakness in handgrip while 1 patient presented with convulsion and had cerebral cortical calcification in NCCT brain.

Effect on reproductive health includes increased incidence of miscarriages, stillbirths<sup>8</sup>, low birth of weight<sup>9</sup>, cognitive impairments<sup>10,11</sup> in babies with



Fig 6 — Cortical calcification in a patient with chronic lead poisoning

high maternal bone lead level. Higher maternal blood pressure and 3rd trimester hypertension has also been associated<sup>12</sup>. We had only 3 females in our study, who did not encounter any of the above.

Lead nephropathy is a potential complication of prolonged high level lead exposure. In our study 4 out of 14 (28.5%) patients suffered from nephropathy. Of them, 50% had nephropathy as main presenting symptom. Nephropathy was detected in these patients through routine screening of Serum Creatinine, emphasizing role of routine screening process in detection of this potential life threatening condition in high risk professional group. Although in our study participants blood lead level was in higher range (lowest being 50 mcg/dL) and thus explaining this high percentage of nephropathy. Rokho Kim et al demonstrated even low blood level of lead is a strong predisposing factor for developing nephropathy<sup>13</sup>.

Prolonged low level lead exposure appears to be associated with increased risk of cataract<sup>14</sup>, hearing loss<sup>15</sup>, carcinogenicity in animals-particularly renal tumours<sup>4</sup>. The National Toxicology program of the US Department of Health and Human services determined that lead has a carcinogenic role in human<sup>16</sup>.

## CONCLUSION

The clinical feature of chronic lead poisoning in adults are mainly nonspecific. The classical clinical presentation like blue line in the gum, wrist drop, basophilic stippling of RBCs in peripheral blood film etc are not always found. A proper history taking including occupational history and narrow threshold of clinical suspicion is important to diagnose and prevent progression this clinical condition which is a silent killer

Our study showed main clinical presentations of lead toxicity being neurological, abdominal colic and renal involvement. Most frequently involved system in lead toxicity are hematopoietic, neurological and renal. Most common possible sources of lead exposure were found to be battery industry, followed by painting, smelting and wire factory. Our study was limited by small sample size. More studies are required in this area to further investigate into sources and distribution of symptomatology of chronic lead toxicity.

**Limitation :** Main limitation in this study is small sample size.

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**Conflict of Interest :** None

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