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Lethal effects of Mercury as insecticide on Zn status, Thyroid production and Lung capacities of Human body

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Abstract
Mercury is a naturally occurring element that is found in air, water and soil. Exposure to mercury – even small amounts – may cause serious health problems, and is a threat to the development of the child in utero and early in life. Mercury may have toxic effects on the nervous, digestive and immune systems, and on lungs, kidneys, skin and eyes. Mercury is considered by WHO as one of the top ten chemicals or groups of chemicals of major public health concern. Mercury is well absorbed through the lungs, the gastrointestinal tract, and the skin. Methyl mercury compounds vaporize easily and if inhaled in large amounts, can destroy lung tissue. The most common sensory effects of mercury toxicity are paresthesia, or a tingling sensation, pain in limbs, and visual and auditory disturbances. Motor disturbances are exhibited by changes in gait, weakness, falling, slurred speech, and tremors. Other symptoms are headaches, rashes and various emotional disturbances. We observed that suddenly some swimmers they had severe hair loss and they felt abnormally extreme parasthenia, we came to know that some mercury based algalicide was added and the results may be because of this. Discontinuation of swimming bring back normal to the affected children, but it took many months. Based on this finding we studied the effect of Parad Vati, a mercury containing tablet added to grains and cereal sin common practice in India (Made by Sacrom Pharma Pvt Ltd, Caode No- 03, Product mane- Parazzest). We found that that as micro-organisation infection convert mercury in to methyl mercury compound that is not only more toxic but also more potentially absorbed in human body. As children and aged persons are the vulnerable persons of any family, so we made two groups of children and aged persons of the Parad Vati user family and also from the non-user family. So estimate their serum Zn level –Akita Abba method was adopted, Lung Capacities was estimated in District hospital Bilaspur by Spirometry, Visual symptoms as abbesses in legs, rashes, twingling, and vertigo also studied. The Status of Thyroid gland was estimated by $T^{3,}$ T^4 and TSH levels in both the groups. We found a significant differences in lung capacities of both the group- the user group showed an Asthma like spirometry picture with reduced lung capacities, also their serum has body samples has lower level of Zn, although this is insignificantly defferent. The $T^{3,}$ T^4 levels were lower is Parad Vati users, TSH level was high in comparison to non-users. (T3 -3.5 - 6.5 pmol/L, T4 10 - 23 pmol/L, TSH-0.5 - 4.70 mIU/L, Serum Zn -89 µmol /l. This study suggests the possibility of mercury toxicity by using Parad Vati in the studied subjects especially in aged persons and children below 8 years of age.

Keywords: Mercury, Thyroid production, Lung capacities.

Introduction

Mercury exists in various forms: elemental (or metallic) and inorganic (to which people may be exposed through their occupation); and organic (e.g., methylmercury, to which people may be exposed through their diet). These forms of mercury differ in their degree of toxicity and in their effects on the nervous, digestive and immune systems, and on lungs, kidneys, skin and eyes. Mercury occurs naturally in the earth's crust. It is released into the environment from volcanic activity, weathering of rocks and as a result of human activity. Human activity is the main cause of mercury releases, particularly coal-fired power stations, residential coal burning for heating and cooking, industrial processes, waste incinerators and as a result of mining for mercury, gold and other metals. Once in the environment, mercury can be transformed by bacteria into methyl mercury. Methyl mercury then bio accumulates (bioaccumulation occurs when an organism contains higher concentrations of the substance than do the surroundings) in fish and shellfish. Methyl mercury also biomagnifies. For example, large predatory fish are more likely to have high levels of mercury as a result of eating many smaller fish that have acquired mercury through ingestion of plankton. People may be exposed to mercury in any of its forms under different circumstances. However, exposure mainly occurs through consumption of fish and shellfish contaminated with methyl mercury and through worker inhalation of elemental mercury vapours during industrial processes. Cooking does not eliminate mercury.

All humans are exposed to some level of mercury. Most people are exposed to low levels of mercury, often through chronic exposure (continuous or intermittent long term contact). However, some people are exposed to high levels of mercury, including acute exposure (exposure occurring over a short period of time, often less than a day). An example of acute exposure would be mercury exposure due to an industrial accident.

Factors that determine whether health effects occur and their severity include:

- the type of mercury concerned;
- the dose;
- the age or developmental stage of the person exposed (the foetus is most susceptible);
- the duration of exposure;

- The route of exposure (inhalation, ingestion or dermal contact).
- Generally, two groups are more sensitive to the effects of mercury. Foetuses are most susceptible to developmental effects due to mercury. Methylmercury exposure in the womb can result from a mother's consumption of fish and shellfish. It can adversely affect a baby's growing brain and nervous system. Mercury is well absorbed through the lungs, the gastrointestinal tract, and the skin. Methyl mercury compounds vaporize easily and if inhaled in large amounts, can destroy lung tissue. Organic complexing produces methyl mercury compounds, which are more toxic, especially to the central nervous system. Only seven percent of ingested inorganic mercury is absorbed, but at least 95% of ingested methyl mercury is absorbed. Zinc, cadmium, and manganese can enhance absorption of inorganic mercury.

  For many years, no one realised that the fish were contaminated with mercury, and that it was causing a strange disease in the local community and in other districts. At least 50 000 people were affected to some extent and more than 2000 cases of Minamata disease were certified. Minamata disease peaked in the 1950s, with severe cases suffering brain damage, paralysis, incoherent speech and delirium.

  Elemental and methylmercury are toxic to the central and peripheral nervous systems. The inhalation of mercury vapour can produce harmful effects on the nervous, digestive and immune systems, lungs and kidneys, and may be fatal. The inorganic salts of mercury are corrosive to the skin, eyes and gastrointestinal tract, and may induce kidney toxicity if ingested.

  Neurological and behavioural disorders may be observed after inhalation, ingestion or dermal exposure of different mercury compounds. Symptoms include tremors, insomnia, memory loss, neuromuscular effects, headaches and cognitive and motor dysfunction. Mild, subclinical signs of central nervous system toxicity can be seen in workers exposed to an elemental mercury level in the air of 20 μg/m3 or more for several years. Kidney effects have been reported, ranging from increased protein in the urine to kidney failure.There are several ways to prevent adverse health effects, including promoting clean energy, stopping the use of mercury in gold mining, eliminating the mining of mercury and phasing out non-essential mercury-containing products.Burning coal for power and heat is a major source of mercury. Coal contains mercury and other hazardous air pollutants that are emitted when the coal is burned incoal-fired power plants, industrial boilers and household stoves.

  Mercury is an element that cannot be destroyed; therefore, mercury already in use can be recycled for other essential uses, with no further need for mercury mining. Mercury use in artisanal and small-scale gold mining is particularly hazardous, and health effects on vulnerable populations are significant. Non-mercury (non-cyanide) gold-extraction techniques need to be promoted and implemented, and where mercury is still used safer work practices need to be employed to prevent exposure.

  Mercury is contained in many products, including:
- batteries
- measuring devices, such as thermometers and barometers
- electric switches and relays in equipment
- lamps (including some types of light bulbs)
- dental amalgam (for dental fillings)
- skin-lightening products and other cosmetics
- Pharmaceuticals.

A range of actions are being taken to reduce mercury levels in products, or to phase out mercury-containing products. In health care, dental amalgam is used in almost all countries. A 2009 WHO expert consultation concluded that a global near-term ban on amalgam would be problematic for public health and the dental health sector, but a phase down should be pursued by promoting disease prevention and alternatives to amalgam; research and development of cost-effective alternatives; education of dental professionals and the raising of public awareness.

Mercury use in some pharmaceuticals, such as thiomersal (ethyl mercury), which is used as a preservative in some vaccines, is very small by comparison with other mercury sources. There is no evidence that suggests a possible health hazard resulting from the amounts of thiomersal currently used in human vaccines. Inorganic mercury is added to some skin-lightening products in significant amounts. Many countries have banned mercury-containing skin-lightening products because they are hazardous to human health. The continued release of mercury into the environment from human activity, the presence of mercury in the food chain, and the demonstrated adverse effects on humans are of such concern that in 2013 governments agreed to the Minamata Convention on Mercury. The Convention obliges government Parties to take a range of actions, including to address mercury emissions to air and to phase-out certain mercury-containing products.

The World Health Organization publishes evidence about the health impacts of the different forms of mercury, guidance on identifying populations at risk from mercury exposure, tools to reduce mercury exposure, and guidance on the replacement of mercury-containing thermometers and blood pressure measuring devices in health care. WHO leads projects to promote the sound management and disposal of health-care waste and has facilitated the development of an affordable, validated, non-mercury-containing blood pressure measuring device.

Mercury is a naturally occurring element that is found in air, water and soil. Exposure to mercury – even small amounts – may cause serious health problems, and is a threat to the development of the child *in utero* and early in life. Mercury may have toxic effects on the nervous, digestive and immune systems, and on lungs, kidneys, skin and eyes. Mercury is considered by WHO as one of the top ten chemicals or groups of chemicals of major public health concern. Mercury is widely used in industry and in a variety of products, e.g., felt, fungicides, algicides used in swimming pools, adhesives, floor waxes, fabric softeners, slimicides, and in the production of chlorine. Mercury is well absorbed through the lungs, the gastrointestinal tract, and the skin. Methylmercury compounds vaporize easily and if inhaled in large amounts, can destroy lung tissue. Organic complexing produces methylmercury compounds, which are more toxic, especially

to the central nervous system. Only seven percent of ingested inorganic mercury is absorbed, but at least 95% of ingested methylmercury is absorbed. Zinc, cadmium, and manganese can enhance absorption of inorganic mercury. Mercury compounds inhibit ATPase, an enzyme that breaks down ATP, inhibiting energy release in all cells. Degeneration of nerve fibers occurs, particularly the peripheral sensory nerve fibers. Besides sensory nerve damage, motor conduction speed was reduced in persons with high hair mercury. The most common sensory effects of mercury toxicity are paresthesia, or a tingling sensation, pain in limbs, and visual and auditory disturbances. Motor disturbances are exhibited by changes in gait, weakness, falling, slurred speech, and tremors. Other symptoms are headaches, rashes and various emotional disturbances.

The Hypothesis

We observed that suddenly some swimmers in Bilaspur Taal, a swimming pool run by Bilaspur Municipal Corporation had severe hair loss and they felt abnormally extreme parasthenia, we came to know that some mercury based algalicide was recently added and the results might be because of this. Discontinuation of swimming bring back most of the children and adults almost normal, but it took many months.Based on this finding we stududied the effect of Parad Vati,a mercury containing tablet added to grains and cereals in common practice in India (Made by Sacrom Pharma Pvt Ltd, Caode No- 03, Product mane- Parazzest)

Materials & Method

We found that as micro-organisal infection in cereals convert mercury in to methyl mercury compound that is not only more toxic but also more potentially absorbed in human body. As children and aged persons are the vulnerable persons of any family, so we made two groups of children and aged persons of the Parad Vati user family and also from the non-user family. The controls and subjects were selected randomly and all the formalities related to medical ethics was followed including written permission was taken from each person involved in this study.

- Study duration- July 1013-December 2015 (29 months)
- Experimental Group- Parad Vati users (Approxmately more than five years of use)
- Children -14 (age range 5-15 yeras)
- Elderly – 14 (above 55 yeras)
- Control Group-Non users of Parad Vati
- Children -14 (age range 5-15 yeras)
- Elderly – 14 (above 55 yeras)
- Study Area- Bilaspur City and near by outskirt area

Biochemical Estimations-

Zinc Estimation

As some previous studies concluded that mercury toxicity is parallel related with deficiency of Zinc, because mercury blocks the absorptive pathway of Zn and as Zinc is not deposited in body thus daily supplementation of Zn is essential to make its regular availability. So, due to mercury toxicity Zn is the first and farmost material affected. (Renee Dufault, Roseanne Schnoll, Walter J Lukiw, Blaise LeBlanc, Charles Cornett, Lyn Patrick, David Wallinga, Steven G Gilbert, and Raquel Crider - Published online Behav Brain Funct. 2009; 5: 44. 2009 Oct 27. doi: 10.1186/1744-9081-5-44)

So for the estimation of serum Zn level –Tulip Group's Zinc Estimation Kit was used, Akita Abe method was adopted for Zn estimation through this kit. 0.05 ml sample of serum wasused with addition of 1 ml reagent, after 5 min s of incubation time the reading was taken on 578 nm weavelength range, I have chosen this method, because of high lenarity of this method (up to 200 ug / dl level)

Also as previous literature said that minute Mercury toxicity resulted in reduced lung capacities. (JD Glezos, MD FRCPC, JE Albrecht, MD, and RD Gair, BSc (Pharm) Can Respir J. 2006 Apr; 13(3): 150–152.) Mercury crosses the alveolar membrane during respiration, leading to rapid systemic absorption and wide distribution into tissues. Lung Capacities was estimated in District hospital Bilaspur by using Spirometry method. The patient was asked to take the deepest breath they could, and then exhaled into the sensor as hard as possible, for as long as possible, preferably at least 6 seconds. It is sometimes directly followed by a rapid inhalation (inspiration), in particular when assessing possible upper airway obstruction. This test wasbe preceded by a period of quiet breathing in and out from the sensor (tidal volume), and the rapid breath in (forced inspiratory part) came before the forced exhalation. During the test, soft nose clips were used to prevent air escaping through the nose. Filter mouthpieces were also used to prevent the spread of microorganisms. Spirometry of all the subjects was done in study duration alteast once.

I have also estimated PEFR (Peak Expiratory Flow Rate) of 6 experimental subjects (3 children & 3 adults) and also 6 persons from control group were under gone PEFR (3 children & 3 adults). Peak expiratory flow (PEF) is the maximal flow (or speed) achieved during the maximally forced expiration initiated at full inspiration, measured in liters per minute or in liters per second. For the PEFR estimations the pulmonary volumes were measured with a peak flow meter, a small, hand-held device used to monitor a person's ability to breathe out air. It measured the airflow through the bronchi and thus the degree of obstruction in the airways.

Spirometry Analysis

Through Spirometry –FVC (Forced Vital Capacity) and FEV (Forced Expiratory Volume in one second) were measured.

- FEV_1/ FVC (80-120 %) : Normal
- FEV_1/ FVC (60-80 %) : Mild Obstruction
- FEV_1/ FVC (40-59 %) : Moderate Obstruction
- FEV_1/ FVC (< 40 %) : Severe Obstruction

- **Peak Expiratory Flow Rate (PEFR)** -It was measured by Peak Flow-meter.
- The Calculation was based on the following formula-

$$\text{Daily Variability} = \frac{\text{PEFR Evening - PEFR Morning}}{{}^{1}/_{2}\,(\text{PEFR Evening + PEFR Morning})} \text{ X } 100$$

- If variability is > 20% for at least two weeks –asthma is present.
- If variability is > 40% asthmatic condition is severe.
- If variability is > 60% it's an urgent condition.

Apart from these observations we had also taken the anterior-posterior diameter of the patients, because the diameter is increased in asthmatic patients.

Thyroid Hormonal Profile

Organic Murcury causes severe damage to both endocrine and natural systems. Studies have documented that mercury causes hypothyroidism, damage Thyroid RNA, causes inflammation of the gland along with the impairment in conversion of T3 in to T4. (Teresa K. Rowles, National Oceanic and Atmospheric Administration, National Ocean Service, Hollings Marine Laboratory, 331 Fort Johnson Road, Charleston, SC 29412, USA). Thus the Status of Thyroid gland was also estimated by assessing $T^{3,}$ T^4 and TSH levels in both the groups. For the estimation of Thyroid hormone status we used Mini Vidas 30 of Bio Merieux's Company.

Visual symptoms as abesses in legs, rashes, twingling, vertigo, gingivitis, stomatitis, oesophageal, gastric small and large bowel erosions haematemesis, bloody diarrhoea, hypotension, lactic acidosis were also examined in the experimental subjects.

Mercury poisonings resulted asthma is the cause of increased RBCs and increased Lymphocytes and Eosinophils in blood. Also serum Hemoglobin level was said to be increase due to severe hypoxia. So the biochemical testing of the above data's was done. Serum Hemoglobin gm% value was measured by Sahil's hemoglobinometer. The Serum values of Eosionophils and Lymphocytes were measured by using Neubar's chamber of Differential Counting.

Pulse Measurement

The pulse is measured because "Pulsus Paradoxus" is common symptom in an mercury poisoned patient.

Differential Counting

As due to Mercury toxicity, the resultant reduced pulmonary capacity changed the RBC and WBC count, thus the estimation of blood cells was included in this study. The differential counting was done by using Hematology Analyserof STA Compact Max.

Hemoglobin gm % value was also estimated in cases and controls by using Hemoglobinometer by using Acid Hematin Method.

Results & Conclusion

- The estimated mean Serum Zinc level in Experimental subjects was 7.9 umol/ L, while in control subjects it was near normal values-10.3 umol/L (Approx 33 % lower than normal values)
- We found a significant differences in lung capacities of both the group- the user group showed an Asthma like spirometry picture with reduced lung capacities.

Table 1: Results of Spirometry Analysis Experimental subjects and Controls

S. No.	Results of Spirometry Analysis in Cases	Results of Spirometry Analysis in Controls
1	51.17	22.23
2	40.80	14.28
3	37.14	18.44
4	50.90	19.16
5	64.13	21.04
6	65.58	18.81
7	43.18	11.82
8	61.42	19.88
9	40.50	29.18
10	52.45	11.43
11	62.27	19.24
12	44.54	22.11
13	54.51	10.70
14	39.04	14.30

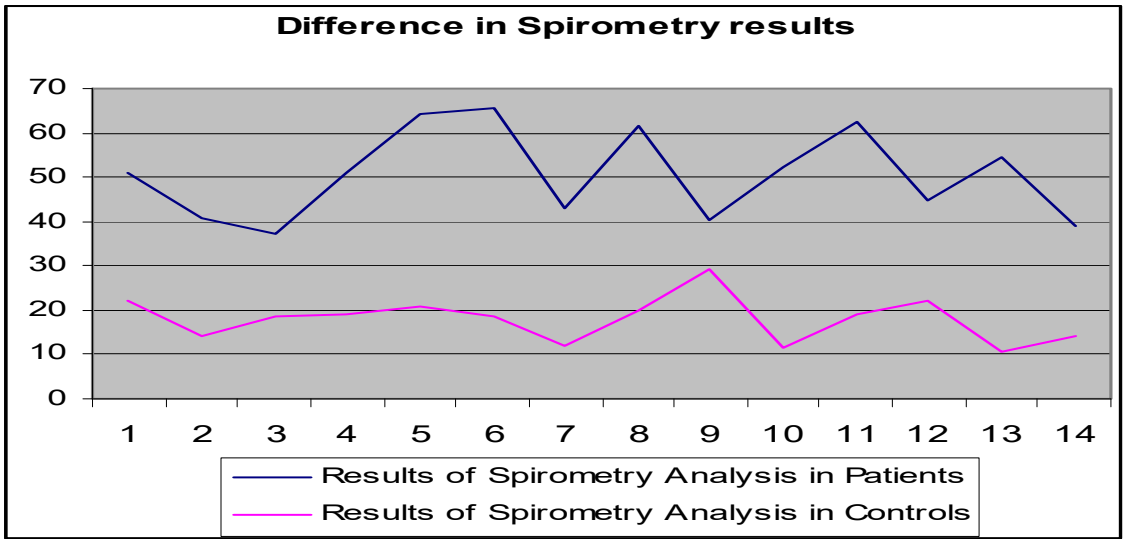

Fig 1: Defference in Spirometry Results

Table-2 Results of Peak Expiratory Flow Rate (PEFR)

S. No.	PEFR In Subjects/day in percentage	PEFR in Controls/day in percentage
1	60.8	10.2
2	22.8	8.4
3	40.4	10.7
4	66.7	11.3
5	26.8	7.3
6	39.0	13.6
7	54.7	16.4
8	25.1	4.6
9	67.5	10.4
10	33.8	12.5
11	57.8	17.4
12	44.2	7.4
13	52.9	15.4
14	37.6	15.4

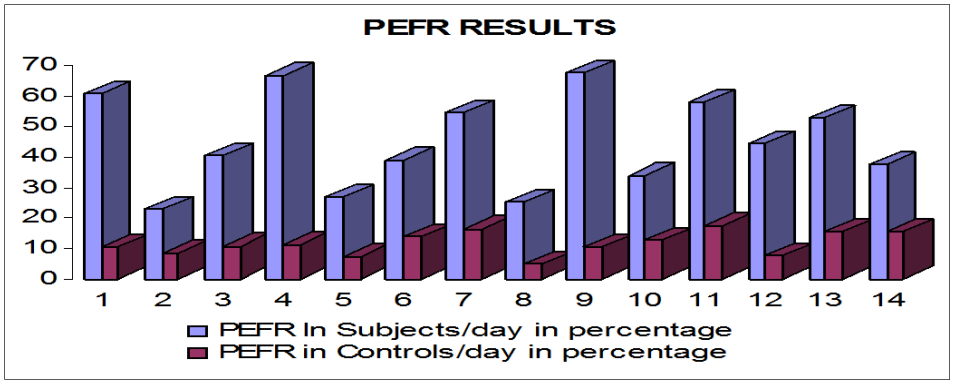

Fig 2: Deference in PEFR Results

Table 3: Vital Capacity Analysis in Cases and Controls

S. No.	Results of Vital Capacity Analysis in Cases [ml]	Results of Vital Capacity Analysis Controls [ml]
1	2100	3100
2	2000	3000
3	2200	3300
4	2230	2900
5	2000	3000
6	2300	3200
7	2100	3100
8	1930	3300
9	2400	3100
10	2000	3300
11	1890	3400
12	2000	3200
13	2100	3300
14	2200	3100

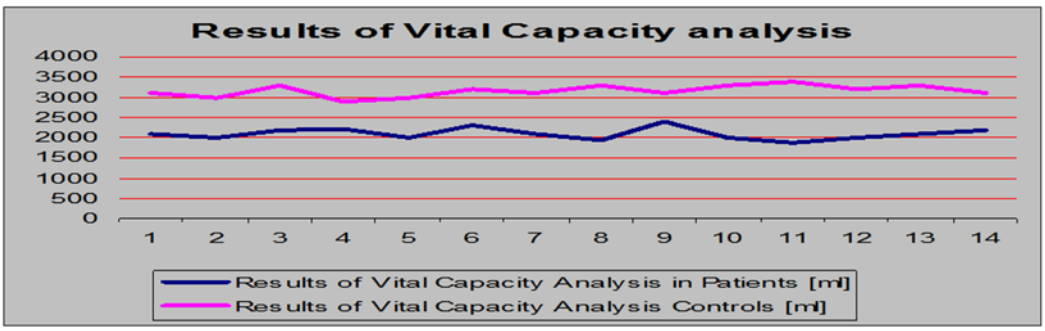

Fig 3: Results of Vital Capacity Analysis

Table 4: Results of Pulse Rate Analysis in Asthmatics and Controls

S. No.	Results of Pulse Rate Analysis in Cases	Results of Pulse Rate Analysis in Controls
1	81	66
2	70	71
3	89	70
4	78	72
5	77	75
6	79	72
7	90	77
8	81	65
9	67	63
10	79	72
11	88	70
12	80	73
13	82	71
14	88	73

- The $T^{3,}$ T^4 levels were lower is Parad Vati users, TSH level was high in comparision to non-users.(T3 -3.5 - 6.5 pmol/L, T4 10 - 23 pmol/L, TSH-0.5 - 4.70 mIU/L, Serum Zn -89 µmol /l. This study suggests the possibility of mercury toxicity on Thyroid gland by using Parad Vati in the studied subjects.

Table 5: RBC Count in Cases and Controls

S. No.	RBCs million/cubic mm in Cases	RBCs million/cubic mm in Controls
1	4.8	4.1
2	4.5	4.2
3	5..1	4.5
4	4.6	4.3
5	4..8	4.2
6	4.7	4.4
7	4.4	4.2
8	5.2	4,4
9	5,0	4.3
10	4.8	4,5
11	4.9	4.4
12	4.8	4.3
13	5.4	4.3
14	5.1	4.5
	Mean = 4.83	Mean = 4.308

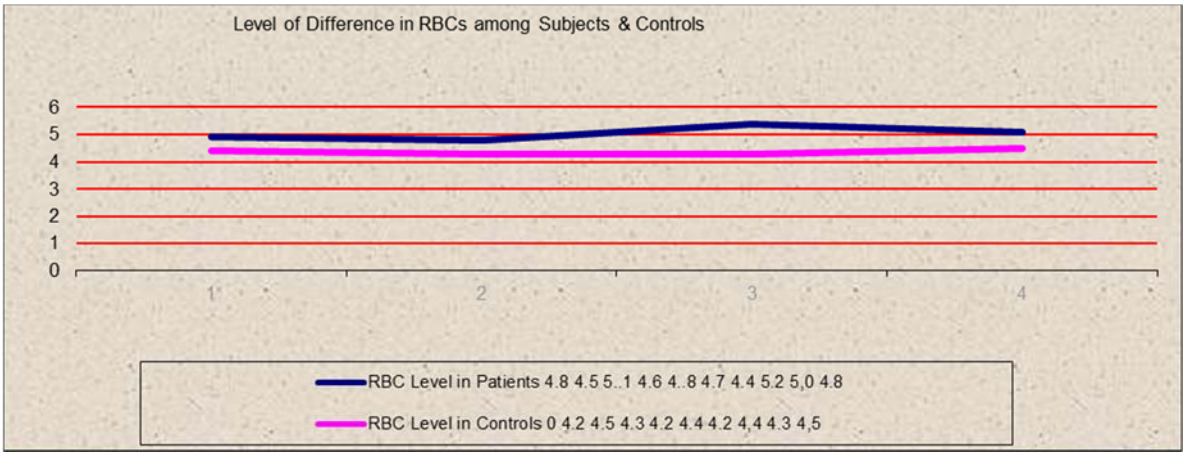

Fig 5: RBC Count in Cases and Controls

Table 6: WBC Count in Cases and Controls

S. No.	WBCs thousands/cubic mm in Cases	WBCs thousands/cubic mm in Controls
1	11,300	8,000
2	15,200	10,200
3	14,450	11,000
4	12,800	12,100

5	15,500	9,800
6	16,000	11,200
7	14,600	11,100
8	14,600	12,100
9	14,800	9,300
10	15,300	11,000
11	17,200	12,500
12	15,800	11,210
13	16,200	9,800
14	11,700	11,800
	Mean = 4.836364	Mean = 4.308

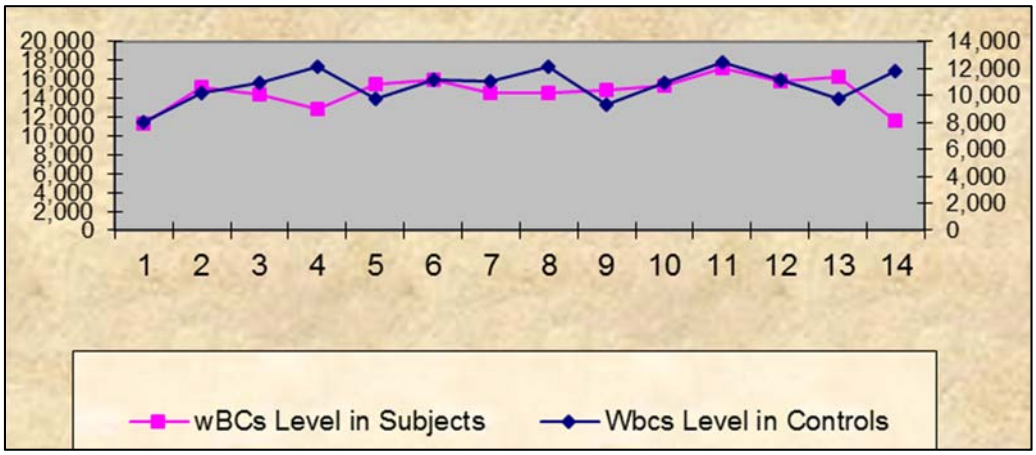

Fig 6: WBC Count in Cases and Controls

Table 7: Hemoglobin/gm % value in Cases and Controls

S. No.	Hg/gm % values in Patients	Hg/gm % values in Controls
1	14.8	12.1
2	12.9	12.2
3	15.3	11.5
4	14.9	12.3
5	14.8	11.2
6	12.9	10.4
7	12.9	9.2
8	14.6	10.4
9	15.0	11.3
10	14.8	11.5
11	14.9	12.4
12	14.8	11.3
13	15.4	12.3
14	15.1	10.5

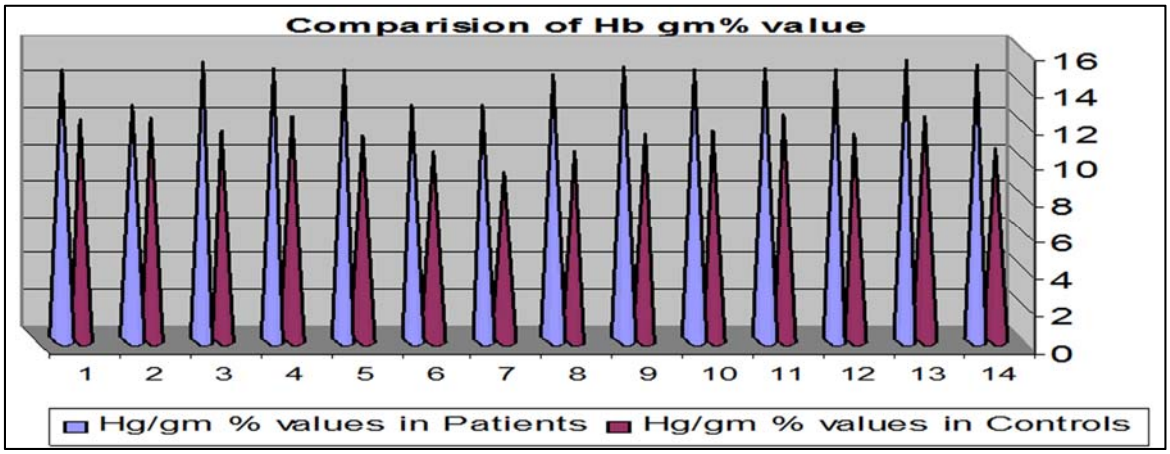

Fig 7: Deference in Hb gm % Results

Discussion

The Parad Vati user group showed some observations that might be due to chronic use of mercury containg vati, the user group had significantly lower serum value of Zinc, as Zinc is related with immunity status, so the user group had skin absees, gingivitis, stomatitis etc. Also the lung capacities of the vati user group showed spirometric and PEFR results with reduced lung volumes. The Vital capacity of the vati users was found drastically affected. The hemogram picture of the experimental group showed hypoxic hematology picture –low RBCs, high WBCs count with somewhat low Hemoglobin gm % values. Pulsus Paradosus was observed in most of the cases. The results of the study showed that the Parad Vati users had affected the Zinc Status, Thyroid functioning, Lung Volumes and hematology picture, We found a significant differences in lung capacities of both the group- the user group showed an Asthma like spirometry picture with reduced lung capacities (TLC- 1890 ml, VC-2200 ml, variability- > 40% was observed. This study suggests the possibility of mercury toxicity by using Parad Vati in the studied subjects specially in aged persons and children below 8 years of age. But it will be too early to say that the biochemical, hematologic, thyroidic and spitometic profile of the subjects were only because of use of parad vati, but the present study suggests the possibility of association. A more deep, community based study is required to conform the results.

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