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Assessment of Salivary Lead Level in Relation to Oral, Cytological and Haematological Findings in Traffic Police Personnel in Baghdad

A Thesis

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Dedication

to my mother, my father and my beloved fiancée for their continual and comprehensive support…

Ali Al-Khasaki

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Abstract

Background: Lead is a toxic metal that widespread use has created major environmental contamination and health problems in many parts of the world. Traffic policemen are the most exposed population to lead (Pb) from automobile exhaust. There has been increasing concern about the possible harmful effects of Pb from automobile exhaust on health of traffic policemen.

The concentration of lead in whole blood has gained wide acceptance as the most useful tool for screening and diagnostic testing, however, saliva has been suggested as a non-invasive biological matrix for assessing exposure.

Aims of the study: To study the possibility of using salivary lead concentration as alternative to blood lead concentration and estimate (clinical, hematological and salivary cytological) changes traffic policemen.

Materials and methods: a prospective study include 53 traffic policemen working heavily traffic areas in Baghdad city as study group and 38 subjects not occupationally exposed to lead as control group. Our institutional review board approved the study, and all the workers gave written informed consent to participate. Collection of personal information as well as blood and saliva samples, examination oral cavity for signs of lead toxicity. Subjects were advised not to smoke, eat, or drink (except water) for one hour prior to saliva collection. After rinsing their mouth with water thoroughly, unstimulated saliva sample accumulated over five minutes was obtained. Atomic Absorption Spectrophotometer was used for quantitative analysis of lead, blood sample analyzed by the use of computerized blood analyzer, blood films were tested by

specialized hematologist and salivary sediments slides inspected by specialized cytologist.

Results: The result of this study showed a significant increase of blood lead level in study group (19 µg/dl) in comparison to control group (14.1 µg/dl) that indicate a significant exposure to lead from car exhausted, booth level are above the critical level of lead (10 µg/dl) which may represent an increase in lead environmental pollution.

This study revealed highly significant correlation between blood lead level and salivary lead level seen in study and control group $p = 0.001$ and 0.018 respectively; significant correlation between blood lead level and other hematological, clinical and cytological parameters, decrease in pH in study group in comparison to control group, highly significant decrease in salivary inflammatory cells and significant increase in red cells distribution width in study group comparing to control group.

Conclusions: While the idea of measuring salivary lead level for biological monitoring is attractive, our findings do not support its use for this purpose.

List of Contents

List of tables

List of figures

List of Abbreviations

%	Percentage
+ve	positive
-ve	negative
<	Less than
>	More than
±	Plus- minus
≥	More than or equal
µg	Microgram
µm	Micrometer
µg/dl	Microgram per deciliter
µmol	Micromole
µmol/l	Micromole per liter
13th	Thirteenth
Å	ångström
App.	Appendix
ALAD	δ-aminolevulinic acid dehydratase
ALT	Alanine transaminase
AST	Aspartate transaminase
ATSDR	Agency for Toxic Substances and Disease Registry
BASO	Basophiles
BnPb	bone lead level
C.V%	Coefficient of variance
C°	Degree centigrade
CAS	Chemical abstracts service
CBC	Complete blood count
CDC	Centers for Disease Control and Prevention
cm^2	square centimeter
CNS	Central nervous system
DNA	Deoxyribonucleic acid
DPCs	Deoxyribonucleic acid -protein cross-links
e.g.,	"exempli gratia" for example

ECG	electrocardiographic
EDTA	Ethylenediaminetetraacetic acid
EOS	Eosinophiles
EPb	Enamel lead level
et al.,	"et alii" (masculine plural)
fig.	Figure
g/cm^3	gram per cubic centimeter
g/l	Gram per liter
GI	gastrointestinal
GOT	glutamic oxaloacetic transaminase
GPT	glutamic pyruvic transaminase
Hct	hematocrit
HFCs	high- sister chromatid exchanges frequency cells
HGB	Hemoglobin
Histio.	Histiocytes
HPb	hair lead level
HRV	heart rate variability
LYM	Lymphocytes
Max	Maximum
MCH	mean corpuscular hemoglobin
MCHC	mean corpuscular hemoglobin concentration
MCV	mean corpuscular volume, or "mean cell volume
Min	Minimum
ml	Milliliter
ml/min	Milliliter per minute
MN	Micronuclei
MONO	Monocytes
MPV	Mean platelet volume
NEU	Neutrophils
ng/m^3	nanogram per cubic meter
NHANES	National Health and Nutrition Examination Survey
nmol/l	Nano mol per liter
No.	Number

NPb	Nail lead level
NS	Non- significant
P	Probability value
P5N	pyrimidine 5′-nucleotidase
Pb	Lead
Pb-B	Blood lead level
Pb-P	Plasma lead level
Pb-S	Salivary lead level
pH	Potential Hydrogen
PLT	platelet
PVC	polyvinyl chloride
r	Pearson’s correlation coefficients
r.p.m.	Revolution per minute
RBC	red blood cell count
RDW	Red cell distribution width
RNA	Ribonucleic acid
S	Significant
SCEs	sister chromatid exchanges
SCN^-	thiocyanate ion
SD	Standard deviation
SE	Standard error
sIgA	Salivary immunoglobulin A
sIgM	Salivary immunoglobulin M
SPSS	Statistical Package for the Social Sciences
t-test	Student's t-test
TCA	Trichloroacetic acid
UPb	Urine lead
WBC	White blood cell
XRF	x-ray fluorescence
ZPP	zinc protoporphyrin

Introduction

The toxic nature of lead has been recognized for millennia, with the earliest published reports dating back to 2000 BC **(Needleman, 1999).** Lead is a slivery-grey, soft, metal with atomic weight 207.21 D and atomic number 82. It has low melting point, 327.4 °C and boils at 1620 °C at atmospheric pressure **(minerals yearbook, 2010).** It is a particularly insidious hazard with the potential for causing irreversible health effects, including hypotension, central nervous system problems, anaemia and diminished hearing acuity before it is clinically recognized **(Staudinger** and **Roth, 1998).**

The toxicity depends on a number of factors; the total dose absorbed, and whether the exposure was acute or chronic. The age of the person can also influence toxicity. The route of exposure is also important; elemental pollutant is relatively inert in the gastrointestinal tract and also poorly absorbed through intact skin, yet inhaled or injected element may have disastrous effects **(Adefris, 2013).**

Lead is absorbed and stored in several body compartments. Five to ten percentage is found in the blood, most of which is located in erythrocytes; 80-90% is taken up in the bone and stored with the hydroxyapatite crystals, where it easily exchanges with the blood. Some authorities list the half-life of lead in the bone as long as 30 years, while others estimate the lead half-life in bone to be 105 days **(Soghoian, 2006).**

Although leaded petrol is not the only source of lead in the environment, it is a good indicator of exposure to lead **(Landrigan *et al.*, 2000).** Multiple studies have shown reductions in blood-lead concentrations in parallel with decreases in levels of lead in petrol **(Thomas *et al.*, 1999).** The combustion in

vehicles of petrol containing antiknock additive lead has become a major source of atmospheric lead **(Settle** and **Patterson, 1980).**

Lead is a purely toxic element and theoretically; its levels in any body fluid should be zero, which is not possible in an industrial society. Acute lead toxicity may irreversibly give rise to increased cerebrospinal pressure, convulsions, memory loss, acute encephalopathy and death **(Marcus** and **Cothern, 1986).** The adverse toxic effects of lead may cause anemia **(Needleman** and **Bellinger, 1991).**

It has been shown that traffic police constables working at various traffic control stations who were regularly exposed to vehicle exhaust fumes in controlling traffic, had alarmingly higher blood lead levels (above the safety limits) as compared to common men **(Sadaruddin** and **Manser, 1992).**

Lead is present in the saliva of exposed and unexposed individuals, and various degree of correlations have been reported with lead level in blood suggest that saliva may be a valuable tool for assessing lead exposure (**DiGregorio *et al.*, 1974; Fung *et al.*, 1975; P'an, 1981** and **Brodeur *et al.*, 1983).**

For this reason this study was carried out to throw some light on the degree of lead exposure on traffic police personnel and the effect of that exposure in oral cavity.

Aims of the study

1. Assess the level of lead in blood and saliva in personnel working in crowded traffic area.
2. Explore the reliability of salivary lead as an alternative to blood lead level.
3. Study the oral manifestations of the study group and compare it with control group.
4. Identify the cytological changes in shedded epithelial cells with saliva of subjects (morphological and nuclear changes).
5. Examine peripheral blood for the presence or absence of basophilic stippling of red blood cells and changes in haematological parameters.

Chapter one

Review of literature

1.1. General view:

Lead has been with mankind almost from the beginning of civilization, throughout this long journey to the present, this metal has been both angel and demon **(Casas and Sordo, 2006),** lead is useful, surprising, unpredictable, dangerous and deadly **(Emsley, 2005),** lead is universally present in plants, but is a nonessential element for plants and animals, lead is a soft, heavy metal of bluish color, which tarnishes to dull grey and is the most corrosion resistant of the common metals **(Woodbury, 1993),** the large amount of the metal that is produced, the high economic value of its trade and the fact that its production and transformation employs a large number of people, all make lead an extremely important material, this situation is not new and there is evidence of the use of lead from very early times, well before the time of the Roman Empire **(Bermejo, 1982),** lead is one of the seven metals of antiquity, it was present in all the metal ages and has played a significant role in the progress of mankind (**Casas** and **Sordo, 2006).**

Lead (Pb: CAS 7439-92-1); atomic weight, 207.21 (1 μg = 0.004826 μmol) Density, 11.3 g/cm3; melting point, 327.4 C°; boiling point 1620 C°; oxidation state, metallic lead is hard to dissolve in water but will dissolve in nitric acid and concentrated sulphuric acid, most lead salts are hard to dissolve (e.g., lead sulfide and lead oxides), but exceptions are found in, for example, lead nitrate, lead chlorate and—to some extent—lead sulphate and lead chloride, in addition, some salts with organic acids are insoluble **(Nordberg *et al.,* 2007).**

The element is a bluish-white lustrous heavy metal from group 14 of the periodic table (appendix 1), lead crystals are face-centered cubic and have a short lead-lead distance of 3.49Å (ångström), lead has physical properties common to other metals: it has a metallic lustre with shiny freshly cut surfaces, a high density, a low melting point, it is a conductor of electricity and heat and is soft, ductile and malleable, the freshly cut metal rapidly loses it metallic shiny lustre in moist air due to the formation of a layer of lead oxide on the surface, the oxide can further react with carbon dioxide to form lead carbonate **(Casas** and **Sordo, 2006).**

Lead is currently used for lead-acid storage batteries, for construction purposes (As sheets and pipes), for cable sheathing, radiation shielding, in alloys and other minor applications, lead compounds are also present in batteries, polyvinyl chloride PVC additives, pigments and other paint additives, glass, glazes and enamels and functional ceramics **(Thornton *et al.*, 2001).**

Lead can exist in both organic and inorganic forms **(Gossel** and **Bricker, 1994),** Inorganic lead poisoning usually result from industrial inhalation of large quantity of lead oxide **(Correia** and **Becker, 1995).**

The interest for organic lead compounds was stimulated by the discovery that their thermal decomposition generates free radicals **(Paneth** and **Hofeditz, 1931),** and by the large scale use of tetraethyl lead as gasoline additive **(Seyferth, 2003),** the major use of organic lead compounds was as antiknock gasoline additive, the major player being tetraethyl lead, the whole dramatic story of rise and fall of this compound, which is gradually eliminated because of environment pollution concerns **(Jarvie, 1988).**

The most important organic lead compounds are tetra ethyl and tetra methyl lead, which have been used in enormous quantities in leaded petrol, they are easily absorbed through inhalation and through the skin **(Nordberg *et al.,* 2007).**

The history of lead pollution is very long: around 3500 Before Christ, a method for extracting silver from lead ores appeared, with the subsequent popularity of silver in jewelry and coins followed an increasing release of the by-product lead into the environment, peaking during the age of the Roman Empire **(Nriagu, 1998),** then there was a widespread lead technology (aqueducts, etc.), and lead acetate was used as a sweetener in wine, in the 19th century, tin-containing lead was widely used in household utensils, with the start of the industrial revolution came a new rapid increase of lead production and emission, which peaked around 1970–1980, large-scale use of lead during the 20th century was in the form of organic lead compounds used as anti-knocking agent in gasoline, until the 1970s, the addition was approximately 1 g/l **(Nordberg *et al.,* 2007).**

Annual global lead emissions to the environment were in the order of 400,000 metric tons during the 1960s– 1980s, but have decreased since, as a consequence of the phase-out of lead in gasoline **(Nriagu, 1996),** however, leaded petrol is still used in many countries **(Nordberg *et al.,* 2007).**

1.2. Exposure:

The body burden of lead in the general population has been estimated to be in the order of 1000 times higher than that of the prehistoric human **(Patterson *et al.,* 1991),** main sources of this general lead exposure are lead added to gasoline, industrial emissions, and lead paint, in many countries, especially industrialized

wealthy ones, these exposures of the general population are now significantly decreasing, mainly as a consequence of elimination of lead additives to gasoline, in contrast, high environmental exposures to lead are still common in developing countries, even higher exposure to lead is prevalent in many occupations **(Nordberg *et al.*, 2007).**

1.2.1. Sources:

Lead is a multimedia pollutant, with several sources and media contributing to the exposure, any attempt to picture all major sources and exposure routes for lead ends up in a complex pattern (Figure 1-1) **(Nordberg *et al.*, 2007).**

Lead has a widespread use as pigment in house paint in some countries, and weathering, chalking, and peeling paint may cause heavy exposure **(Rosner *et al.*, 2005),** another large-scale source of exposure is organic lead added to gasoline, at combustion in the engine, organic lead is transformed into the inorganic lead oxide and is emitted almost entirely as such, this causes exposure to inorganic lead, in particular in people living in areas with heavy traffic **(Nordberg *et al.*, 2007).**

1.2.1.1 Inhalation:

The exposure through ambient air largely depends on any use of leaded gasoline in cities where leaded gasoline is still in use, or has only recently been phased out, mean air-lead levels in the order of 200–400 ng/m3 is common in residential areas **(He *et al.*, 2004),** levels are higher in areas with heavy traffic, for example reported 2000–3900 ng/m3 in such areas in the city of Lucknow, India **(Kaul *et al.*, 2003),** an average of 2860 ng/m3 in urban Beirut **(Hashisho** and **El-Fadel, 2004),** similar levels (yearly mean, 2800 ng/m3) were observed in the

Valley of Mexico in 1987, when lead was still added to gasoline in relatively high concentrations, Until 1997, lead in gasoline was reduced by > 98.5%, and in 2002, the yearly mean air-lead concentration had dropped to 70 ng/m^3 **(Schnaas *et al.*, 2004).**

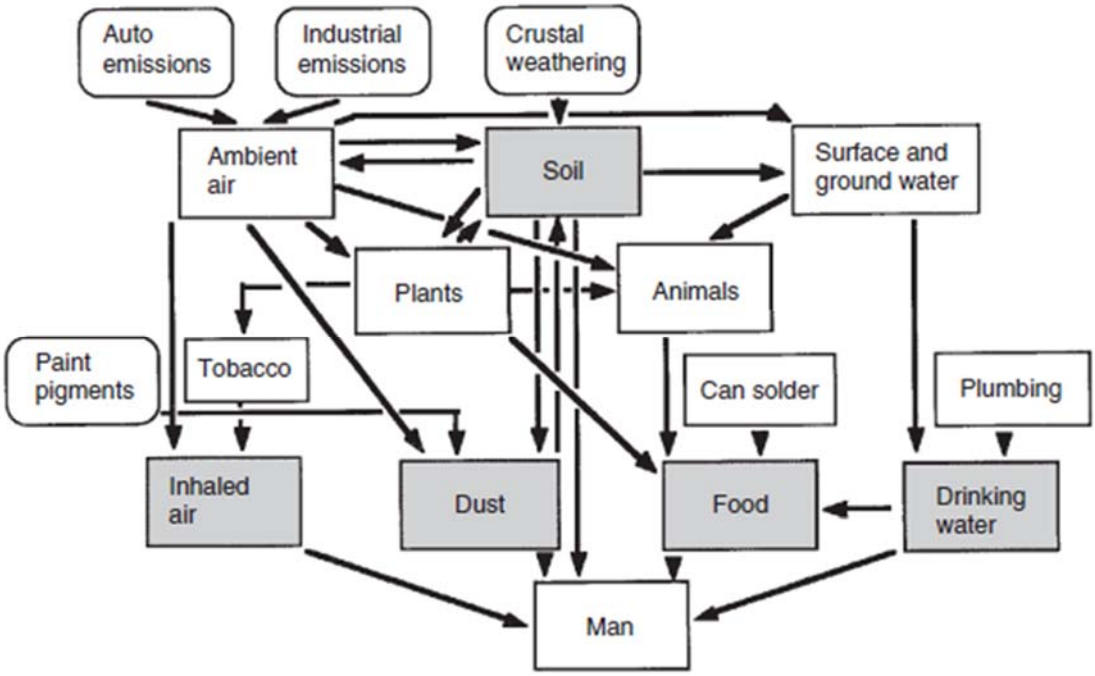

Figure 1-1 Sources and routes of Lead exposure in the general population (Skerfving, 1993)

Additional inhalation exposure occurs through cigarette smoking, although the association between smoking and blood-lead concentration may, to some extent, be confounded by alcohol intake **(Grandjean *et al.*, 1981),** the lead content in a cigarette is 3–12 µg, approximately 2% of this is inhaled into the active smoker, leaving most of the lead in the environmental tobacco smoke (**Willers *et al.*, 1992).**

1.2.1.2 Ingestion:

In the diet, fruits and vegetables, cereals, bakery wares, and beverages are major sources of lead, together supplying most of the intake **(EU SCOOP, 2004).**

Alcoholic beverages cause lead exposure **(Grandjean *et al.*, 1981),** earlier lead acetate was used as a sweetener in wines **(Morgan *et al.*, 2003),** even less spectacular alcoholic beverages, especially wines, may contain considerable lead concentrations, partly because of use of lead arsenate as a fungicide in vineyards and contamination from containers, including crystal decanters and glasses **(Graziano** and **Blum, 1991),** further intake of herbal medicine products (ayurvedic) may cause lead exposure **(Saper *et al.*, 2004).**

1.2.1.3. Skin Exposure:

Skin exposure to inorganic lead occurs, and there is an uptake through the skin however, the major influence of skin exposure seems to be that lead contamination of the hands contributes to the oral intake, this is certainly of importance in children **(Kranz *et al.*, 2004),** but also in occupationally exposed adults **(Askin** and **Volkmann, 1997),** exposure may occur from cosmetics **(Al-Ashban *et al.*, 2004),** in occupationally lead-exposed workers, contamination of cigarettes by the hands seems to cause inhalation exposure to smokers **(Dykeman *et al.*, 2002).**

1.2.1.4 Geographical Differences:

Because leaded gasoline has for a long time been a significant source of environmental lead, living close to a road with heavy traffic is a determinant of

exposure level **(Osman *et al.*, 1992; 1994),** people living in city centers have higher blood lead concentrations than people living in rural areas **(Skerfving *et al.*, 1999).**

1.3. Toxicokinetics: A simple model of the toxicokinetics of lead is shown in Figure (1-2).

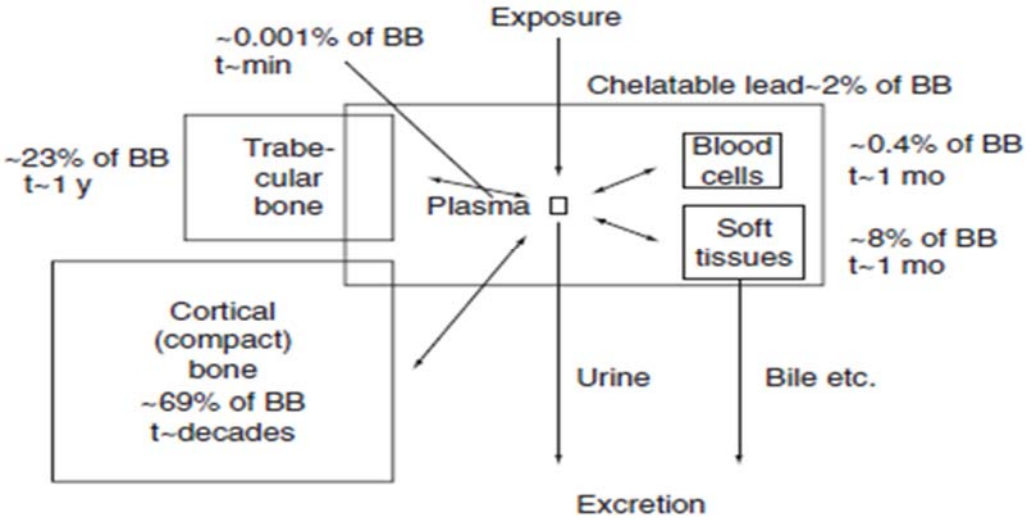

Figure 1-2 metabolic compartment model for lead in an adult human (Skerfving *et al.,* 1995)

1.3.1. Absorption:

The absorption of lead occurs by different routes of exposure which include:

1.3.1.1. Inhalation:

lead may be inhaled as an aerosol, the pattern of deposition of inhaled lead in the respiratory tract depends on the particle size, most of the lead deposited in the alveolar part of the lung is absorbed **(Nordberg *et al.*, 2007),** the rate of absorption depends on the solubility of the chemical species of lead, in human

radiotracer experiments, the absorption has generally been completed within 24 hours **(Chamberlain, 1985),** amounts and patterns of deposition of particulate aerosols in the respiratory tract are affected also by breathing patterns such as nose breathing vs. mouth breathing, air way geometry and airstream velocity within respiratory tract **(James, *et al.*, 1994).**

1.3.1.2. Gastrointestinal Tract:

The extend and the rate of gastrointestinal absorption of ingested inorganic lead are influenced by physiological states of the exposed individual e.g. age, pregnancy, nutritional calcium and iron status which mean is an inverse relationship between dietary calcium intake, iron status and blood lead concentration **(Ziegler *et al.*, 1978; Mahaffey** and **Annest, 1986),** also the gastrointestinal absorption is generally inversely proportional to particle size and directly proportional to solubility of the lead compound **(Boweler** and **Cone, 1999).**

1.3.1.3. Skin:

A fraction of soluble inorganic lead salt applied on the skin is absorbed **(Stauber *et al.*, 1994),** in one study, the absorption was only 0.06% during one month **(Moore *et al.*, 1980),** probably, the absorption of lead soaps (lead naphtenate and lead stearate) is considerably higher **(Ong *et al.*, 1990).**

1.3.2. Distribution:

Absorbed inorganic lead appears to be distributed in essentially the same manner regardless of the rout of absorption **(; Chamberlain *et al.*, 1978; Kehoe, 1987).**

Lead is distributed to blood, soft tissues and calcified tissues, within blood most of the lead is present in the erythrocytes (red cells), leaving only a fraction of less than 1% in plasma **(Nordberg *et al.*, 2007).**

From the blood plasma, the absorbed lead is distributed to other organs, Among the soft tissues, the liver and the kidney attain the highest concentrations **(Barry, 1975; Skerfving *et al.*, 1985;Baheman-Hoofmeister *et al.*, 1988),** in those organs, lead occurs as intra-nuclear inclusion bodies **(Fowler** and **Du Val, 1991),** lead does, to some extent, pass the blood–brain barrier **(Barry, 1975; Skerfving *et al.*, 1985),** the distribution within the nervous system is uneven, with high levels in the hippocampus and the amygdala **(Grandjean, 1978)** and the choroids plexus **(Manton** and **Cook, 1984),** the lead level in cerebrospinal fluid is very low **(Conradi *et al.*, 1980; Manton and Cook, 1984);** it is correlated with plasma lead (although even lower) lead is distributed to the gonads and other parts of the male reproductive system **(Nordberg *et al.*, 2007).**

A large proportion of the absorbed lead is incorporated into the skeleton **(Gusserow, 1861; Barry, 1975; Wittmers *et al.*, 1988 Silbergeld *et al.*, 1993; McNeill *et al.*, 1997),** the skeleton contains >90% of the body burden of lead **(Barry, 1975).**

1.3.3. Biotransformation:

There is only circumstantial evidence that microorganisms may methylate inorganic lead, it is not known whether this may occur in the gastrointestinal tract, there are no indications of methylation or any other biotransformation in the tissues **(Nordberg *et al.*, 2007).**

1.3.4. Elimination:

Independent of rout of exposure absorbed lead is excreted primary in urine and faeces; sweat, saliva, hair, nails and breast milk are minor routes of excretion **(Chamberlain *et al.*, 1978; Kehoe, 1987; Stuaber *et al.*, 1994).**

At low exposures, the excretion in the faeces is approximately half that in the urine, at higher levels probably less **(Nordberg *et al.*, 2007).**

Lead is also, to some extent, excreted in saliva **(Koh *et al.*, 2003)** and sweat **(Omokhodion** and **Crawford, 1991),** amounts without practical importance are excreted in nails and hair **(Foo *et al.*, 1993),** lead is also incorporated into semen, the placenta, the fetus, and milk **(Nordberg *et al.*, 2007).**

1.4. Organ Effects:

Lead can cause toxic effects on a long series of organs and tissues.

1.4.1. Nervous System:

Exposure to lead may cause encephalopathy, the classical signs in severe toxicity are ataxia, coma, and convulsions, after elimination of exposure and treatment by chelating agents, the signs of acute encephalopathy may improve,

but residual symptoms may remain **(Nordberg *et al.*, 2007),** at less severe exposure, there are symptoms indicating less dramatic CNS effects such as of irritability, hostility, anxiety, fatigue, tension, depressed mood, interpersonal problems, and difficulties in concentrating **(Ehle and McKee, 1990; Maizlish *et al.*, 1995).**

Occupational lead exposure affects the autonomous nervous system, hence, associations between decreased electrocardiographic (ECG) heart rate variability (HRV) and blood lead level (Pb-B) have been reported in several studies **(Murata** and **Araki, 1991; Teruya *et al.*, 1991; Murata *et al.*, 1995),** and this indicates effects on the sympathetic and (less) parasympathetic nervous systems, possibly at the brain stem level, in some reviews, it was concluded that such effects may occur at Pb-B of 1.5 μmol/L and higher **(Araki *et al.*, 2000; Skerfving *et al.*, 2005),** lead also affects auditory and visual functions **(Otto** and **Fox, 1993),** there is an association between impaired visual contrast and Pb-B **(Lucchini *et al.*, 2000),** the mechanism behind lead-induced neurotoxicity is not clear **(Rice** and **Silbergeld, 1996),** however, several possibilities have been proposed, Hence, lead interferes with heme synthesis, which may impair the energy metabolism in the nervous system **(Nordberg *et al.*, 2007),** experimentally: lead can induce significant function impairment in vivo in the nervous system at doses below cytotoxicity **(Rice** and **Silbergeld, 1996).**

1.4.2. Blood and Blood-Forming Organs:

Heavy lead exposure can cause anemia, lead induced anemia is characterized by basophilic stippling of peripheral erythrocytes, because the inhibition of pyrimidine 5′-nucleotidase (P5N) causes an accumulation of pyrimidine

nucleotides; normal depolymerization of reticulocyte ribosomal RNA does not occur, and granulae are formed, lead inhibits enzymes in the heme synthesis and maybe also interfere with iron transport (δ-aminolevulinic acid dehydratase "ALAD" and heme chelatase), in the bone marrow, there are sometimes sideroblasts, probably because iron fails to be incorporated into heme, moreover, lead inhibits the synthesis of α- and ß-chains of globulin **(Nordberg *et al.*, 2007),** also, there might be an anemic effect mediated by erythropoietin deficiency as a result of tubular kidney toxicity with impaired stimulation of erythroid progenitors **(Osterode *et al.*, 2006)** erythrocyte ALAD and hepatic activities were correlated directly with each other and correlated inversely with Pb-B in the range of 12-56 μg/dl **(Secchi *et al.*, 1974).**

Basophilic stippling is a non-specific finding in many other conditions such as; hemolytic anemia, malaria, leukemia and exposed to other toxins **(Ibles** and **Pollock, 1986)** and should be regarded as unreliable index in lead intoxication **(Peter** and **Bryson, 1996).**

1.4.3. Kidneys:

Heavy lead exposure may cause renal dysfunction characterized by glomerular and tubulointerstitial changes, resulting in hypertension, hyperuricemia and gout ("saturnine gouty arthritis"), and chronic renal failure (**Nordberg *et al.*, 2007),** there are indications that environmental lead exposure in the general population plays a role in the etiology and/or progression of kidney disease, at least in populations with high exposure **(Lin *et al.*, 2001).**

At lower lead exposures in the occupational and general environments, there were associations between blood lead concentrations and increased serum levels

of urate, as well as urinary excretion of low molecular weight and lysosomal enzymes **(Endo *et al.*, 1993; Chia *et al.*, 1994a, 1994b; 1995; Santos *et al.*, 1994; Shadick *et al.*, 2000; Weaver *et al.*, 2003a; 2005a, b),** the effect on serum urate may be more pronounced at old age, It has been proposed that a urate increase may be the mechanism behind lead-induced tubulointerstitial changes, although other mechanisms may also operate **(Weaver *et al.*, 2005b),** slight tubular proteinuria has also been reported to be associated with lead exposure in children **(Bernard *et al.*, 1995; Verberk *et al.*, 1996; Fels *et al.*, 1998; Osman *et al.*, 1999),** the findings indicate an effect on the proximal tubuli, with deficiencies in excretion of urate and reabsorption of proteins, which have been filtered in the glomeruli, and shedding of tubular cells, although hyperuricemia in itself may also reflect oxidative stress **(Waring *et al.*, 2001).**

1.4.4. Cardiovascular System:

Cardiovascular changes have been noted in association with increasing lead body burdens and/or lead exposure in humans; these include changes in cardiac conduction and rhythm **(Kirkby** and **Gyntelberg, I985; Cheng *et al.*, 1998)** which may be secondary to lead induced impairment of peripheral nerve conduction, numerous epidemiological studies have examined the association between lead exposure (as indicated by Pb-B or bone lead concentration) and blood pressure, quantitatively this association amounts to an increase in systolic blood pressure of approximately l mmHg with each doubling of Pb-B **(Nawrot *et al.*, 2002).**

A variety of diverse mechanisms may contribute to the increased blood that is observed with chronic exposure to lead, lead affects important hormonal and

neural systems that contribute to the regulation of vascular resistance, heart rate and cardiac output **(Carmignani *et al.*, 2000).**

1.4.5. Endocrine System:

There is some indication of effects in lead workers on the hypothalamus-pituitary-thyroid/adrenal axes **(Tuppurainen *et al.*, 1988),** although the picture is not consistent **(Erfurth *et al.*, 2001),** perhaps because of varying exposure levels, furthermore, associations between serum prolactin and Pb-B have been reported **(Lucchini *et al.*, 2000).**

Hence, there are indications that lead causes endocrine disruption, Skerfving *et al.,* (2005) concluded that there were some indications of such effects at occupational lead exposure in the range of 1.5– 2.0 μmol/l and higher **(Skerfving *et al.*, 2005).**

There are associations between lead and serum levels of vitamin D metabolites, In children, very high Pb-B was associated with low concentrations of 1,25- dihydroxycholecalciferol **(Mahaffey *et al.*, 1982),** possibly because of deficient hydroxylation in the kidney tubuli, no such relationship was seen in children with lower Pb-B **(Koo *et al.*, 1991),** however, the picture is complicated, hence, in lead workers, high Pb-B was associated with high serum concentrations of 1,25- dihydroxycholecalciferol **(Kristal-Boneh *et al.*, 1998),** the latter may be due to compensatory increase of formation to compensate for lead-inhibited intestinal lead absorption **(Fullmer, 1990).**

1.4.6. Gastrointestinal Tract:

Gastrointestinal symptoms (lead colic) are often the only clinical ones in lead poisoning, they appear in the beginning, often remain during the entire course of the disease and are often the reason why lead poisoning is diagnosed, they are often not characteristic, they most often start as protracted constipation, indigestion, and loss of appetite, but only occasionally diarrhea, the abdominal cramps are intermittent, often with pain-free intervals, most often localized in the hypogastrium (sometimes in the epigastrium), sometimes radiating to the urinary bladder, scrotum, and kidney, they may be very intensive, Vomiting is prevalent, as is tenesmus without defecation and miction without much urine **(Nordberg *et al.*, 2007).**

Skerfving *et al.*, (2005) was concluded that gastrointestinal symptoms usually occur at Pb-B of 3 μmol/l and higher **(Skerfving *et al.*, 2005).**

1.4.7. Reproductive system:

Lead is distributed to the testis **(Barry, 1975),** also lead accumulates in other parts of the male reproductive tract epididymis, seminal vesicles, and prostate **(Johansson** and **Wide, 1986).**

There were associations between exposure and sperm count, motility, and morphology **(Telisman *et al.*, 2000).**

Even in subjects without occupational lead exposure, there was an association between seminal fluid Lead and sperm count **(Xu *et al.*, 2003),** decreased libido, erectile dysfunction, and ejaculation problems have been reported in lead workers **(Lancranjan *et al.*, 1975).**

1.4.8. Oral cavity:

Lead is excreted in the saliva **(Koh *et al.,* 2003),** which may explain the gingival "lead line" (Burtonian line) sometimes seen in lead workers (alternately, the origin is lead in the gingival tissue), the greyish color is due to precipitated lead sulfide, which is formed by sulfur produced by bacteria, hence, the sign is most prevalent in lead workers with bad oral hygiene and bacterial paradentosis **(Nordberg *et al.,* 2007),** this line is usually absent in edentulous patients or in patients who take care of their teeth **(Peter** and **Bryson, 1996),** other oral manifestations include ulcerative stomatitis, grey spots on the buccal mucosa and heavy coating on the tongue **(Ibles** and **Pollock,1986).**

In the oral cavity, high levels of lead can damage the acinar cells of parotid gland, resulting in altered salivary secretion of protein, calcium and lysosomal enzymes **(Abdollahi *et al.,* 2001).**

Several ecologic and cross-sectional studies, conducted in the 1960s and 1970s, implicated lead as a risk factor for dental caries **(Stack 1983),** these studies, however, were inconclusive, In recent years, lead has been identified as a risk factor for dental caries in 2 cross-sectional studies conducted in Spain **(Gil *et al.,* 1996),** however, the most compelling basis for a causal relationship between lead exposure and dental caries showed prenatal and perinatal lead exposure to be linked to increased incidence of caries in a well-controlled animal study **(Watson *et al.,* 1997).**

Three different mechanisms can be hypothesized concerning lead exposure and dental caries: salivary gland function, enamel formation, and interference with fluoride in saliva **(Mark *et al.,* 1999),** exposure to lead may have adversely affected the ability of the salivary gland to produce adequate amounts of saliva

(Watson *et al.*, 1997), saliva has several protective properties that operate against caries: it acts as a buffering agent when acids are produced, it physically removes debris from tooth surfaces, and it has immunologic and bacteriostatic properties **(Mandel, 1984),** lead also incorporates into tooth structure before the tooth erupts into the mouth and this may result in defective enamel that is more susceptible to caries **(Brudevold *et al.*, 1977),** also lead may interfere with the bioavailability of fluoride by binding to fluoride ions in saliva and plaque, thereby reducing the preventive capacity of fluoride to remineralize enamel after an acid challenge **(Rao, 1984).**

1.4.9. Other Organs:

Lead exposure is associated with a low skeletal growth, even at levels of exposure in the general population **(Frisanch** and **Ryan, 1991).**

The mechanism is not known, however, there are possibilities of interaction with both calcium metabolism and bone cell proteins **(Sauk *et al.*, 1992).**

1.5. Immunotoxicology:

There is only limited information on immunotoxic effects of lead **(McCabe, 1994),** and the picture is not consistent, Some of the interstudy discrepancies may be due to the variations in exposure intensity and methodological differences, there is no evidence of a marked immunotoxic effect of lead at the exposure levels studied, however, there are probably various effects on the humoral immunity—immunoglobulin levels in serum and saliva **(Pinkerton *et al.*, 1998)** in lead workers.

Moreover, in lead-exposed workers, varying effects on leukocyte and lymphocyte subtypes and function have been described **(Sata *et al.*, 1997;**

Pinkerton *et al.*, 1998), their health implications are not clear, but there are some indications of increased sensitivity to infections in Japanese lead refinery workers **(Horiguchi *et al.*, 1992).**

1.6. Alcoholics and Smokers:

Alcoholics, and people who consume excess amounts of alcohol, may be at increased risk of hematological, neurological, and hepatotoxic effects, in animal studies, lead and alcohol synergistically inhibited blood ALAD activity and hepatic glutamic oxaloacetic transaminase (GOT, AST) and glutamic pyruvic transaminase (GPT, ALT) activity, depressed dopamine and 5-hydroxy lead tryptamine levels in rat brain, increased lead burdens in tissue organs, and elevated blood zinc protoporphyrin ZPP **(Dhawan *et al.*, 1989),** smokers are also at elevated risks of lead intoxication since cigarette smoke contains lead and other heavy metals such as cadmium and mercury **(Calabrese 1978),** which have been shown to be synergistic in experimental animals **(Fahim** and **Khare, 1980).**

1.7. Sign and symptom of Lead poisoning:

Adults with occupational lead exposure may manifest numerous signs and symptoms representing disorders of several organ systems, true acute poisoning is rarely occur after very high respiratory exposures **(Keogh, 1992),** large ingestions or intravenous exposures **(Norton *et al.*, 1989),** such patients may present with colic, hepatitis, pancreatitis, hemolytic anemia and encephalopathy in days or weeks **(Cullen *et al.*, 1983).**

The clinical presentation of chronic lead poisoning varies widely, depending upon the age at exposure, the amount of exposure, and the duration of exposure, younger patients tend to be affected more than older children and adults, because

lead is absorbed from the gastrointestinal (GI) tract of children more effectively than from that of adults **(Kathuria *et al.*, 2014).**

No pathognomonic symptoms exist, When symptoms do occur, they are typically nonspecific, Common nonspecific symptoms include the following: temperamental lability, irritability, behavioral changes, hyperactivity or decreased activity Loss of developmental milestones, language delay, more significant exposure to lead may cause symptoms that are more likely to lead to a medical evaluation, They are as follows: abdominal pain, loss of appetite, vomiting, constipation, headache, ataxia, lethargy, seizures, stupor, and coma, the presence of fever does not rule out the diagnosis, which still must be given full consideration, adults with chronic exposure may develop other symptoms, such as Weakness of extensor muscles (e.g., foot drop, wrist drop), delirium, and hallucinations, adults with lead poisoning frequently have sleep disorders, they may be hypersomnolent or have difficulty falling asleep at the appropriate time **(Kathuria and Ramachandran, 2014).**

Currently, three forms of lead nephropathy are recognized, the first is acute lead poisoning resulting from acute massive exposure to lead, which causes classic symptoms, including colic, encephalopathy, and anemia, neuropathy, and Fanconi syndrome, the second is chronic lead nephropathy (fig. 1-3), which is a slowly progressive interstitial nephritis resulting from excessive cumulative exposure to lead and is frequently associated with hypertension and gout, the third is lead-induced hypertension. Furthermore, lead exposure, at much lower levels than those causing lead nephropathy, acts as a cofactor with more established renal risk factors to increase the risk of chronic kidney disease and the rate of progression, adverse renal effects have been reported at mean blood lead levels of

less than 5 µg/dl, cumulative lead dose has also been associated with worse renal function **(Kathuria *et al.*, 2014).**

In addition to its effects on renal function, lead has been associated epidemiologically with the development of hypertension **(Fadrowski *et al.*, 2010),** research on the effects of lead on adults has prompted the suggestion that acceptable levels of lead in adults be dropped almost to those of children **(Murata, 2009).**

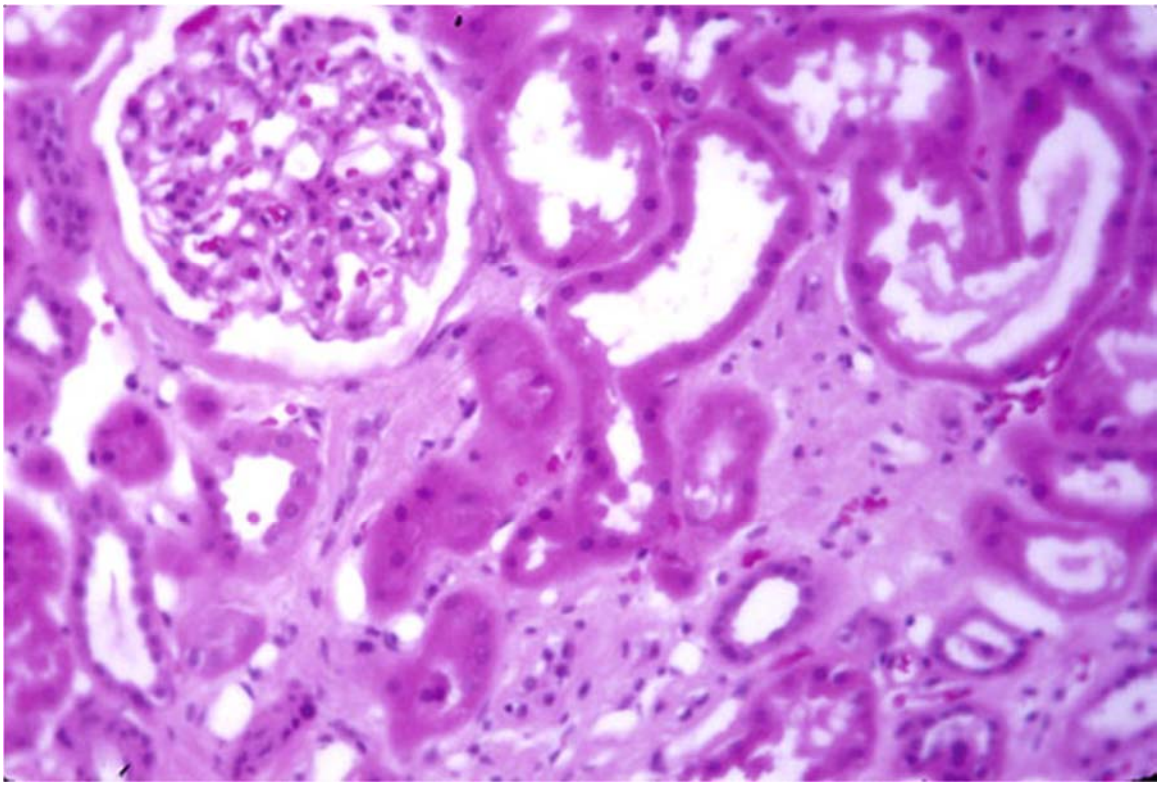

Figure 1-3 Kidney biopsy results from patient with chronic lead nephropathy show nonspecific tubular atrophy and interstitial fibrosis, Note absence of interstitial infiltrate Single glomerulus included in section is normal (Batuman *et al.*, 2014)

1.8. Biomarkers/biological monitoring of lead exposure:

Biological monitoring has been defined as the measurement and assessment of agents or their metabolites either in tissues, secreta, excreta, expired air or any combination of these to evaluate exposure and health risks compared with an appropriate reference **(Berlin *et al.*, 1982),** the term biological marker (biomarker) is a general term used for a system that specifically measures an interaction between a biological system and a chemical, physical, or biological environmental agent, biological monitoring techniques are useful for risk assessment of toxic agents in the field of environmental health, biomarkers are generally classified into three groups: biomarkers of exposure, effect, and susceptibility, different biologic tissues and fluids (blood, urine, bone, tooth, hair, and nail) have been used to test for lead exposure, no biomarker of bioavailable lead has been generally accepted **(Sanders *et al.*, 2009).**

The difficulty in assessing the exact nature of lead exposure depends on the complex toxico-kinetics of lead within various body compartments (namely, cycling of lead between bone, blood, and soft tissues).

Blood lead (Pb-B)

erythrocyte lead, is a representative of soft tissue lead and the primary biomarker used for the assessment of Lead exposure, both for screening and diagnostic purposes and for biomonitoring body burden and absorbed (internal) doses of the metal, In adult humans, up to 50% of inhaled lead is transferred to bloodstream and of the ~10% absorbed dietary lead, more than 98% is found in blood cells **(Schütz *et al.*, 1996),** blood lead measurements reflect both recent and past exposures, the latter resulting from mobilization from bone back into blood **(Gulson *et al.*, 1996),** and even in persons without excessive exposure to Lead,

bone can contribute from 45% to 55% of Pb-B **(Smith *et al.*, 2002),** 90% or more of Pb-B consists of mobilized bone-lead **(Barbosa *et al.*, 2005),** the time required for Pb-B to decline to < 10 µg/ dl in non-chelated having Pb-B levels between 25–29 µg/ dl was about 2 years and was linearly related to the Pb-B peak **(Smith *et al.*, 2002),** Pb-B was found to be associated with: (a) environmental concentrations of lead; (b) the duration of exposure **(Roy *et al.*, 2003),** an important weakness of Pb-B is its poor response to changes in exposure at high levels **(Bergdahl and Skerfving 2008).**

In certain cases bone or teeth (for past exposures), feces (for current gastrointestinal exposure), or urine (for organic lead) are sometimes more useful than blood **(Sanders *et al.*, 2009).**

Plasma lead (Pb-P)

As the plasma fraction is rapidly exchangeable in the blood, the toxic effects of lead are assumed to be primarily associated with plasma lead (Pb-P) **(Barbosa *et al.*, 2005),** although Pb-P should be more germane than Pb-B to lead exposure and distribution, little is known about the association between Pb-P and clinical outcome, the determination of Pb-P is problematic because erythrocyte hemolysis can shift the metal into the plasma and artificially increase Pb-P levels **(Sanders *et al.*, 2009),** the concentration of lead in plasma is extremely difficult to measure accurately because levels in plasma are near the quantitation limits of most analytical techniques **(Bergdahl and Skefing, 1997)** and because of hemolysis that may occurs with typical analytical practices can contribute substantial measurement error **(Smith *et al.*, 1998).**

Bone Pb (BnPb)

Many researchers accept that a cumulative lead exposure integrated over many years, in bone for example, rather than a single Pb-B measurement of lead dose may be the most important determinant of some forms of toxicity, bone Pb (BnPb) accounts for > 94% of the adult body burden of lead (70% in children) **(Hu *et al.*, 1998),** there is a strong association between BnPb levels and serum lead levels of adults exposed to lead **(Hernandez *et al.*, 1998).**

Lead in bone is considered a biomarker of cumulative exposure to lead because lead accumulates in bone over life time and most of the lead body burden resides in bone, lead is not distributed uniformly in bone, lead accumulates in regions of bone undergoing the most active calcification at the time of exposure **(Aufderheide** and **Wittmers, 1992).**

The development of non-invasive x-ray fluorescence (XRF) techniques for measuring lead concentrations in bone has enabled the exploration of bone Lead as biomarker of lead exposure in children and adult **(Hu *et al.*, 1995; Rosen *et al.*, 1993).**

The most informative epidemiologic studies of the impact of lead on health are those that could derive estimates of both recent (Pb-B) and cumulative (BnPb) exposure for each participant **(Sanders *et al.*, 2009),** in a review of studies measuring both Pb-B and BnPb at exposure levels encountered after environmental exposure, the associations between the biomarkers of cumulative dose (mainly in tibia) and cognitive function in adults were stronger and more consistent than were the associations with Pb-B levels **(Shih *et al.*, 2007) ,** Patella (kneecap) lead, representing a pool that may capture aspects of both current

bioavailable and cumulative lead dose thus offering advantages over tibia or Pb-B **(Wright *et al.*, 2003).**

Saliva lead (Pb-S)

Lead is excreted in human saliva and sweat **(Stauber *et al.*, 1994),** Saliva is a convenient source and therefore a potential substitute for blood as a biomarker for lead exposure **(Silbergeld, 1993),** nevertheless, saliva has not been generally accepted as a reliable biomarker of lead exposure because of conflicting and unreliable saliva lead (Pb-S) measurements **(Sanders *et al.*, 2009).**

Early research suggested an association between Pb-S levels and Pb-B and Pb-P levels **(P'an, 1981; Omokhodion** and **Crockford, 1991),** subsequently, data from a study compared Pb-B and Pb-S in an area highly contaminated from lead mining, suggesting that saliva is not suitable material for biological monitoring with respect to lead exposure due to environmental contamination **(Thaweboon *et al.*, 2005),** similarly, another study evaluated the use of parotid Pb-S levels as a surrogate of Pb-B or Pb-P levels to diagnose lead exposure, only a weak correlation was found between Pb-S and Pb-B, and between Pb-S and Pb-P **(Barbosa *et al.*, 2006),** a later study by this group did show a clear relation between Pb-S and environmental contamination by lead, the authors suggested that further studies on Pb-S should be undertaken to investigate the usefulness of saliva as a biomarker of lead exposure **(Costa *et al.*, 2008).**

Moreover, it has been argued that Pb-S is direct excretion of Pb fraction in diffusible plasma namely, the fraction not bound to proteins **(Omokhodion** and **Crockford, 1991).**

Alternatively other study found highly significant correlation between Pb-S and Pb-B, suggesting the use of Pb-S for lead exposure monitoring **(Gonzalez *et al.*, 1997; Mudher, 2008; Matloob, 2011).**

Urine lead (UPb)

The collection of urine lead (UPb) is favored for long-term biomonitoring, especially for occupational exposures, urine Pb originates from Pb-P that is filtered at the glomerular level and excreted through the kidneys **(Sanders *et al.*, 2009),** UPb levels adjusted for glomerular filtration rate can serve as a proxy for Pb-P **(Tsaih *et al.*, 1999; Barbosa *et al.*, 2005)** other study concluded that the correlation of UPb with Pb-B among workers occupationally exposed to lead was close enough to suggest that UPb can be a good alternative to Pb-B on a group basis, but not close enough to allow UPb to predict Pb-B on an individual basis **(Fukui *et al.*, 1999).**

Hair lead (HPb)

Although lead excreted in hair has been suggested for the assessment of lead exposure **(Schumacher *et al.*, 1991),** although there is an extensive debate ensues about hair lead (HPb) as a biomarker **(Barbosa *et al.*, 2005)** Hair is a biological specimen that is easily and non-invasively collected with minimal cost and is easily stored and transported to the laboratory for analysis, Such advantages should make hair an attractive biomonitoring substrate, at least superficially **(Sanders *et al.*, 2009).**

Nail lead (NPb)

Similar to hair, nails have many superficial advantages as a lead exposure biomarker, especially as specimen collection is non-invasive and simple and specimens are very stable after collection, not requiring special storage

conditions, Nail lead (NPb) is considered to reflect long-term exposure because this compartment remains isolated from other metabolic activities in the body **(Takagi *et al.*, 1988),** because toenails are less affected than fingernails by exogenous environmental contamination, toenails have been preferred for lead-exposure studies **(Sanders *et al.*, 2009).**

Tooth enamel lead (EPb)

In comparison to bone, teeth accumulate lead over the long term, some evidence has shown that teeth are superior to bone as an indicator of cumulative lead exposure because the losses from teeth are much slower, moreover, teeth are relatively easy to analyze and are very stable for preservation purposes, **(Maneakrichten *et al.*, 1991),** the concentrations of Pb-B is related to the lead concentrations in surface tooth enamel (EPb) in long term but correlated with Pb-S only in the short term **(Cleymaet *et al.*, 1991; Silbergeld, 1993).**

Micronuclei (MN)

are chromosome fragments that are not incorporated into the nucleus at cell division, the MN assay in peripheral blood is considered a reliable biomarker of genotoxic exposure to both physical and chemical agents **(Fenech, 1993; Vaglenov *et al.*, 1998)** increases in MN frequency indicate exposure to clastogenic and/or aneugenic agents **(Sanders *et al.*, 2009),** sister chromatid exchanges (SCEs), high-SCE frequency cells (HFCs), and DNA-protein cross-links (DPCs) have also been shown to be reliable biomarkers for monitoring exposure to lead and clearly indicate health effects from occupational exposure to lead **(Wu *et al.*, 2002).**

Enzymes

Several enzymatic processes responsible for heme synthesis can be used as biomarkers for the toxic effects of lead, primarily δ-aminolaevulinic acid dehydratase (δ-ALAD), which catalyzes the condensation of two molecules of 5-aminolevulinic acid to form the heme precursor, porphobilinogen, As the activity of δ-ALAD is inhibited by lead binding, this enzyme is accepted as the most sensitive measurable biological index of lead toxicity **(Barbosa *et al.*, 2005).**

1.9. Oral fluid (whole saliva):

Oral fluid (whole saliva) is for the larger part produced and secreted by the various salivary glands, such as the submandibular, sublingual, and parotid glands) **(Schenkels *et al.*, 1995),** also minor salivary gland situated on the tongue, palate, and buccal and labial mucosa **(Ferguson, 1999),** in addition, it contains serum components that enter the oral cavity via damaged oral mucosa or the periodontium (crevicular fluid), each type of gland secretes a fluid with a characteristic protein composition, thus, whole saliva is a mixed secretion **(Schenkels *et al.*, 2005),** whole saliva also contains a number of constituents of non salivary origin to form what is called "oral fluid" which include gingival crevicular fluid, blood cells, bacteria, bacterial products, desquamated epithelial cells, cellular components, viruses, fungi, food debris, fluoride, some bronchial secretions and acid liquid from stomach in case of gastric reflux **(Fejerskove and Kidd, 2008).**

In healthy adults about 0.5-1 ml of saliva is present at any time in the mouth, spread out a total surface area of approximately 200 cm^2 resulting in a thin film of 10- 100 μm in thickness **(Queimado *et al.*, 2008).**

1.9.1. Functions of saliva:

Saliva is a complex fluid that plays an important role in the lubrication, digestion, antibacterial functions, oral clearance, maintenance of healthy tissue, speech and taste, in addition to that stimulated saliva provides a powerful buffer that protects the oral cavity against the damaging effect of pH changes following acid production by plaque bacteria and acts as a reservoir for ions that facilitate remineralization of teeth after demineralization caused by bacterial acids, however, functions of saliva depend on its flow rate and composition **(Katie *et al.*, 2008; Fejerskove and Kidd, 2008)** (table 1-1).

Saliva is the key element in the maintenance of oral health, its function depends on its rate of secretion and composition; alterations in salivary composition appear to be related in its viscosity and oral complaints **(Chimenos-Kustner *et al.*, 2002).**

Saliva provides an important excretory route for several blood components, including urea, uric acid, ammonia and thiocyanate, the majority being subsequently reabsorbed in the gut, toxic blood levels of heavy metals may also reflect salivary lead, mercury and bismuth secretion, subsequently leading to characteristic oral soft tissue deposits **(Christopher, 1988),** saliva coats the oral mucosa, mechanically protecting it from trauma during eating, swallowing and speaking **(Maton, 1993)** (fig. 1-4).

The dissolution of foodstuffs is probably one of the major salivary functions by facilitating comminution and digestion, **(Christopher, 1988),** the lubrication action of saliva is important for oral health, it facilitates the movements of the tongue and lips during swallowing and eating and is important for clearly articulated speech, the efficacy of saliva as lubricant depend on its viscosity and how it changes with shear rate **(Darwell** and **Clark, 2000).**

In addition to protecting the oral tissues from dehydration, saliva has a major function in mechanical food and microbial debris lavage, salivary mucus tends to take a relatively constant course along specific routes to the esophagus **(Bloomfield 1921, 1922),** with the salivary flow rate, tongue movements and swallowing reflexes all involved in this mechanism is probably responsible for

Table 1-1 functions of saliva (Whelton, 1996).

Fluid/lubricant	**Coats mucosa and helps to protect against mechanical, thermal and chemical irritation, Assists smooth air flow, speech and swallowing.**
Ion reservoir	**Solution supersaturated with ions facilitates re-mineralization of the teeth.**
Buffer	**Help to neutralize plaque pH after eating, thus reducing time for demineralization.**
Cleansing	**Clears food and aids swallowing.**
Antimicrobial action	**Specific (e.g. sIgA) and non-specific (e.g. lysozyme, lactoferrin and sialoperoxidase), Anti-microbial mechanisms help control the oral micro flora.**
Agglutination	**Aggregation and accelerated clearance of bacterial cells.**
Pellicle formation	**Protective diffusion barrier formed on enamel from salivary proteins.**
Digestion	**Due to the presence of the enzyme amylase, starchy food and debris on the teeth is broken down.**
Taste	**Saliva acts as a solvent thus allowing interaction of food stuff with taste buds to facilitate taste.**
Excretion	**As the oral cavity is technically outside the body, substances which are secreted in saliva are excreted, This is a very inefficient excretory pathway as re-absorption may occur further down the intestinal tract.**
Water balance	**Under conditions of dehydrations, salivary flow is reduced, dryness of the mouth and information from osmoreceptors are translated into decreased urine production and increased drinking (integrated by the hypothalamus).**

the low incidence of primary oral infections and inflammatory lesions in normal patients **(Christopher, 1988),** human salivary mucins have a multifunctional role in the oral cavity in that they lubricate oral surfaces, provide antimicrobial protective barrier for oral tissue, and aid in mastication, speech and swallowing **(Baughan *et al.*, 2000),** mucins have the ability to interact with oral microorganisms when infectious organism enter the body **(Thomsson *et al.*, 2002),** humans salivary proline-rich proteins are present in the initially formed acquired pellicle and mature pellicle, considered as inhibitors of calcium phosphate crystal growth, interact with oral bacteria, have lubricatory roles in saliva **(Lit *et al.*, 2001).**

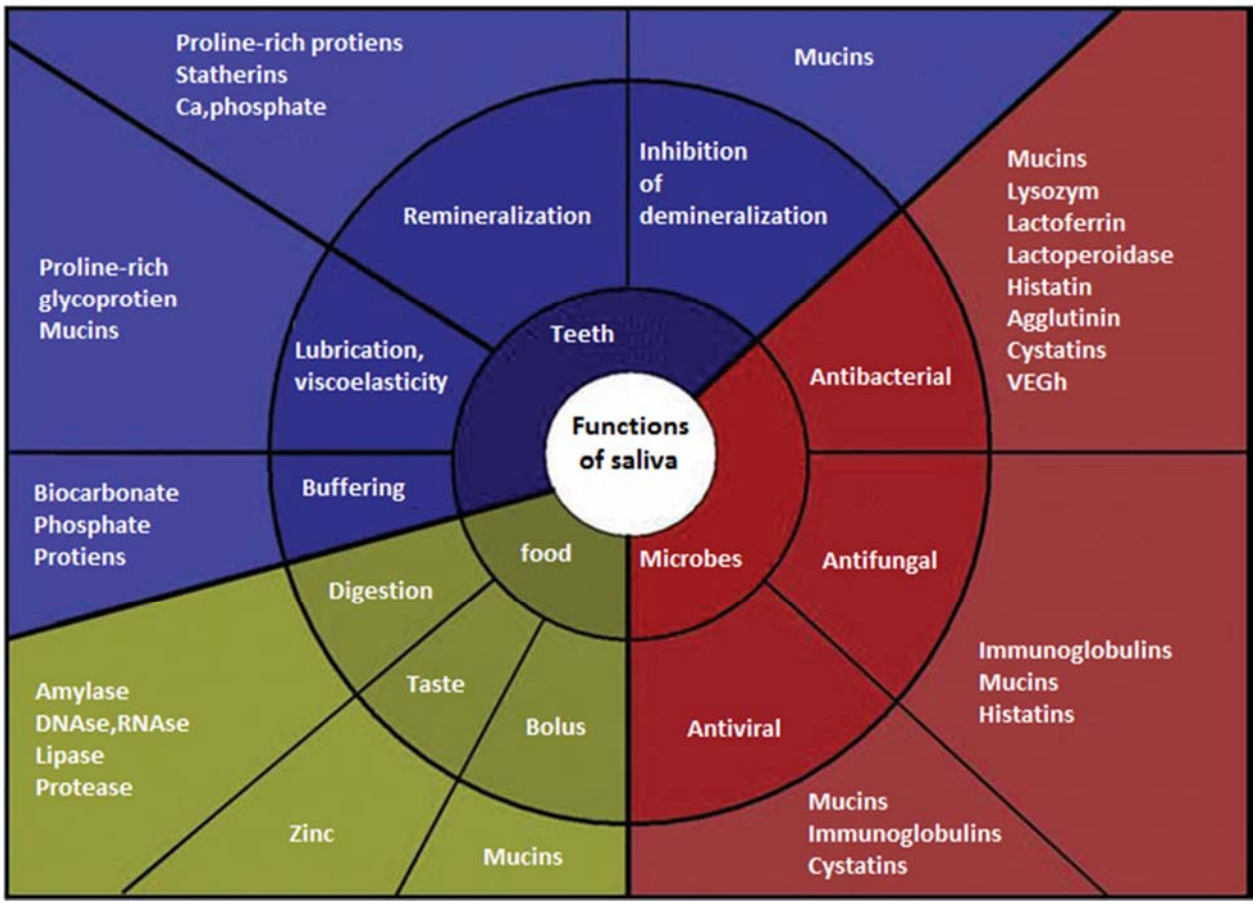

Figure 1-4 Functions of saliva (Wong, 2008)

Salivary immunoglobulins (sIgA and sIgM) originate from immune cells are produced as a host response to an antigenic stimulus, the immunoglobulin may be directed at specific bacterial molecules, inducing cell surface molecules such as adhesions, or against enzymes, by binding to such molecules, adhesion of specific bacteria to oral surface may be blocked, so preventing colonization by the affected species **(Zee *et al.*, 2001)**, these immunoglobulins considered as first line of mucosal defense against microbial invasion **(Proctor** and **Carpenter, 2001).**

Salivary lysozyme is secreted mainly by the submandibular and sublingual gland **(Noble, 2000),** hydrolysis specific bands in exposed bacterial cell wall, causing cell lyses and death, so it has been proposed as a lytic factor for bacteria with immunoglobulins have bound and mimicking, lysozyme to mucosal protection and modulates candida populations in the oral cavity **(Samaramyaka *et al.*, 200l).**

Salivary peroxidase and myeloperoxidase, catalyze a reaction involved inhibition of bacterial growth and metabolism, and the prevention of peroxide accumulation, thus protecting proteins from the action of reactive oxygen species **(Salvolini *et al.*, 2000),** salivary analyses the oxidation of thiocyanate ion (SCN^-) to generate oxidation products that inhibit the growth and metabolism of many microorganisms **(Battino *et al.*, 2002).**

Salivary agglutinins are glycoproteins which have the capacity to interact with unattached bacteria, resulting in clumping of bacteria into large aggregates which are more easily flushed by saliva and swallowed and induced the aggregation and clearance of streptococci from the oral cavity **(Carlen *et al.*, 1998).**

Salivary agglutinins may mediate the adherence of various bacterial species to the tooth surfaces **(Stenudd *et al.*, 2001),** salivary lactoferrin has antibacterial activity, bind iron, making it unavailable for microbial use, and also has a direct bactericidal effect on some microorganisms including streptococcus mutans strain **(Van der Strate *et al.*, 1999).**

The most significant function of histatins may be their antifungal activity against candida albicans; tennin-binding proteins in human saliva and bind to enamel surfaces and hydroxyapatite in a complex manner **(Wrnblowski *et al.*, 2001).**

1.9.2. Composition of saliva:

The composition of saliva varies depending on whether it is stimulated or unstimulated (resting), the unstimulated saliva is the mixture of secretions which enter the mouth in the absence of exogenous stimuli such as taste or chewing while the stimulated saliva is secreted in response to masticatory or other less common stimuli such as activation of the vomiting center **(Bradley, 1995),** The main constituents of whole saliva is water (99.4% and 99.5%) for unstimulated and stimulated saliva respectively, the remaining is composed of organic substances (protein, carbohydrate, lipids, vitamins, hormone-like substance, free amino acids, urea, as well as antimicrobial substances) and inorganic constituents (calcium, phosphate, magnesium, potassium, bicarbonate, hydrogen ions, oxygen and nitrogen, in addition to trace elements as zinc, copper, fluoride, strontium, iron, chromium, etc.) **(Pesce and Spitalnik, 2007; Wong, 2007).**

The salivary major and minor glands are controlled by both parasympathetic and sympathetic stimuli of various types which affect salivary compositions; in

general the parasympathetic stimuli increase the output of water and electrolytes, if this reversed the output will contain a greater amount of macromolecules, in particular mucous **(Tenovuo** and **Lagerlof, 1994; Tenovuo, 1997).**

There are several factors affecting the composition of saliva, the main factor are the salivary flow rate, as the salivary flow rate and the concentration of total protein, urea, sodium, calcium, chloride and bicarbonate increase, while the concentration of inorganic phosphorous, iodide and magnesium decrease, on the other hand potassium and fluoride concentration remain unchanged **(Dawes, 1996; Pesce and Spitalnik, 2007; Zimmermenn *et al.*, 2007).**

Another factor is the duration of stimulation, saliva collected during the first minutes has different composition from saliva collected after 15 minutes of constant stimulation, for example bicarbonate, calcium and protein levels increase, while the chloride level falls with prolonged stimulation **(Tenovuo** and **Lagerlof, 1994; Dawes, 1996),** while **Atwood *et al.*, (1991)** found that the concentration of sodium, potassium, calcium and phosphate showed no significant relation with the duration of stimulation.

Circadian rhythms affect salivary zinc, copper, sodium, potassium, chloride and protein **(Atwood *et al.*, 1991; Tenovuo and Lagerlof, 1994),** while calcium, phosphate and urea showed no significant relation to rhythms **(Suddick *et al.*, 1980),** also the nature of the stimulus has an effect on saliva composition with salt taste stimulates higher protein content **(Tenovuo and Lagerlof, 1994; Dawes, 1996),** saliva composition is also influenced by the glandular source, for example most of the amylase in the saliva is produced by the parotid gland **(Dawes, 1996; Wong, 2007),** other factors affecting the composition of saliva include plasma concentration, diet, hormones, pregnancy, genetic polymorphism, antigenic stimulus, exercise and drugs **(Dawes, 1987).**

Regarding the effect of gender on saliva composition, **El-Samarrai (2001)** and **Agha-Hosseini *et al.*, (2006)** found that the females had higher calcium concentration than that among the males, while **Tulunoglu *et al.*, (2006)** and **Al-Jobouri (2007)** found that calcium concentration among the males were higher than that among females, several studies tried to determinate the effect of aging on saliva composition but the results were controversial, many studies showed that old persons have higher concentration of electrolytes than do younger persons **(Finkelstein *et al.*, 1984; Tulunoglu *et al.*, 2006),** in contrast, **Ben-Aryeh *et al.*, (1986)** recorded no significant difference between young and old persons regarding the salivary concentration of sodium, potassium, calcium and magnesium, while **Bales *et al.*, (1990)** found significant age related decrease in magnesium concentration in mixed saliva supernatant and parotid saliva, the composition of saliva is also affected with the increase in the body weight such as zinc and copper levels which shown to be higher among the overweight persons **(Kennedy *et al.*, 1986).**

1.9.3. Inflammatory cells:

There are five types of white blood cell (leucocyte). These are divided into two main classes

- **Granulocytes:**

Neutrophils are the commonest type of white blood cell they are born in the bone marrow and circulate in the blood for 6-10 hours, and then enter the tissues. They are motile, and phagocytic and will destroy damaged tissue and bacteria. They self-destruct after one burst of activity, the neutrophils are 12-14 μm diameter, and so look bigger than the surrounding red blood cells. There is a single nucleus, which is multilobed, and can have between 2 and 5 lobes.

Eosinophils are making up 1-6% of the total white blood cells, these cells are born in the bone marrow, and migrate from the peripheral blood system after a few hours, into loose connective tissue in the respiratory and gastointestinal tracts. These cells are 12 - 17 μm in diameter - larger than neutrophils, and about 3 times the size of a red blood cell, these cells have large acidophilic specific granules - these stain bright red, or reddish-purple.

Basophils are the rarest type of inflammatory cells, making up only 1% of the white blood cells, They are 14-16 μm in diameter, contain lots of deep blue staining granules (basic) and a bilobed.

•Agranulocytes:

Lymphocyte are the second most common inflammatory cells (20-50%),Most of the lymphocytes are small; a bit bigger than red blood cells, at about 6-9μm in diameter, They have a small spherical nucleus and has abundant dark staining condensed chromatin. Not much cytoplasm can be seen, and it is basophilic (pale blue/purple staining).

Monocytes are the third most common type of red blood cell; about 2-10% of leucocytes are monocytes, Monocytes in the circulation are precursors of tissue macrophages that are actively phagocytic. Monocytes circulate in the blood for 1-3 days, and then migrate into body tissues, where they transform into macrophages. They will phagocytose dead cells and bacteria. These are the largest type of white blood cells, and can be up to 20μm in diameter, they have a large eccentrically placed nucleus, which is kidney bean shaped, They have abundant cytoplasm, and some fine pink/purple granules in cytoplasm **(Nanci, 2013).**

1.9.4. Salivary hydrogen potential (Saliva pH):

Salivary pH dependent mainly on the bicarbonate ion concentration **(Lagerlof, 1994; Dawes, 1996),** maintenance of physiology pH at mucosal epithelial cells and tooth surface is an important function of salivary buffers **(Carranza, 1979),** the pH of whole saliva ranges from 6.7 to about 7.4 **(Bhaskar *et al.*, 1986)**, although it is fairly constant for each individual, the pH varied hourly and daily **(Grossman** and **Brickman, 1937).**

It has been found that there is an increase in the pH of saliva afternoon than the pH in the morning **(Eisenbrandt, 1943),** moreover the salivary pH increase with flow rate, it may reach a pH of 7.8 at high flow rate **(Suddick *et al.*, 1980),** the stimulated salivary secretion has more effective diluting and flushing action and higher buffer capacity than unstimulated or resting saliva **(Jarvinen *et al.*, 1988).**

Unstimulated saliva is less over saturated than stimulated saliva due to its higher dissolving capacity, this in return is induced by the lower pH and higher buffer capacity of the unstimulated saliva **(Rathje, 1956),** at the pH of 6 or higher, saliva is super saturated with the respect to pH which forms the dental enamel, apatite begins to dissolve below the critical pH of 5.5 **(Suddick *et al.*, 1980).**

1.9.5. Salivary flow rate:

Salivary flow rate is a clinical measure of the total secreted output of the salivary gland, either individually or in combination **(Cataldo *et al.*, 2000),** the amount of saliva in the mouth is not constant and varies within a person over time and between individuals, unstimulated whole saliva flow rate in a normal person is 0.3–0.4 ml per minute **(Ship *et al.*, 1991),** factors affecting unstimulated saliva

flow rate are degree of sex, age, time of collection, previous stimulation, drugs, psychic effects and functional stimulation **(Dawes, 1987).**

Reduced salivary flow may cause a variety of mostly non-specific symptoms to the patient, so the establishment of salivary flow rates is of primary importance in oral medicine and dentistry **(Chezzi *et al.,* 2000),** saliva influences carries attack mainly by its flow rate, its fluoride content and buffering action, the salivary flow rate influences to a high degree the rate of oral and salivary clearance of bacterial substrates **(Lagerlof** and **Oliveby, 1994).**

1.10. Oral histology of normal squamous epithelium:

The oral epithelium is a stratified squamous epithelium, the cells of the epithelium consist of two functional populations: a progenitor population (the function of which is to divide and provide new cells) and a maturing population (which continually differentiate or mature to form a protective surface layer), In general, maturation in the oral cavity follows two main patterns:

- Keratinization: The epithelial surface of the masticatory mucosa (hard palate and gingiva)
- Nonkeratinization: which is present on the lips, buccal mucosa, alveolar mucosa, soft palate, underside of the tongue, and floor of the mouth **(Nanci, 2013).**

1.11. Diagnostic cytology:

Is the art and science of the interpretation of cells from human body; it's based on three basic sampling technique:

- Collection of exfoliative cells.

- Collection of cells removed by brushing.
- Aspiration biopsy or removal of cells from non-surface bearing tissues by needle **(Koss** and **Melamed, 2006).**

This laboratory diagnostic technique is being used more frequently, particularly in the differentiation of tumors from inflammatory or degenerative lesions, the advantage of this technique include the simplicity of obtaining the specimen (from patients without need for anesthesia) and the speed and ease with which can evaluated **(Thomas, 1989).**

1.11.1. Exfoliative cytology:

Exfoliative cytology is the study of cells which have been extracted or removed from the epithelial surface of several organs **(Mehrotra, 2012).**
It's based on spontaneous shedding of cells derived from the lining of an organ into a cavity **(Koss** and **Melamed, 2006),** or be harvested from the surface with wooden spatula **(Thomas, 1989)** to examine the morphological characteristics of exfoliated or scraped cells, this has been used in the oral cavity for many purposes mainly the diagnosis of oral mucosal lesions of the mouth **(Banoczy, 1976)** and offers a cheap , rapid, simple and painless method for determining the precise nature of most of the lesions **(Zuher, 1985).**

1.11.2. Cytology of normal oral squamous epithelium:

The uniformity of the squamous epithelium lining the oral cavity renders the interpretation of a smear relatively simple, normal squamous epithelium shed cells resembling superficial and intermediate squamous cells of the vagina in cervix, except that nuclear pyknosis is not observed, smaller, deeper parabasal

cells may be observed if the epithelium is vigorously scraped, or if there is an epithelium defect, such as ulceration is present, fully keratinized squamous cells without visible nuclei are common component of oral smears, especially from the palate, and do not necessarily reflect a significant abnormality, all stages of transition between non keratinized and keratinized cells may be observed **(Koss** and **Melamed, 2006).**

A longitudinal condensation of nuclear chromatin in the form of a nuclear bar, similar to that observed in Antischkow cells in the myocardium in rheumatic heart disease, has been recorded in squamous cells by Wood *et al.*, the significance of this changes is unknown **(Wood *et al.*, 1975).**

Chapter two

Subjects, materials and methods

2.1. The Sample:

A Prospective study started from the 13th of January 2014 to the end of April 2014, the sample consisted of 91 subjects, divided into two groups:

The first group consisted of 53 lead exposed subjects (member of traffic police who work in crowded traffic intersections in Baghdad for eight hours six days a week with no systemic diseases), have been in police service since age of 18, considered as a study group.

The second group consisted of 38 subjects with no history of occupational lead exposure nor systemic diseases as control group.

Interviews, clinical examinations, and collection of blood and saliva samples were conducted at the general directorate of traffic police headquarter for subjects from Al-Karkh, subjects from Al-Russafa and subjects of control group were examined at the teaching laboratories of medical city.

All the samples were analyzed at the teaching laboratories of medical city (hematology and cytology departments), poisoning consultation center and Department of Oral Diagnosis at College of Dentistry, University of Baghdad, Oral and Maxillofacial Pathology Laboratory.

2.2. Instruments and materials:

The instruments, equipment and materials used in this study including:

Diagnosis and sample collection

- Disposable diagnostic tool kit.
- Disposable sterile gloves.
- Mask and white coat.
- pH meter (Jenway 3320) (Fig. 2.5).
- Ice box (Goldenstars)
- Dry ice (Rubbermaid)
- Portable light torch.

Cytology

- Graduated glass tubes (for saliva collections).
- Glass microscope slides (Fisherbrand™ positive charged slides).
- Adjustable micropipette with disposable tips.
- Glass jars.
- Centrifuge (universal 16 A) (Fig. 2.2).
- Light microscope. 95% ethanol alcohol.
- Papanicolaou stain.

Hematology

- Blood analyzer (Abbott cell-dyn Ruby) (Fig. 2.6).
- Light microscope.
- Disposable 5ml plastic syringe.
- EDTA tube.
- Methanolthe solution.

- May–Grünwald staining solution.
- Giemsa stain (azure–eosin) solution.

Lead analysis

- Sterile disposable plain tubes.
- Adjustable micropipette with disposable tips.
- Wooden sticks (fig.2.1).
- Trichloroacetic acid (TCA) 20% w/v (fig. 2.1).
- Centrifuge (universal 16 A) (Fig. 2.2).
- Shaker (Kahn-Shaker Tka 226-100S) (Fig. 2.3).
- Atomic absorption spectrophotometer (NovAA 300) (Fig 2.4).

Figure 2-1 blood mixed with TCA by wooden stick

Figure 2-2 Centrifuge (universal 16 A)

Fig. 2-3 Shaker (Kahn-Shaker Tka 226-100S)

Figure 2-4 Atomic absorption spectrophotometer (NovAA 300)

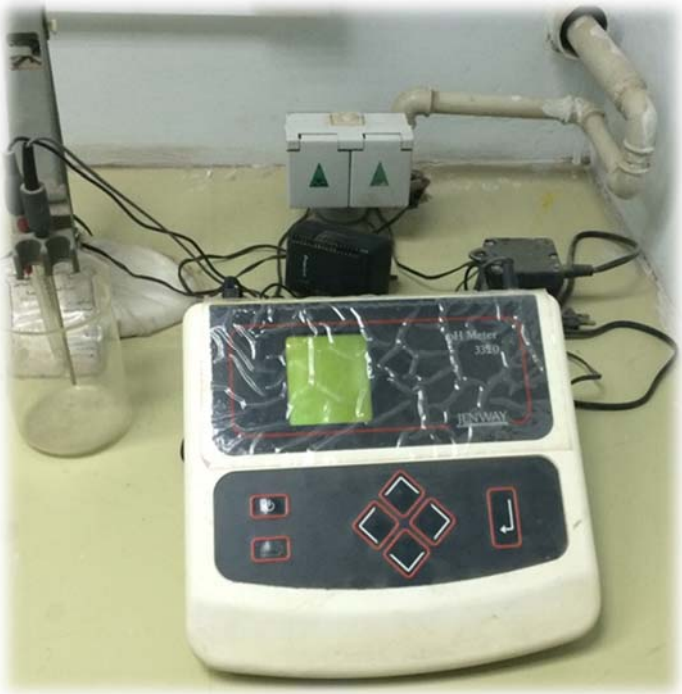

Figure2-5 pH meter (Jenway 3320)

Figure 2-6 Blood analyzer. (Abbott cell-dyn Ruby)

2.3. Methods:

2.3.1. Questionnaire:

All the subjects answered a written questionnaire regarding their name, age, duration of service (App. II).

2.3.2. Oral Examination:

Oral examination, using sterile mirror and a portable light torch, oral findings recorded in term of presence or absence which include: gingival lead line, ulceration and any other abnormal signs.

2.3.3. Examination of Physical Properties of Saliva:

1. Saliva collection:

Unstimulated whole saliva samples were collected by asking the subjects to refrain from eating, drinking, smoking, or oral hygiene procedures for at least one hour before the collection.

Each subject instructed to wash and rinse his mouth with water several times to ensure the removal of any possible food debris and contaminating materials and asked to accumulate saliva in their mouth by spitting method, spit the saliva into graduated glass tube, after estimating the pH value, saliva sample was centrifuged at 4500 r.p.m. for 15 minutes.

After centrifugation the supernatant is aspirated and put in a plain tube and stored in (-20 C°) in a deep freeze till the time of quantitative analysis of lead, while the sediment smeared on glass slide then immersed in 95% ethanol alcohol for fixation of the cells to be stained with Papanicolaou stain.

2. Determination of Salivary Flow Rate and Measurement of Salivary pH:

a. The volume of unstimulated whole saliva collected by spitting method in dried, sterilized, graduated glass tube for each subject of the study and control groups was measured during 10 minutes and recorded after centrifugation of the saliva sample.

The salivary flow rate was calculated by dividing the volume of collected saliva (ml) by the time required for the collection in minute **(Herrera *et al.*, 1990; Rihab, 2006; Mudher, 2008)**

$$flow\ rate(ml/min) = \frac{volume(ml)}{time\ (min)}$$

b. The salivary pH was measured by pH meter:

Calibration the device with buffer standard solutions with pH 7.00 (part No. 025 038), 4.00 (part no. 025 037), 10.05 (part No. 025 039), 9.22 (part No. 025 162) and 2.00 (part No. 025 163) washing with electrode clearing solution (part No. 025 161)

3. Preparation of Saliva for Cytological Examination:

Saliva sample was centrifuged, the sediments was aspirated with micropipette with disposable tips smeared on glass slides wiped with albumin with aid of wooden stick and put in 95% ethanol alcohol for fixation this producer was made at oral and maxillofacial pathology laboratory, after that the slides were dried and then stained with Papanicolaou stain in teaching laboratory of the medical city.

Fixation of smears:

The sediment of saliva are smeared on coded glass slide and rapidly flooded with the fixative to avoid air drying, two fixed slides were taking for each case, the main purposes of cytological fixative are to minimize cell shrinkage and maintain morphologic integrity; the fixative used was 95% ethanol, immediate fixation while the specimen was still wet.

Staining methods:

This was done by Papanicolaou method (figure 2-7):

Wet fixed samples on microscope slides

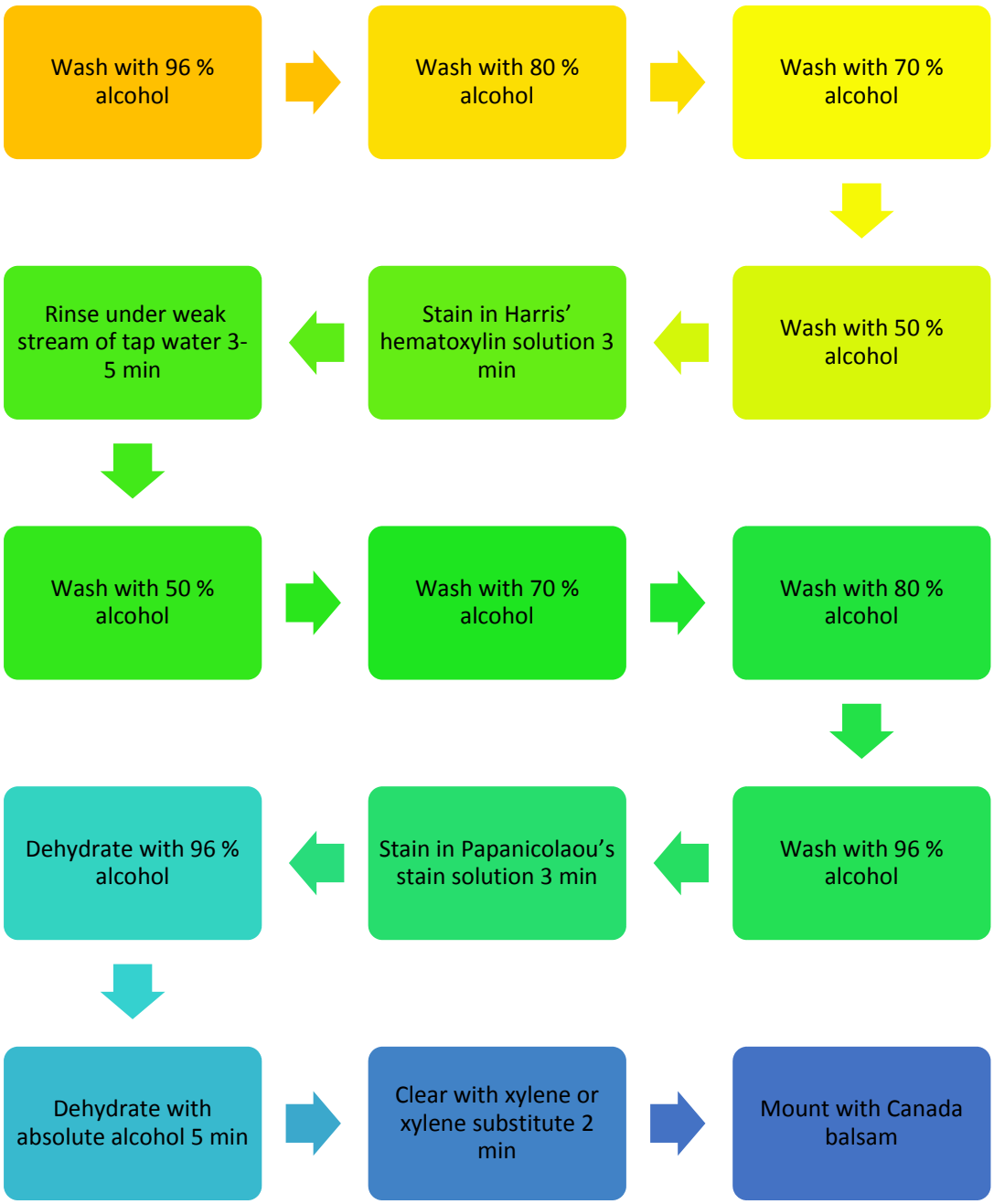

Figure 2-7 Papanicolaou staining method

Epithelial cells:

The smears examined for any morphological cytoplasmic and nuclear changes.

Inflammatory cells:

The field examined at high power field (400x) for the sake of counting inflammatory cells; neutrophils are12-14 µm diameter and have single nucleus which is multilobed 2-5 lobes each and neutrally stained, Eosinophiles are 12-17 µm diameter larger than neutrophils and have large acidophilic granules, basophils are 14-16 µm diameter and contain lots of deep blue granules and bilobed nucleus, lymphocytes are small 6-9 µm diameter single nucleus.

Ten field count in each slide and the mean was calculated.

2.3.4. Blood Samples Collection:

Blood sample conducted on peripheral blood obtained by venesection using disposable syringe, 5ml of blood aspirated then put in two EDTA tube; 2.5ml of blood in each, the EDTA tube labeled with subject name, one tube used for blood analysis the other for lead analysis, the sample put in icebox and transported for measuring CBC and making blood films by placing a drop of blood on one end of a slide, and using a spreader slide to disperse the blood over the slide's length, The slide was left to air dry, after which the blood was fixed to the slide by immersing it briefly in methanol, the peripheral blood film was examined by specialist hematologist for assessment of morphological changes in blood including basophilic stippling of erythrocytes.

Blood film preparation

A droplet of the blood sample is placed close to the edge of the slide, a ground cover glass (spreader slide) is placed in front of the droplet onto the slide at an angle of 30°, the cover slide is then slowly backed into the blood droplet, Upon contact, the blood droplet spreads along the edge of the slide without pressure, the cover glass is now lightly moved over the slide, the smear must be thoroughly air-dried; for good staining, at least two hours' drying time is needed, fixation with methanolthe horizontally stored, air-dried smear is covered with May–Grünwald staining solution (eosin–methylene blue) for three minutes, then about an equal amount of phosphate buffer, pH= 7.3, is carefully added and, after a further three minutes, carefully poured off again, next, the slide is covered with diluted Giemsa stain (azure–eosin), which is prepared by addition of 1 ml Giemsa stock solution to 1 ml neutral distilled water or phosphate buffer, pH= 6.8–7.4, After 15 minutes, the Giemsa staining solution is gently rinsed off with buffer solution and the smears are air-dried with the feathered end sloping upwards **(Theml, 2004).**

2.3.5. Measurement of Lead Level:

The supernatant of the centrifuged saliva were used for quantitative analysis of lead.

For blood we used the following:

a. Shaking EDTA tubes on an electrical shaker for 30 minutes.
b. Mixing the specimen with equal amount of 20% trichloroacetic acid (TCA) vigorously (use wooden stick) (Fig 2.1).
c. Centrifugation on 4500 r.p.m. for 15 minutes.

d. Taking the supernatant by using adjustable micropipettes with disposable tips and put it in a dry, sterilized plastic plain tube.
e. Samples stored in freezer in -20C° to the time of analyses of lead.

Standardized procedure, stock standard (1000 µg/dl) was used to make working standard of different one :(10, 20, 30 µg/dl) and a calibration curve was made, samples, controls and standard were directly aspirated into air-acetylene flame where the lead hallow cathode lamp was used at wavelength of 283.2 nm.

2.4. Statistical analysis:

Statistical analyses were computer assisted using IBM® SPSS® Statistics version 21 release 21.0.0.0 64 bit edition and Microsoft® Office professional plus Excel 2013 for figures.

Statistical analysis of data had done by:

I. Descriptive statistics:

- Number and percentages (%).
- Mean.
- Standard deviation.
- Standard error.
- Minimum.
- Maximum.
- Range.
- Coefficient of variance (c.v. %).

II. Inferential Statistics:

- Chi-square test (probability less than 0.05 to be significant.
- t-test.
- Pearson's linear correlation coefficient.

III. P-Value

- $P<0.05$ significant.
- $P>0.05$ non-significant.
- $P<0.01$ high-significant.

Chapter Three

Results

3.1. The study population:

In this study the total subjects examined were 91 males divided into two groups (study and control groups), 53 subjects in study group with an age ranged from 22-61 and 38 subjects in control group with age ranged from 21-55 years according to the last birthday (table 3-1).

Table (3-1) Descriptive statistics of age control group and study group

	Control group (No. = 38)	Study group(No. = 53)
Mean	37.5	37.2
SD	9.482	10.55
SE	1.529	1.445
Min	21	22
Max	55	61
C.V%	25.2347	28.34389

***t-test =0.051 p=0.96 P>0.05 Non significant**

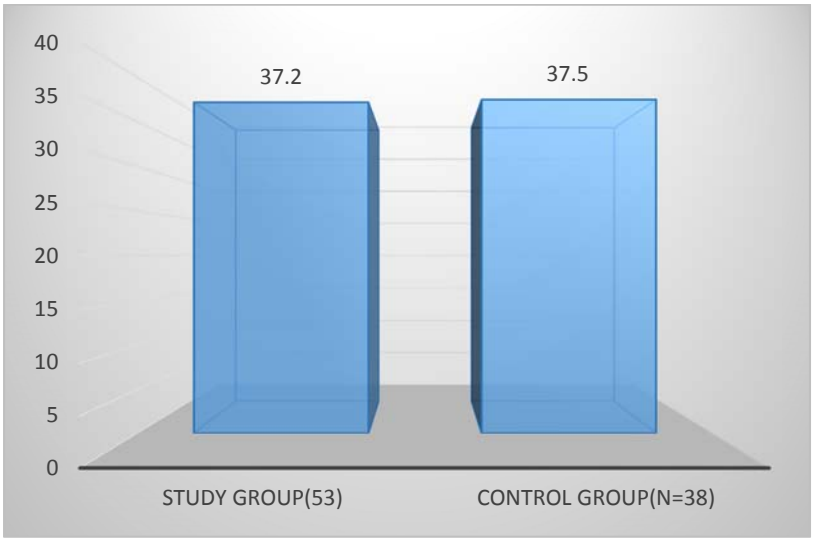

Figure (3-1) means of age in study and control group

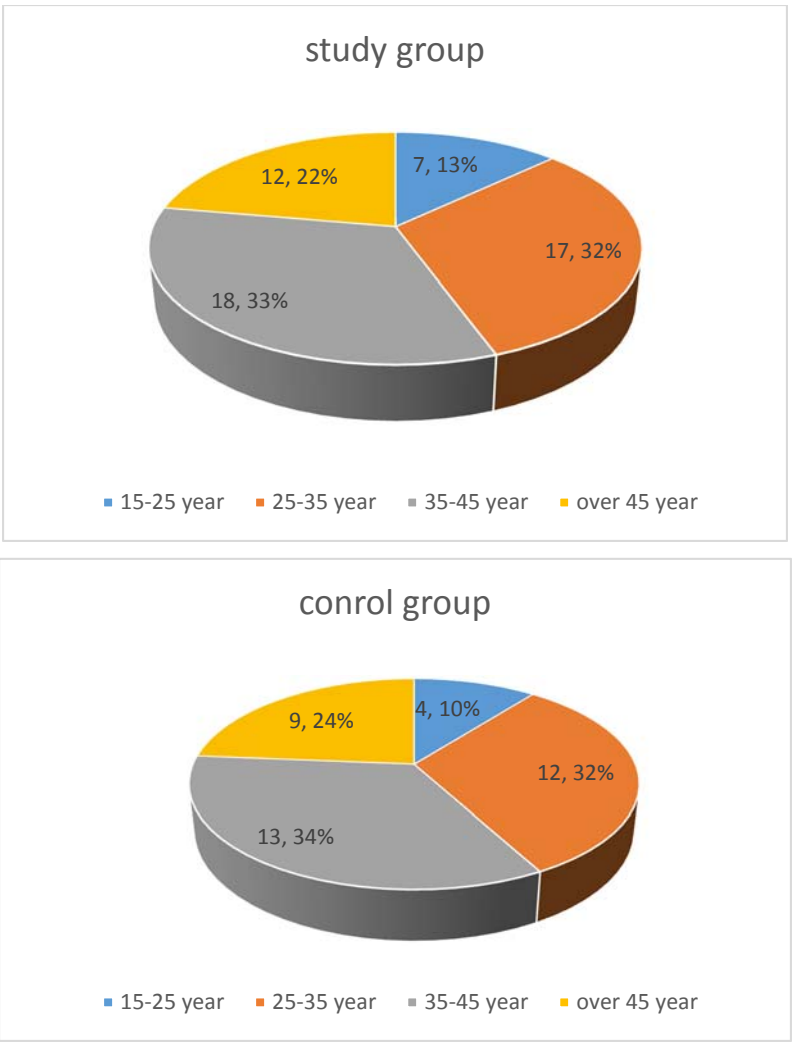

Figure (3-2) age distribution in study and control group

3.2. Frequency of lead toxicity between study and control group:

As shown in (table 3-2) the subjects of both control and study groups were divided according to the blood lead level into low level exposure (which include the subjects with blood level less than 25 µg/dl) and toxic group (which include the subjects with blood level equal or more than 25 µg/dl).

In the lead exposed group the number of subjects with toxic blood level was 15% of this group.

Table (3-2) frequency distribution of lead toxicity

	Study group		Control group	
	No.	Percentage	No.	Percentage
Non-toxic	45	85%	37	97.3%
Toxic	8	15%	1	2.7%
Total	53	100%	38	100%

***Chi-square = 3.857; p value = 0.049 Significant**

3.3. Differences in mean salivary and blood lead concentration between study and control group:

As shown in (table 3-3), (Figure 3-3) the mean, SD, SE, of both salivary and blood Pb concentrations were calculated for both study and control groups.

According to blood lead level; the mean of 19 µg/dl in study group which is significantly higher than 14.1 µg/dl of control group (p=0.001), while according to salivary lead level the mean of study group was 2.23 µg/dl which is highly significant higher than mean lead level 1.42 µg/dl of the control group (p<0.001) (Table 3-4).

Table (3-3) Descriptive statistics of blood lead and salivary lead level

	Control group		Study group	
	Blood lead µg/dl	*Salivary lead µg/dl*	*Blood lead µg/dl*	*Salivary lead µg/dl*
Mean	14.078	1.4236	19.018	2.2283
SD	4.1809	0.5763	5.0668	0.7801
SE	0.6743	0.0929	0.6940	0.1068
Min	8	0.6	9	0.7
Max	26	2.8	30	4
C.V%	29.696	40.4797	26.641	35.010

Table (3-4) Comparing of blood lead and salivary lead level between control and Study groups

	Blood lead	*Salivary lead*
t	3.648	4.291
p-value	0.001	P<0.01
sig	*HS*	*HS*

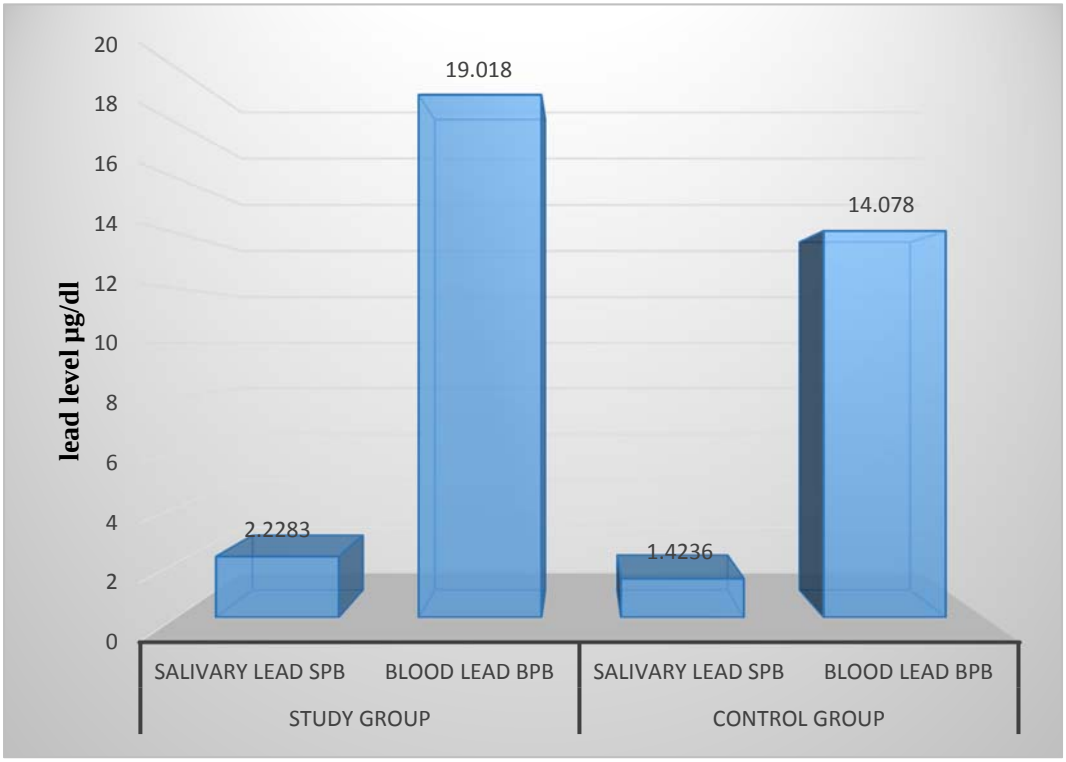

Figure (3-3) means of blood lead and salivary lead level

3.4. Differences in mean salivary flow rate and salivary pH between study and control group:

As seen in (table 3-5), (Figure 3-4) the mean salivary flow rate of study and control groups were 0.299 ml/min (range 0.08-1.36ml/min) and 0.312 ml/min (range 0.08-1.2 ml/min) respectively with no significant differences (p=0.419) (table 3-6).

Alternatively salivary pH were significantly lower in study group in comparison to control group, with mean of 7.411 for study and 7.510 for the control group with r = -0.09 (table 3-6).

Table (3-5) Descriptive statistics of control group and study group

	Control group		Study group	
	flow rate ml/min	salivary pH	flow rate ml/min	salivary pH
Mean	0.31	7.5	0.29	7.4
SD	0.27	0.18	0.29	0.23
SE	0.04	0.028	0.04	0.03
Min	0.08	7.1	0.08	6.9
Max	1.2	7.8	1.36	7.8
C.V%	85.7	2.353	95.9	3.2

Table (3-6) Comparing between control and Study

	flow rate	salivary pH
t	0.058	*2.607*
p-value	0.954	*0.013*
Significance	NS	S
r	*0.135*	-0.09
p-value	*0.419*	0.591

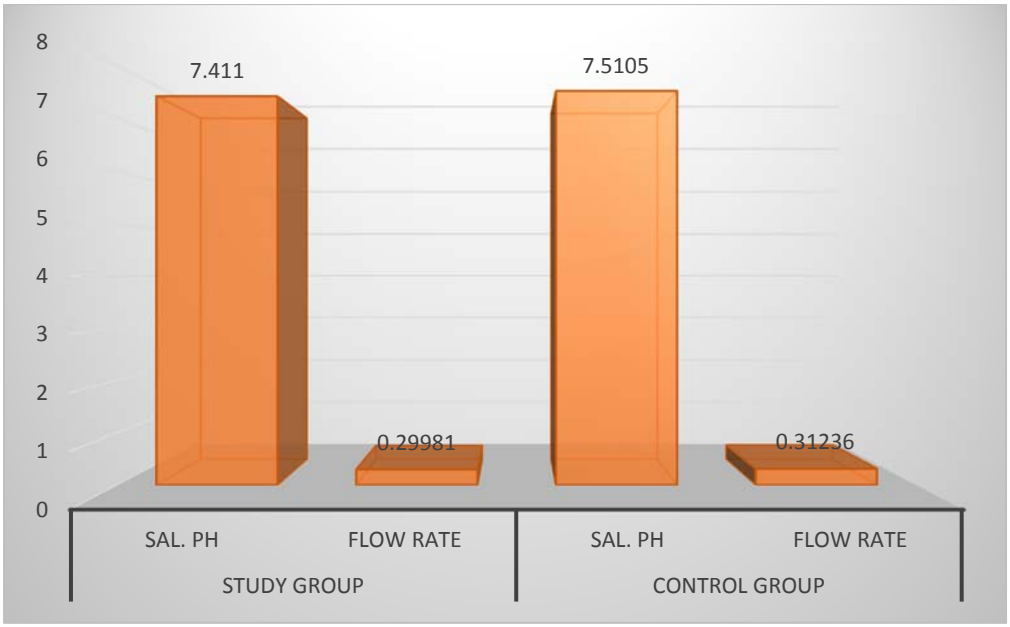

Figure (3-4) means of blood lead and salivary pH and salivary flow rate

3.5. Differences of salivary inflammatory cells count:

As seen in table 3-7, table 3-8 , figure 3-5 , 3-14, 3-15, 3-16,3-16, 3-17, 3-18, 3-19, 3-20 and 3-21there was non-significant difference in cell count of neutrophils, eosinophil and histiocytes in saliva between study and control group.

Highly significant decrease in lymphocytes (p-value <0.01) in study group comparing to healthy control group.

Table (3-7) Descriptive statistics of control group and study group regarding salivary inflammatory cells count

	Control group				Study group			
	Neutro.	*Eosino.*	*Lympho.*	*Histio.*	*Neutron.*	*Eosino.*	*Lympho.*	*Histio.*
Mean	1.32	1.24	5.92	0.58	1.647	1.715	4.03	1.03
SD	1.9	1.5	3.2	0.8	1.2	1.2	2.6	0.9
SE	0.039	0.03	0.064	0.017	0.024	0.026	0.055	0.018

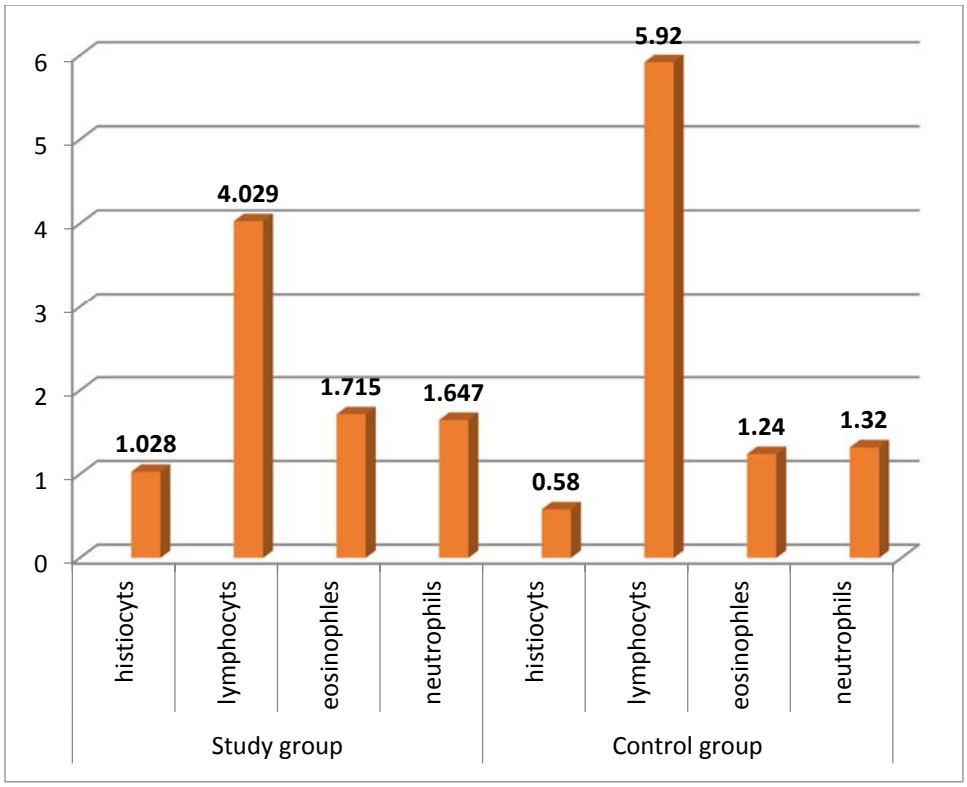

Figure 3-5 means of salivary inflammatory cells count in study and control group

Table (3-8) Comparing salivary inflammatory cells count between control and Study group

	neutrophils	*eosinophiles*	*lymphocytes*	*histiocytes*
t	**0.976**	**0.922**	**3.868**	**1.20**
p-value	**0.334**	**0.361**	**P<0.01**	**0.236**
sig	**NS**	**NS**	**HS**	**NS**

3.6. Differences in hematological parameters between healthy control and lead exposed groups:

3.6.1. Differences in WBC, Neutrophils and Lymphocytes count between study and control group:

As seen in table 3-9, table 3-10 and figure 3-5 there was slightly increased in WBC and lymphocyte count in study group, no significant difference seen in neutrophils count between the groups

Table (3-9) Descriptive statistics of control group and study group regarding WBC, Neutrophils and lymphocytes count in peripheral blood

	Control group			Study group		
	WBC $10^3/\mu l$	NEU $10^3/\mu l$	LYM $10^3/\mu l$	WBC $10^3/\mu l$	NEU $10^3/\mu l$	LYM $10^3/\mu l$
Mean	6.66	3.62	2.11	7.82	4.37	2.65
SD	1.64	1.11	0.77	2.07	1.66	0.72
SE	0.26	0.18	0.12	0.28	0.23	0.09
Min	3.45	1.86	1.08	4.26	1.76	1.5
Max	10.1	6.45	4.01	13.6	9.18	4.5
C.V%	24.63	30.53	36.5	26.4	37.8	27.04 5

Table (3-10) Comparing WBC, Neutrophils and Lymphocytes counts between control and Study group

	WBC	NEU	LYM
t	2.596	1.479	3.619
p-value	0.025	0.167	0.004
sig	S	NS	S
r	0.274	-0.274	0.5
p-value	0.389	0.388	0.097

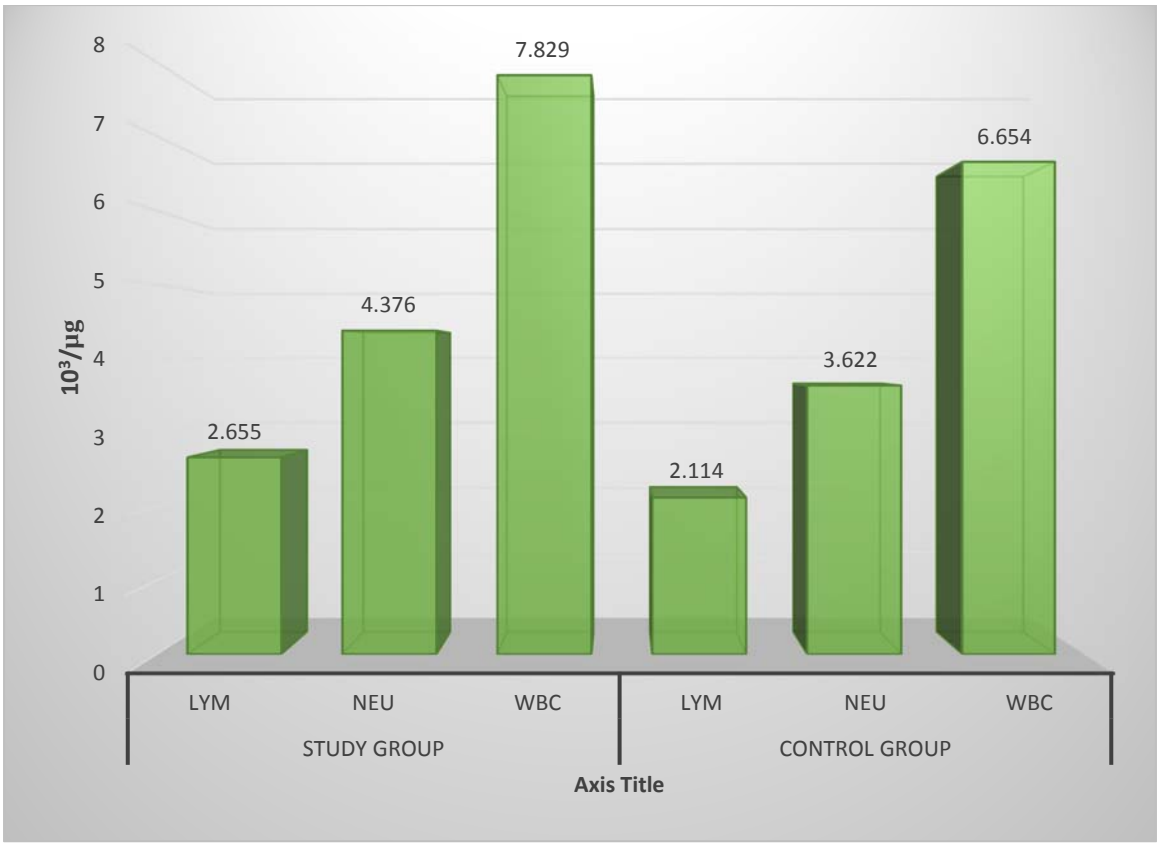

Figure 3-6 mean of WBC, neutrophils and lymphocytes in study and control group

3.6.2. Differences in basophils, eosinophiles and monocytes count between study and control group:

As seen in table 3-11, 3-12 and figure 3-7 there is slight increase in basophils count in study group in contrast; there is no significant difference seen in monocytes, eosinophiles count between the groups.

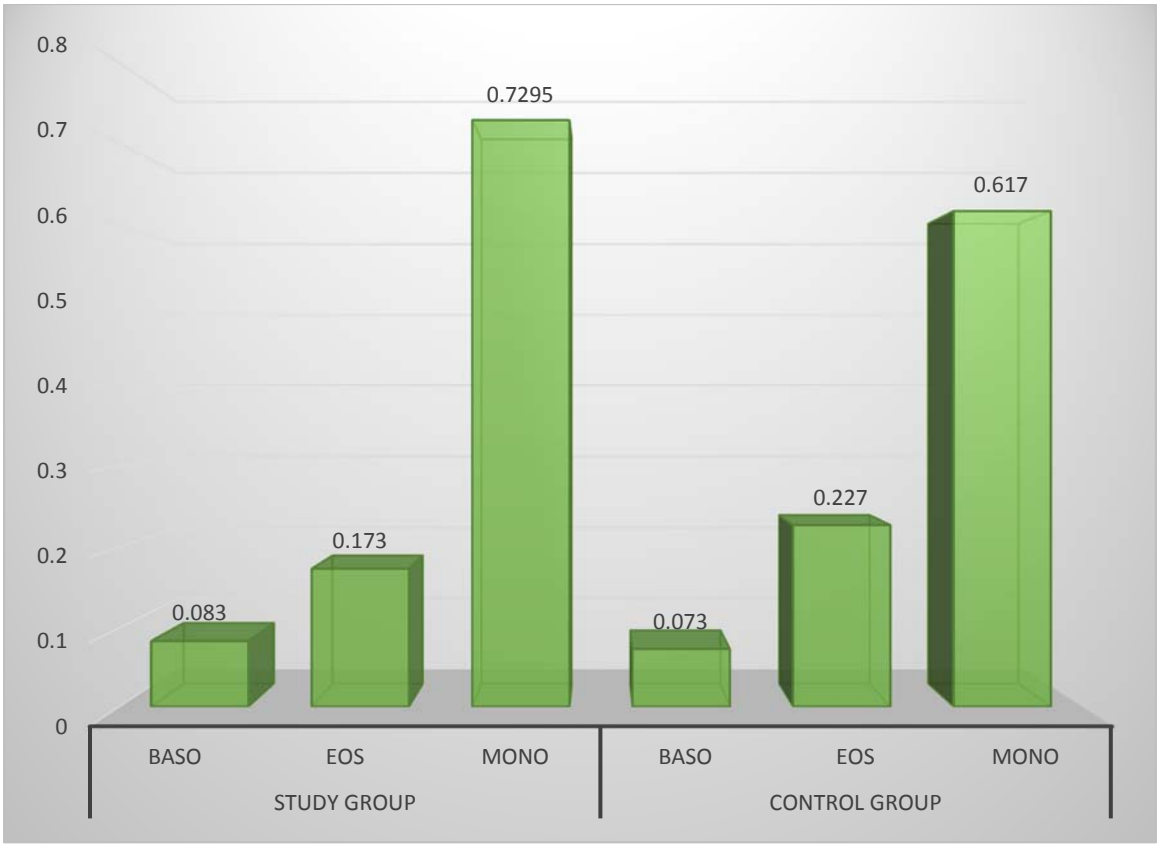

Figure (3-7) mean of basophils, eosinophiles and monocytes in study and control group

Table (3-11) Descriptive statistics of control group and study group regarding monocytes, eosinophiles and basophils count in peripheral blood

	Control group			Study group		
	MONO $10^3/\mu l$	EOS $10^3/\mu l$	BASO $10^3/\mu l$	MONO $10^3/\mu l$	EOS $10^3/\mu l$	BASO $10^3/\mu l$
Mean	0.617	0.227	0.073	0.729	0.1736	0.083
SD	0.23	0.22	0.028	0.214	0.092	0.043
SE	0.038	0.036	0.0046	0.03	0.013	0.006
Min	0.332	0.008	0.036	0.318	0.019	0.031
Max	1.48	0.957	0.139	1.2	0.419	0.241
C.V%	37.8	97.6	38.6	29.36	53	50.7

Table (3-12) Comparing Monocytes, Eosinophiles and Basophils count between control and Study group

	MONO	EOS	BASO
t	2.045	1.196	2.266
p-value	0.066	0.243	0.033
sig	NS	NS	S
R	0.406	0.106	0.266
P-value	0.191	0.613	0.199

3.6.3. Differences in RBC, HGB and Htc between study and control group:

There is no significant difference regarding RBC, HGB and Hct between study and control group (table 3-13), (table 3-14) & (figure 3-8).

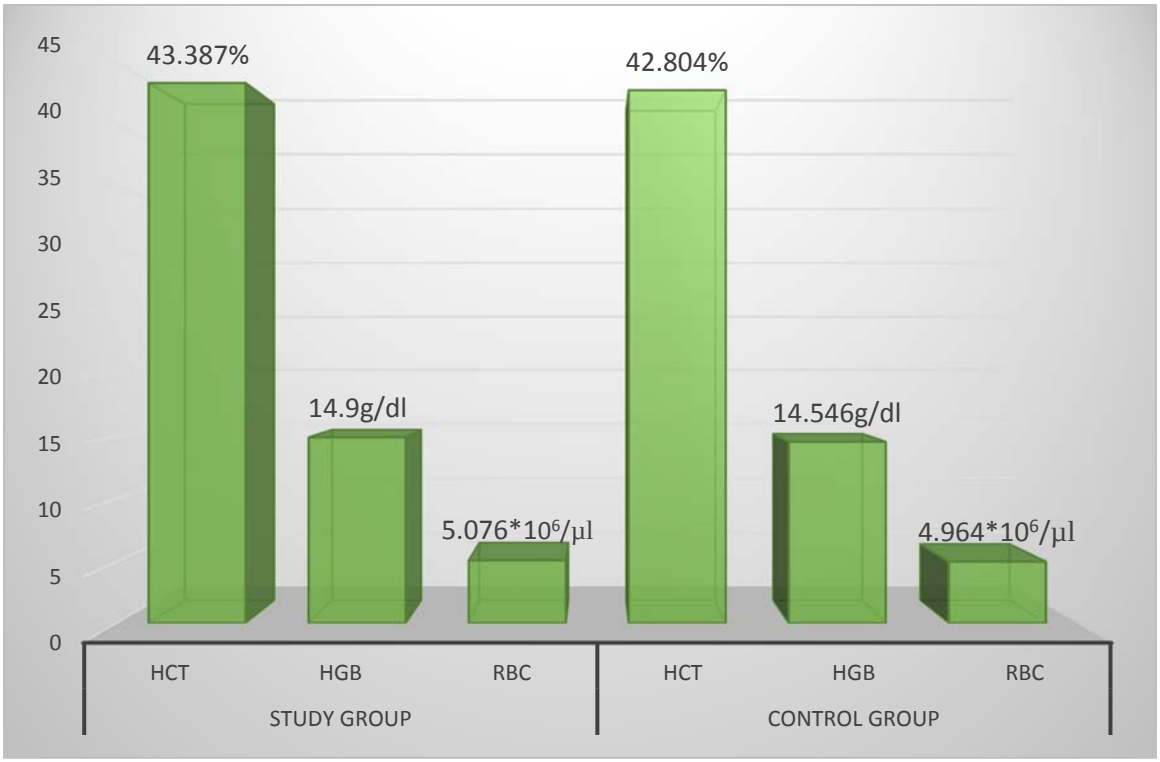

Figure 3-8 mean of Hct, HGB & RBC in study and control group

Table (3-13) Descriptive statistics of control group and study group regarding RBC, HGB and Hct in peripheral blood

	Control group			Study group		
	RBC 10^6/µl	HGB g/dl	Hct %	RBC 10^6/µl	HGB g/dl	Hct %
Mean	4.9648	14.5468	42.804	5.076364	14.9	43.38788
SD	0.637992	1.892443	5.242652	0.582601	1.701286	4.025214
SE	0.102902	0.305233	0.845589	0.079808	0.233053	0.551399
Min	3.03	8.37	25.3	3.14	11.1	34.6
Max	6.07	17.3	50.1	6.09	17.5	50.7
C.V%	12.85031	13.00934	12.24804	11.47674	11.41803	9.277278

Table (3-14) Comparing regarding RBC, HGB and HTC between control and Study group

	RBC	HGB	Hct
t	0.101	1.146	0.729
p-value	0.921	0.276	0.481
sig	NS	NS	NS
r	0.128	0.209	0.006
P-value	0.692	0.515	0.985

3.6.4. Differences in MCHC, MCH and MCV between study and control group:

Non-significant difference seen between study and control group regarding MCHC, MCH and MCV (figure 3-9), (table 3-15).

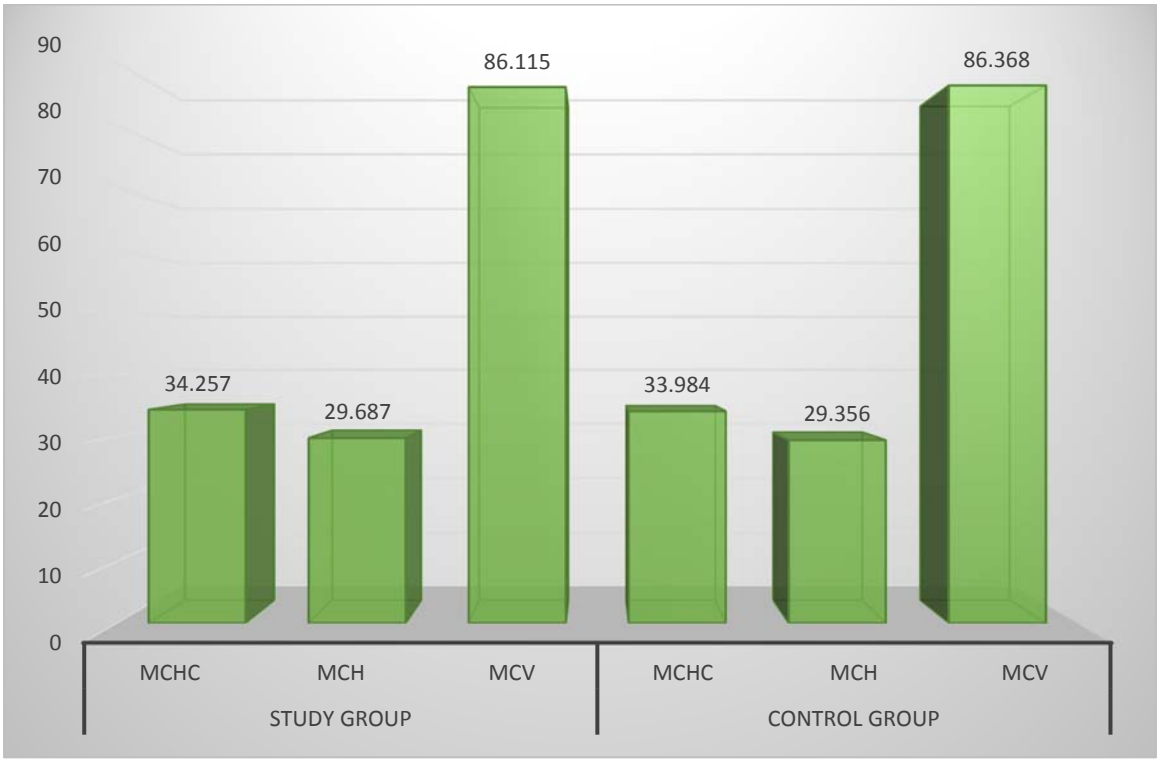

Figure 3-9 mean of MCHC, MCH & MCV in study and control group

Table (3-15) Descriptive statistics of control group and study group regarding MCHC, MCH and MCV.

	Control group			Study group		
	MCV Femto-liter	MCH Picogram/ cell	MCHC g/dl	MCV Femto-liter	MCH Picogram/ cell	MCHC g/dl
Mean	86	29	34	86	30	34
SD	4.38	1.8	1.02	8.33	3.39	1.23
SE	0.71	0.3	0.17	1.14	0.47	0.17
Min	79.3	26.4	32.4	58.9	18.9	31.7
Max	98.3	33.3	36.1	110	39	36.3
C.V%	5.08	6.15	3.03	9.68	11.44	3.59

Table (3-16) Comparing regarding MCHC, MCH and MCV between control and Study group

	MCV	MCH	MCHC
t	1.584	2.097	1.982
p-value	0.142	0.06	0.073
sig	NS	NS	NS
r	0.206	0.069	0.246
P-value	0.522	0.831	0.441

3.6.5. Differences in MPV and RDW between study and control group:

Significant increase in RDW seen in study group, non-significant difference between study and control group regarding MPV and platelets count (figure 3-10, 3-11), (table 3-17, 3-18, 3-19).

Table (3-17) Descriptive statistics of control group and study group regarding MPV and RDW

	Control group		Study group	
	RDW %	MPV Femto-liter	RDW %	MPV Femto-liter
Mean	11.7	7.9	13.5	7.9
SD	0.76	1.44	2.28	1.3
SE	0.12	0.23	0.31	0.18
Min	10.4	5.26	9.62	5.48
Max	12.9	11.1	19.5	12.5
C.V%	6.46	18.28	16.84	16.56

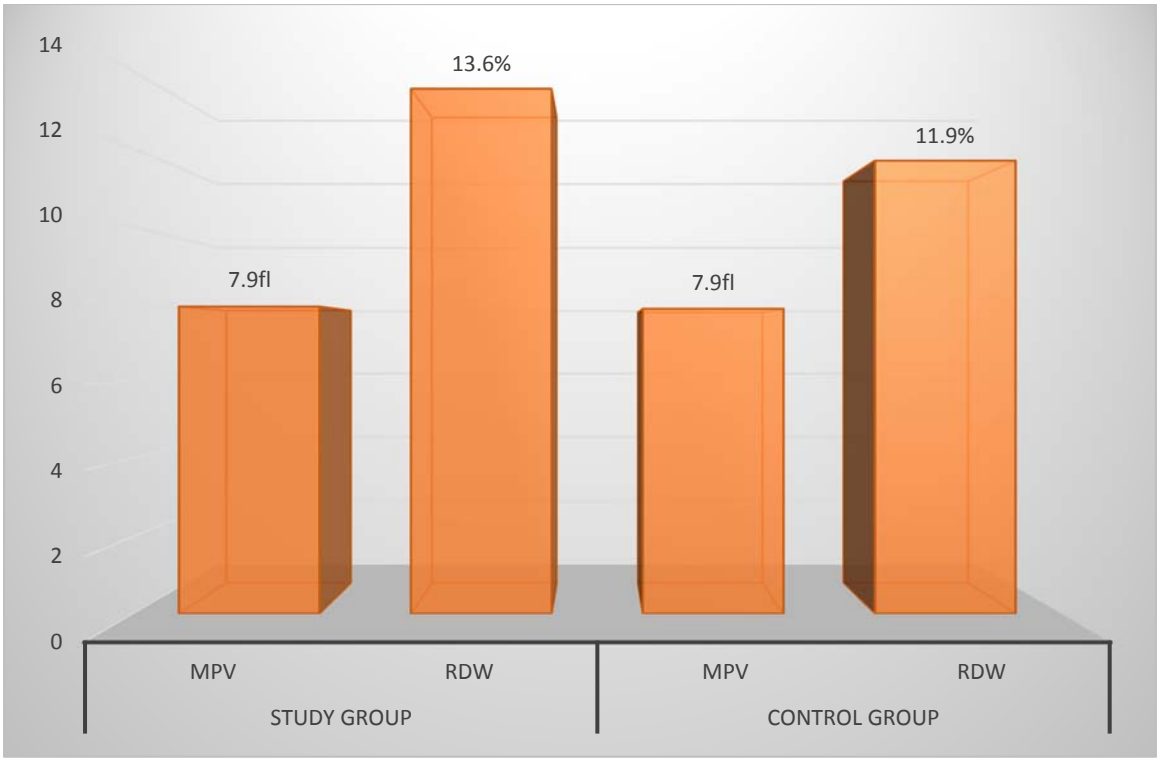

Figure 3-10 means of MPV & RDW IN study and control group

Table (3-18) Descriptive statistics of platelet count in control group and study group

	Control group	Study group
	PLT $10^{3}/\mu l$	PLT $10^{3}/\mu l$
Mean	261.6	272.0606
SD	66.47681	139.4155
SE	10.72207	19.09801
Min	161	119
Max	464	952
C.V%	25.41163	51.24428

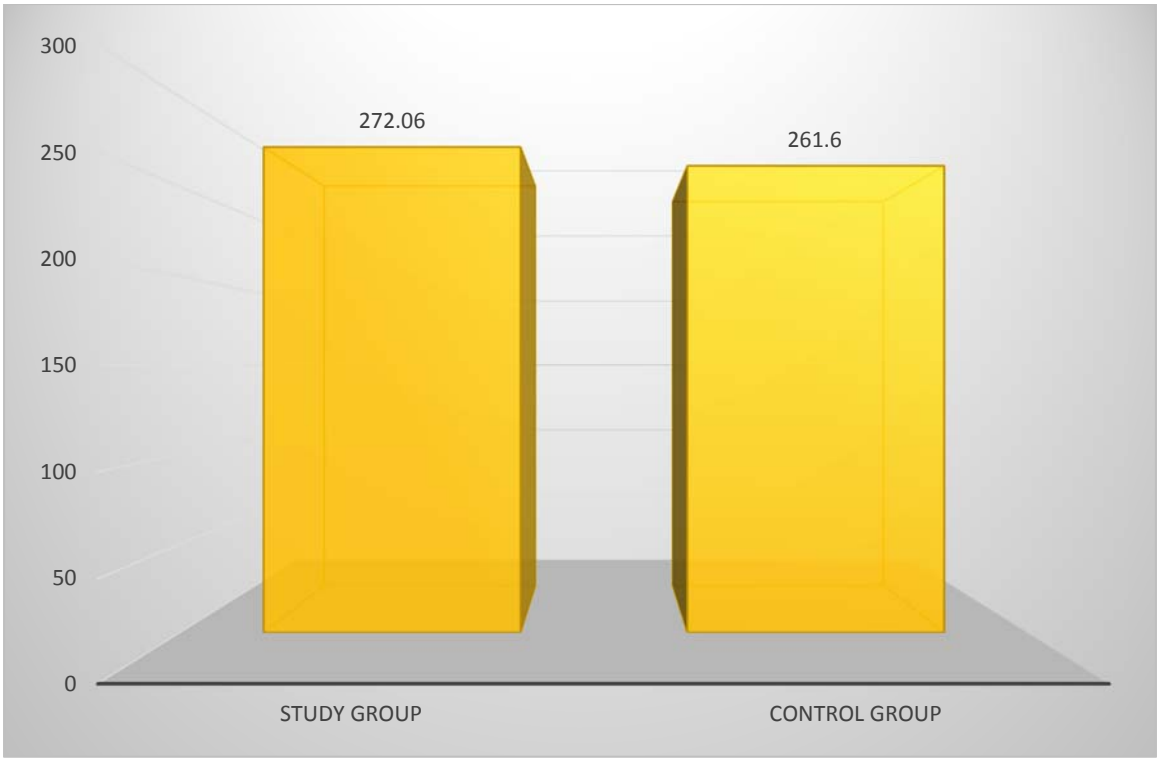

Figure (3-11) mean of platelet count in control group and study group

Table (3-19) Comparing MPV, PLT and RDW between control and Study group

	RDW	PLT	MPV
t	**2.926**	**0.255**	**0.68**
p-value	**0.014**	**0.803**	**0.51**
sig	**S**	**NS**	**NS**
r	**0.617**	**0.742**	**-0.08**
P-value	**0.033**	**0.006**	**0.805**

3.7. Differences in morphological changes in blood between study and control group:

Significant morphological abnormality seen in blood film of study group compared to healthy controls p=0.034 (table 3- 20).

Table (3- 20) Number and percentage of morphological changes in blood of control and study

	Study group		Control group	
	No.	%	No.	%
NORMAL	46	86.79	38	100
RBC morphology +PLT seen in aggregate	1	1.887	0	0
PLT seen in aggregate	1	1.887	0	0
Hypochromic anemia	1	1.887	0	0
Thalassemia	1	1.887	0	0
lymphocytosis	1	1.887	0	0
RBC morphological abnormality	2	3.774	0	0
Total	53	100	38	100

***Chi-square=4.56 p=0.034**

3.8. Correlation between blood lead level, salivary lead level with selected parameter:

As shown in table (3-21), (figure 3-12) highly significant correlation between blood lead level and salivary lead level seen in study and control group p = 0.001 and .018 respectively.

Highly Significant correlation between age and blood lead level seen in study and control group p<0.01 and weak correlation in control group p = 0.038 in contrast there was weak correlation between age and salivary lead level.

Highly significant negative correlation between blood lead level and salivary flow rate seen in study and control group p = 0.005 and p = 0.004

respectively, significant correlation between RDW and Pb-B, no such correlation is seen with salivary lead level.

Table (3-21) Person correlation and p value between blood lead levels, salivary lead levels with selected parameter in study and control group

	Study group				Control group			
	Blood pb		Salivary pb		Blood pb		Salivary pb	
	r	p	r	p	r	p	r	p
B-pb	1	0	.438**	.001	1	0	.378*	.018
S-pb	.438**	.001	1	0	.378*	.018	1	0
age	.485*	.038*	.113	.419	.705**	<0.001	.253	.125
S-Flow rate	-.377**	.005	-.105	.450	-.460**	.004	-.033	.843
Salivary pH	-.231	.96	.126	.368	-.305	.063	-.109	.516
WBC	.142	.429	.235	.188	-.021	.921	-.088	.675
Neutrophil	.211	.237	.196	.274	-.164	.433	-.191	.362
Lymphocyte	-.277	.204	.035	.848	.170	.417	.130	.535
Monocytes	.018	.019	.321	.069	-.111	.598	-.241	.246
Eosinophil	-.039	.780	-.056	.687	.180	.390	.087	.678
Basophils	.142	.304	.162	.241	.092	.662	.126	.550
RBC	.008	.966	-.037	.835	-.291	.158	-.129	.539
HGB	.103	.568	.019	.918	-.393	.052	-.192	.357
Hct	.212	.237	.062	.732	-.358	.079	-.175	.403
MCV	.131	.466	.090	.620	-.134	.525	-.087	.679
MCH	-.020	.913	-.018	.920	-.222	.285	-.129	.538
MCHC	-.188	.296	-.052	.774	-.236	.256	-.115	.585
RDW	.011	.951	-.035	.846	.410*	.042	.176	.401
PLT	.169	.346	-.023	.901	.353	.083	.270	.191
MPV	.129	.475	.092	.609	-.109	.604	-.242	.245

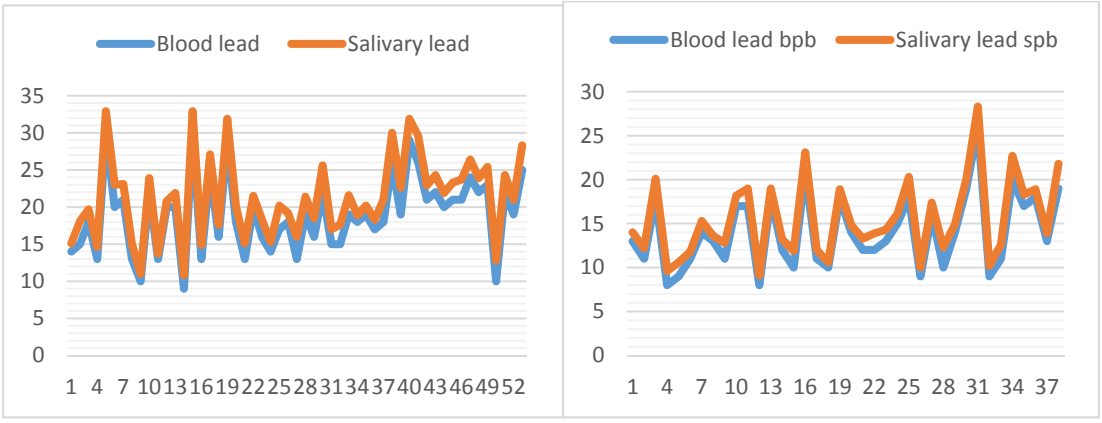

Figure 3-12 correlation between Pb-B & Pb-S in study and control groups

3.9. Effect of toxic lead level in oral cavity in study group:

As shown in table (3-22) no ulceration was seen in oral mucosa in all subjects, statistically the result were non-significance in ulceration and tongue coating and cytoplasmic basophilia (fig3-13 ;3-14), while the result have significant differences in lead line.

Table 3-22 Effect of toxic lead level in oral cavity in study group

	Non-toxic(45)			Toxic(8)			P value
	+ve	-ve	%	+ve	-ve	%	
ulcerations	0	45	0	0	8	0	0.160 NS
Tongue coating	0	45	0	1	7	12.5	0.670 NS
Lead line	0	45	0	3	5	37.5	0.001 S
Cytoplasmic basophilia	16	29	35.56	5	3	62.5	0.191 NS

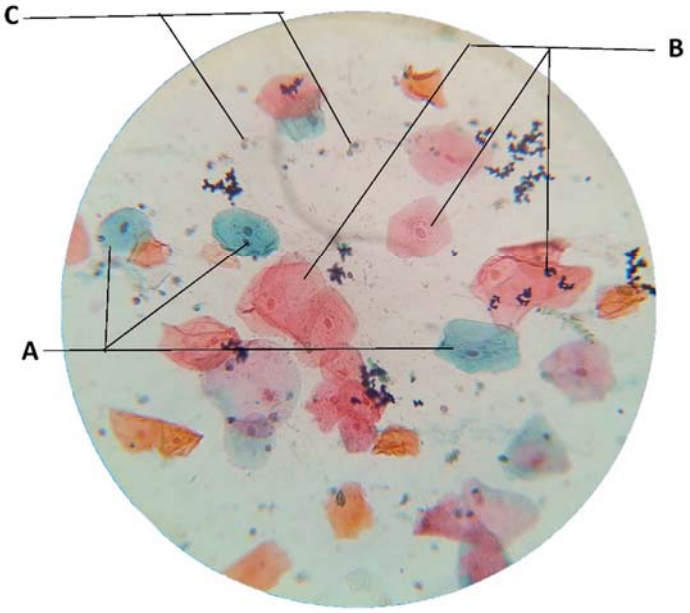

Figure 3-13: Salivary smear of subject of study group with Pb-B 30 µg/dl and Pb-S 2.9 µg/dl; A: non-keratinized squamous epithelium shedded form oral mucosa, B: keratinized squamous epithelium shedded form oral mucosa, C: inflammatory cells.

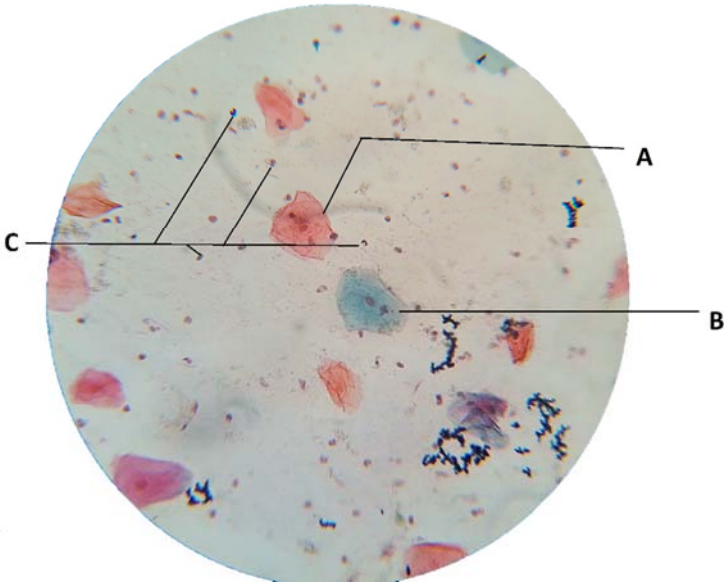

Figure 3-14: Salivary smear of subject of study group with Pb-B 22 µg/dl and Pb-S 1.9 µg/dl; A: keratinized squamous epithelium shedded form oral mucosa, B: non-keratinized squamous epithelium shedded form oral mucosa, C: inflammatory cells.

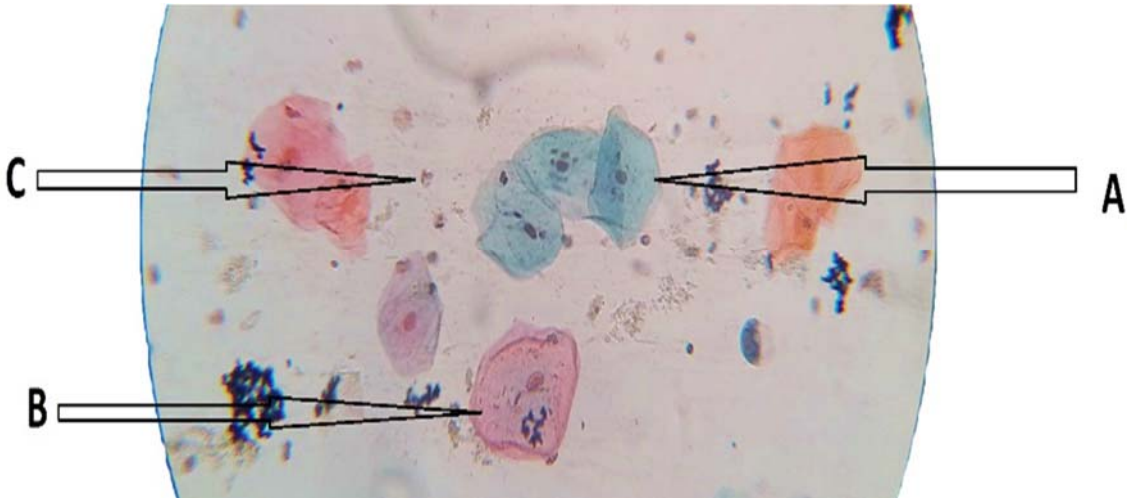

Figure 3-15: Salivary smear of subject of study group with Pb-B 25 µg/dl and Pb-S 2.1 µg/dl(X400); A: non-keratinized squamous epithelium shedded form oral mucosa, B: keratinized squamous epithelium shedded form oral mucosa, C: inflammatory cells.

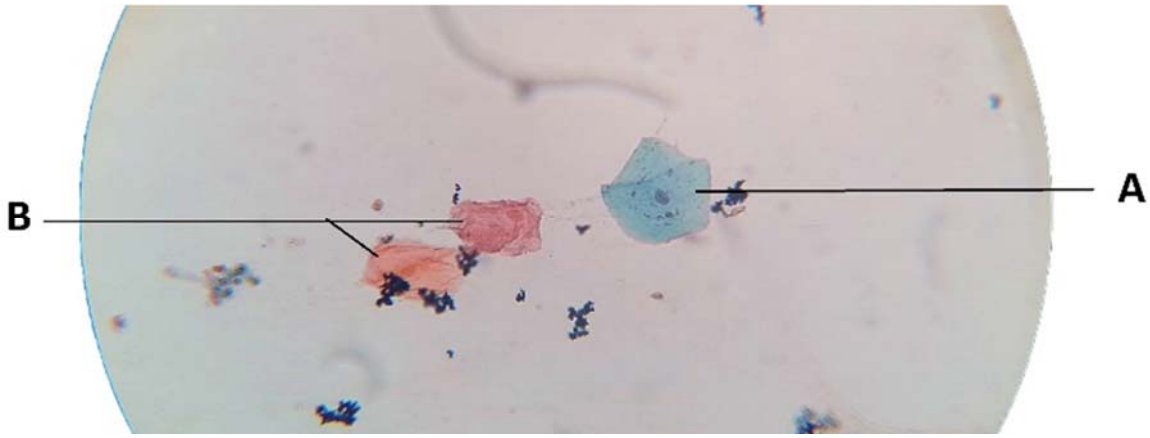

Figure 3-16: Salivary smear of subject of control group with Pb-B 13 µg/dl and Pb-S 1 µg/dl(X400); A: non-keratinized squamous epithelium shedded form oral mucosa, B: keratinized squamous epithelium shedded form oral mucosa.

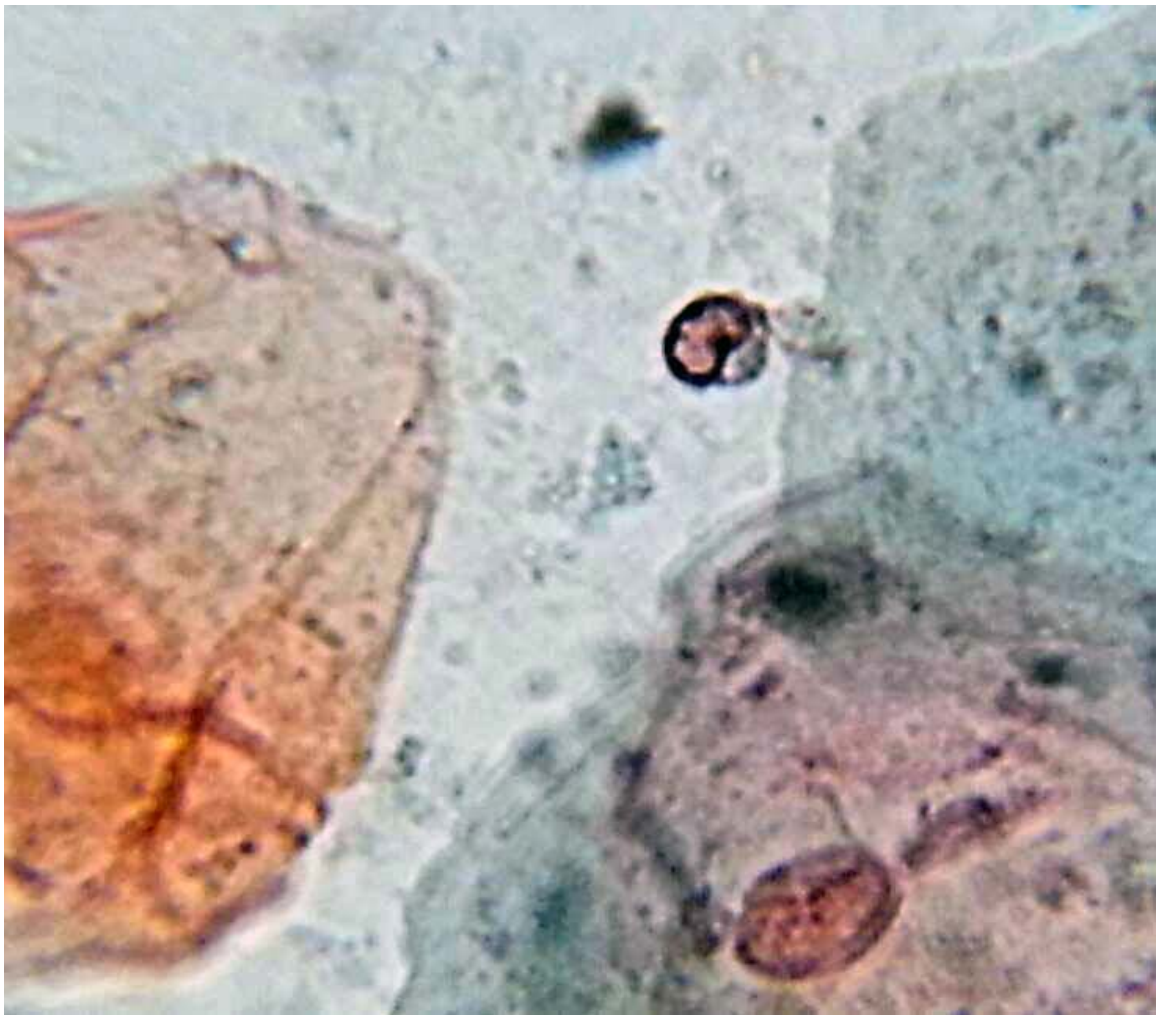

Figure 3-17: Salivary smear of subject of study group with Pb-B 26µg/dl and Pb-S 3.6 µg/dl showing lymphocyte (X1000).

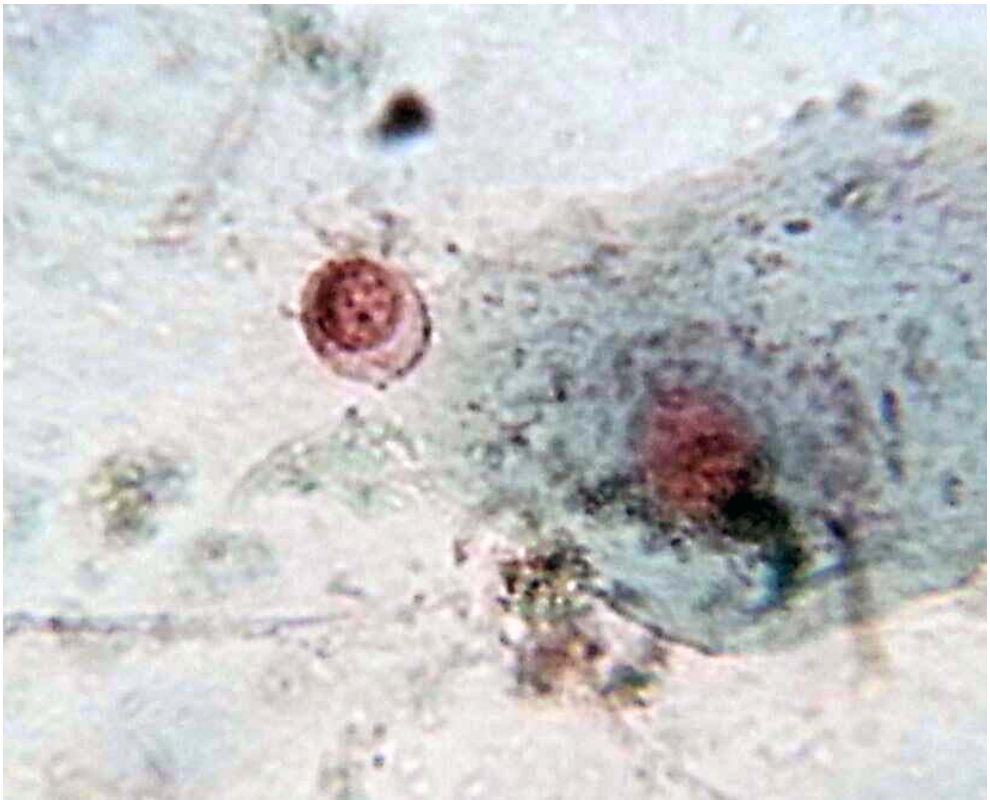

Figure 3-18: Salivary smear of subject of study group with Pb-B 25µg/dl and Pb-S 3.3 µg/dl showing lymphocyte (X1000).

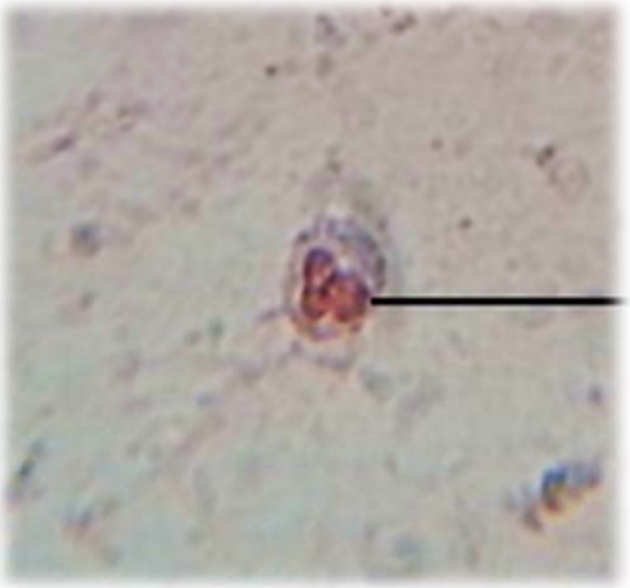

Figure 3-19: Salivary smear of subject of study group with Pb-B 26 µg/dl and Pb-S 4 µg/dl showing neutrophil (X1000).

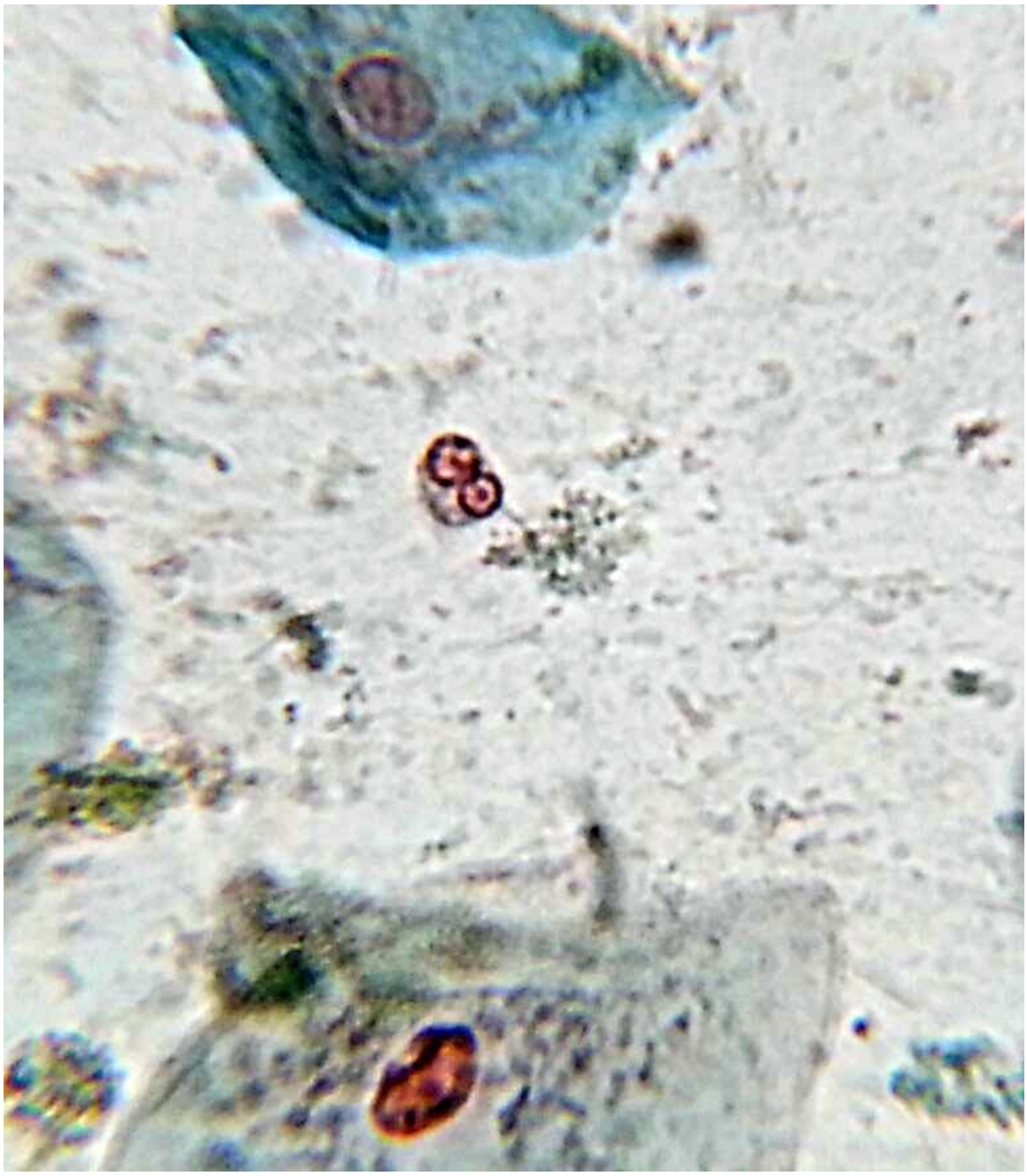

Figure 3-20: Salivary smear of subject of study group with Pb-B 19 µg/dl and Pb-S 2 µg/dl showing eosinophil (X1000).

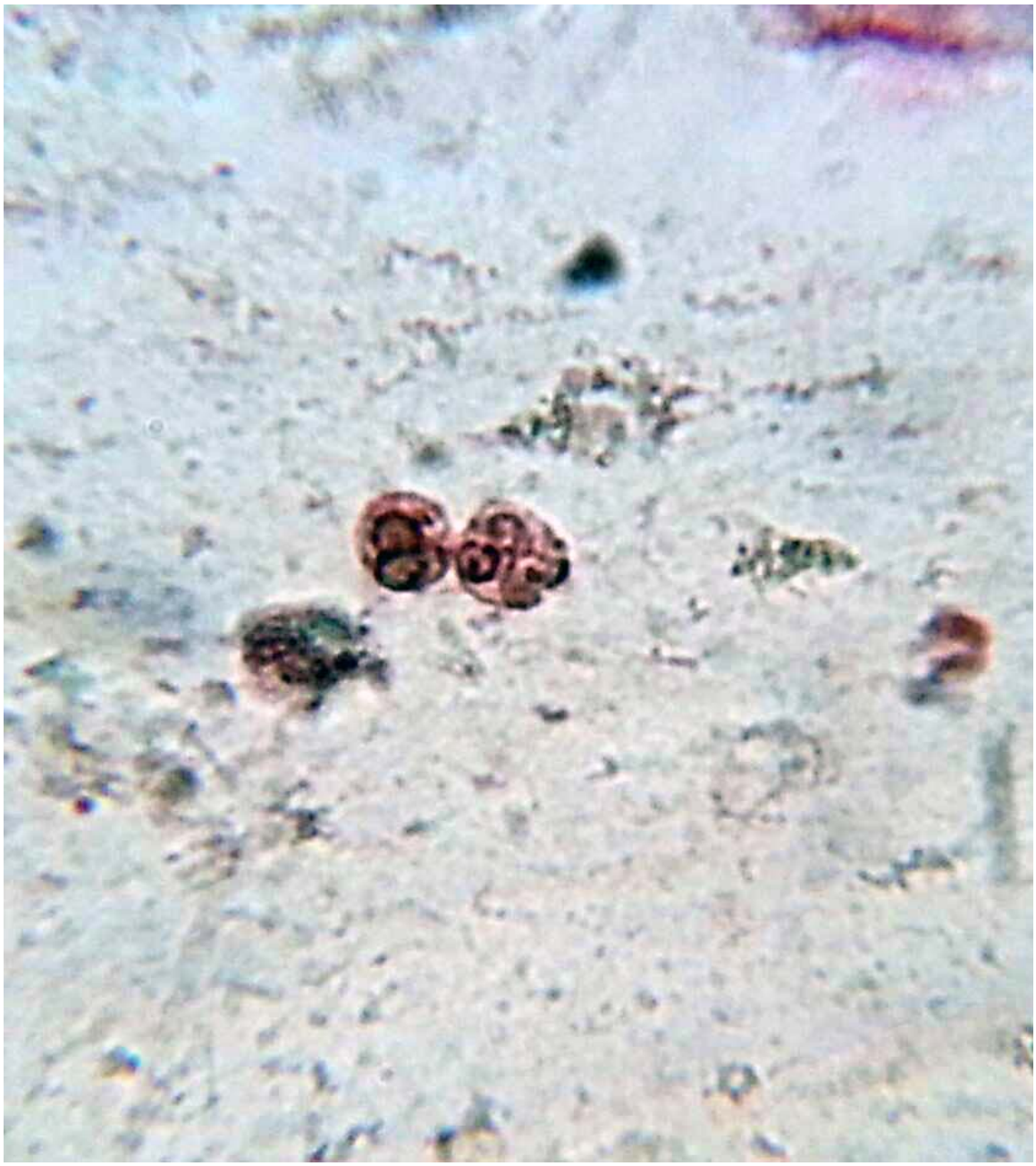

Figure 3-21: Salivary smear of subject of control group with Pb-B 9 µg/dl and Pb-S 1.2 µg/dl showing neutrophils (X1000).

Chapter Four
Discussion

4.1. General:

Lead is the most abundant of the heavy metals in the Earth's crust, it has been used since prehistoric times, and has become widely distributed and mobilized in the environment. Exposure to and uptake of this non-essential element have consequently increased. Both occupational and environmental exposures to lead remain a serious problem in many developing and industrializing countries, as well as in some developed countries **(Tong *et al.*, 2000),** lead is an important toxic substance. Its toxicity can cause aberrant function of multiple organs. Therefore, monitoring its toxicity is very important. **(Barbosa, 2005),** blood and saliva are useful bio-fluids for monitoring the exposure and effects of lead in human population **(Nriagu *et al.*, 2006)**, lead levels in blood (Pb-B) are widely accepted as the standard currency for estimating lead exposure and benchmarking its health effects **(center for disease control CDC, 1991).**

There was considerable interest in the utilization of saliva as a diagnostic fluid including its utility as a biological monitoring medium for drugs and chemical exposures **(Streckfus and Bigler, 2002),** however, before saliva can be confidently utilized for biomonitoring, the kinetic relationship between Pb concentration in blood and saliva needs to be more fully understood to interpret a saliva Pb measurement and how it may or may not relate to systemic dosimetry **(Timchalk *et al.*, 2004).**

4.2. Clinical findings:

4.2.1. Salivary parameters:

The result of this study showed that non- significant difference in salivary flow rate between study and control groups and that have been discordant; **Nriagu *et al.*, (1983)** they found that lead poisoning can impair normal salivary function with xerostomia being one of first recognized clinical symptoms, that might be explained by the lower Pb-B recorded in this result comparing to the mean level recorded in mentioned book, higher lead level in control group might be another possible cause.

Mudher (2008) & **Matloob (2011)** found similar result to this study, both found Pb-B lower than that reported by **Nriagu *et al.*, (1983).**

In this study very strong negative correlation between Pb-B and salivary flow rate, similar findings reported by **Nriagu *et al.*, (1983); Haeckel, (1993),** such correlation might be due to acinar impairment by heavy metals **(Nriagu *et al.*, 1983),** regarding Pb-S have been found weak correlation with salivary flow rate, this might explained in the opposite direction; The flow rate can affect the Pb-S/Pb-B ratio because of its strong influence on saliva pH and membrane permeability **(Haeckel, 1993),** variables that have been shown to influence saliva flow rate include age, medication, circadian rhythm, psychological stress and some disease states **(Rotteveel *et al.*, 2004)** so the relation is complicated and simple correlation can't be established.

Weak non-significant correlation between Pb-S, Pb-B and salivary pH have been reported in this study, this probably due to the effect of lead on salivary flow rate (**Tenovuo** and **Lagerlof, 1994; Bardow *et al.*, 2000).**

In this study significant decrease in salivary lymphocytes in study group saliva; lead induced effects including changes in emotional, hormonal, neurological and immunological status and response as well as metabolic imbalances can change quality and quantity of saliva **(Mandel, 1993)**.

4.2.2. Age and its correlation with lead level:

- In this study Significant positive correlation between age and blood lead level with Pearson correlation ranging from 0.485 to 0.705 (probably due to accumulative effect of lead), this is in agreement with **Nriagu *et al.*, (2006)** who found highly significant correlation with r = 0.48-.049.
- **White** and **Sabbioni (1998)** found gradual increase in Pb-B with age due to long body half-life of excretion and continuous exposure, similar findings were reported by **Jamil *et al.*, (1991)**; **Counter *et al.*, (2000) and Nurcan *et al.*, (2001).**
- Regarding Pb-S a weak non-significant Pearson correlation r = 0.113- 0.253 reported in this study which is close to the result reported by **Barbosa *et al.*, (2006)** who conclude that age does not affect Pb-S levels.

4.2.3. Oral signs and symptoms:

Oral examination revealed occurrence of lead line in gingival margin in patient with toxic Pb-B (p value = 0.001), the dark blue–purplish black seem results from a reaction of the lead with sulfur ions that are formed by bacteria in the oral cavity and that form deposits as lead sulfide along the dental-gingival margin **(Pearce, 2007),** the lead line seem does not correlate with the amount of lead in the blood, but is a reliable indicator for longer term exposure to lead **(Franziska *et al.*, 2008).**

No other significant oral finding was reported in this study.

4.3. Biochemical findings:

4.3.1. Blood lead concentrations:

The results in the current study show that the concentrations of lead in blood (Pb-B) of control group average of 14 µg/dl range from 8 µg/dl to 26 µg/dl, a value that is high compared to international normal value and results of the 1999–2000 National Health and Nutrition Examination Survey **(NHANES 99-00). NHANES 99-00** reported a geometric mean Pb-B value of 1.66 µg/dl for the US population **(CDC, 2003),** and to previously reported values for example; 2.7 ± 0.1µg/dl reported in Detroit by **(Nriagu *et al.*, 2006),** 1.9µg/dl for Japanese population in **(Shimbo *et al.*, 2000),** 3.9µg/dl in different parts of the UK **(White and Sabbioni, 1998),** 4.5 µg/dl for Italian men, in several urban areas **(Apostoli *et al.*, 2002),** 3.1µg/dl in Dusseldorf, Germany **(Wilhem *et al.*, 2002; Becker *et al.*, 2002),** 4.7µg/dl in the city of Badajoz, Spain **(Moreno *et al.*, 1999),** 1.6µg/dl for adolescents in the cities of Uppsala and Trollhattan, Sweden **(Barany *et al.*, 2002).** Countries where leaded gasoline is still being used or has only recently been banned report higher PbB values: 8.2µg/dl in Taiwan **(Liou *et al.*, 1996),** 6.4µg/dl in Korea **(Yang *et al.*, 1996),** and 7.4µg/dl in the middle part of China **(Wang *et al.*, 2004).**

results were close to the average of 12µg/dl Pb-B reported in Mansoura City, Egypt **(Mortada *et al.*, 2002)** and other local studies for example 15 µg/dl **(Mudher, 2008),** 15 µg/dl **(Matloob, 2011).**

In our opinion the increase of Pb-B level in control group compared to international rates might be due to lead pollution in environment from source other than car exhausted that effect general population.

this study revealed increase in Pb-B (average of 19μg/dl and range of 9-30 μg/dl) in traffic police personnel that exposed to car exhausted that contain lead as anti-knocking agent comparing to control group, similar result found by**; Kamal *et al.*, (1991) Khan *et al.*, (1995); Mortada *et al.*, (2001); Naeher *et al.*, (2004); Agha *et al.*, (2005); Eibensteiner *et al.*, (2005)** and **Mormontoy *et al.*, (2006).** Except for **Pala et *al.*, (2002)** and **Rahama *et al.*, (2011) who** found non-significant difference between PbB level in traffic police personnel and control group, different amount of lead addition among countries to gasoline can explain such controversial findings **(Lovei, 1997; UNEP, 2014).**

4.3.2. Salivary lead level:

Because of cultural beliefs, plus growing apprehension about unintended use of blood samples (e.g., genetic screening for crime and drug enforcement), many at-risk members of urban communities are increasingly reluctant to volunteer blood samples for research. The use of other non-invasive methods for assessing environmental lead exposure has become a necessity if the magnitude of this well-documented problem is to be ascertained **(Nriagu, 2006).**

The salivary glands represent a clearance organ for lead in the blood stream. The half-life of lead in saliva is much less than that of blood due to continuous secretion of saliva (**Brodeur *et al.*, 1983).**

The idea of using saliva for biomonitoring is attractive. Its collection is less invasive than venepuncture, and likely to be better accepted by individuals, especially for periodic collections. There is also potential for cost savings, as a skilled technician would not be required to perform the collection **(Koh *et al.*, 2003)**

Average concentration of lead in saliva in study group was 2.2283 μg/dl which is significantly higher than 1.4236 μg/dl of control group**,** observation in control group are among the lowest Pb-S levels reported, other such values reported include 3.4 μg/dl by **DiGregorio *et al.*, (1974),** 5.5 μg/dl for whole saliva by **P'an (1981)** and 3.1 μg/dl for whole saliva by **Gonzalez et al., (1997),** Trace metal measurements made before the late 1980s carried high risk of being compromised by contamination artifacts **(Settle** and **Patterson, 1980)** and most of the Pb-S values published before this period are suspect, a study by **Wilhem *et al.*, (2002)** found that 89% of the lead content of saliva samples was below the limit of .15 μg/dl, and **Nriagu, (2006)** found an average concentration of lead in saliva was 0.24 ± 0.13 μg/dl., local studies tend to be slightly higher to observations; 3.2 μg/dl., by **Mudher (2008**); 3.044 μg/dl., by **Matloob, (2011)** and 7.23 μg/dl by **Hamza (2013);**

Reported Pb-S levels in occupationally exposed individuals tend to be higher than values for example: **Brodeur *et al.*, (1983)** who reported 12.9 μg/dl and **Mudher 2008** who reported 5.3 μg/dl**, Matloob (2011),** reported 7.02 μg/dl**, Hamza, (2013)** reported 15.90 μg/dl, in contrast other international studies show lower value for example **0.48** μg/dl by **Omokhodion** and **Crawford (1991)** and .77 μg/dl by **Koh *et al.*, (2003),** different age group, area of residence, altitude and distance from a gasoline generator might explain such differences **(Al-Dosky *et al.*, 2012).**

The concentrations of lead in saliva were much lower than those in blood, the average Pb-S:Pb-B ratio being only 10-11% for control and study group respectively in this study, except for **Koh *et al.*, (2003)** who found mean Pb-S to be only 3% of the Pb-B, other investigations have reported higher values that ranged from 13% to 56% **(DiGregorio *et al.*, 1974; P'an, 1981** and **Omokhodion**

and **Crawford, 1991;),** local studies ranged from 19.6% to 29% **(Mudher, 2008** and **Matloob, 2011)** The large variation in the previously reported values has been attributed largely to sample contamination (during collection, handling and analysis) and low detection limit for the analytical methods of the time **(Koh *et al.*, 2003).**

4.3.3. Salivary and blood lead association:

A strong association (r = 0.438- 0.378) was found between PbB and Pb-S concentrations in study and control groups respectively where observed in this study, Associations between Pb-B and Pb-S reported in the literature have been discordant; **DiGregorio *et al.*, (1974)** showed poor positive correlation with Pb-S (r = 0.137) while a negative correlation was found between the two parameters by **Omokhodion** and **Crawford (1991).**

Alternatively many international and local studies goes with this study and found moderate to strong association between Pb-B and Pb-S as example; **Youravong *et al.*, (2013)** found that the salivary lead level significantly correlated with the blood lead level (Rs = 0.18, P = 0.05), **P'an (1981)** found a good correlation between PbB and Pb-S (r = 0.72) for adult male occupationally exposed to lead. **Koh *et al.*, (2003)** also reported a strong correlation (r = 0.41) among occupationally exposed individuals with high PbB values, similarly **Mudher, (2008**) found very strong association with p value <0.001, this observation suggests that saliva may be an important route for excretion of lead.

This study reported correlation in study group is stronger than control group and that in our opinion suggest that correlation increased with high lead levels.

4.4. Hematological parameters:

The result of this study showed significant increase in WBC count due to increase of lymphocytes and basophiles (leukocytosis & basophilia) in study group comparing to controls, such findings might be linked to inflammatory effect of lead, similarly **Lorenzo *et al.*, (2006)** report significant leukocytosis in lead exposed worker with respect to non-exposed worker. **MuGahi *et al.*, (2003)** report similar result in experimental study on rat, he revealed a highly significant statistically increase in leucocytes, monocytes and neutrophils count with p value <0.001, such findings might be linked to various effects of lead on the humoral immunity—immunoglobulin levels in serum **(Undeger *et al.*, 1996** and **Pinkerton *et al.*, 1998)**, Moreover, in lead-exposed workers, varying effects on leukocyte and lymphocyte subtypes and function have been described **(Undeger *et al.*, 1996; Sata *et al.*, 1997** and **Pinkerton *et al.*, 1998).**

Regarding RBC, HGB, Hct, MCHC, MCH, MCV, MPV and PLT; non-significant difference between study and control group reported in this study and that have been discordant; **Bryson (1996)** said that hematocrit and HGB value of lead exposed patients may be slightly to moderately reduced, in contrast **Iavicoli *et al.*, (2003)** observed that small increase of blood Pb was associated with increased RBC count and also increased Hb and Hct levels in experimental study in rats; this incongruent probably due to difference of the mean Pb-B in this study and **Bryson (1996)** reports and different mechanism of RBC production between humans and rats**.**

Jacob *et al.*, (2000) reported significant increase in RBC count in children intoxicated with lead, different age group might explain such difference, **Jamil *et al.*, (1987)** found that the effect of lead on these parameter started when blood lead above 50 µg/dl which is higher than what reported in this study.

Except for RDW a significant increase (P-value 0.033) in study group comparing to control group was reported in this study; **Peng *et al.* (2002)** have reported that RDW increased significantly in lead expose workers, **Golalipou *et al.*, (2007)** report similar findings in experimental study on rats, High RDW levels may reflect a disruption in erythropoiesis **(Laso *et al.*, 1990).**

Blood films examination by specialized hematologist revealed some morphological abnormality: thalassemia (single case reported) which is one of the most common genetic diseases worldwide **(Higgs *et al.*, 2012)** it's not correlated to lead merely co-finding, lymphocytosis might be linked to inflammatory effect of lead as previously explained, Hypochromic anemia, probably due to the adverse hematological effects of lead as result of its perturbation of the heme-biosynthesis pathway **(Arun *et al.*, 2006),** basophilic stippling of red cells was reported in two cases with toxic Pb-B which has been considered a classic laboratory sign of lead poisoning since 1899 **(Cheson *et al.*, 1984),** the counting of basophilic stippling of red cells in the blood are both complicated and time-consuming procedures, as they do not offer any particular advantages in the detection or evaluation of lead poisoning they are considered unsuitable **(Haeger-Aronsen, 1971).**

4.5. Cytological findings:

In this study a non-significant difference between study and control group regarding the morphology of normally shedded squamous epithelial cells in saliva, cytological examination revealed that salivary epithelium similar to the normal control, this finding have argument with **Mudher, (2008)** who found that cells are larger, nucleated, cytoplasmic basophilia and cytoplasmic inclusion, the different of the lead level in saliva probably explain such controversy.

No other reported studies are found in exfoliated epithelium cytology, more studies are needed to increase understanding this field.

Chapter five

Conclusions and suggestions

5.1. Conclusions:

1. While the idea of measuring salivary lead level (oral fluid) for biological monitoring is attractive, our findings do not support its use for this purpose.
2. The result of this study revealed gradual increase in lead level with age due to long body half-life and continuous exposure.
3. The counting of basophilic stippling of red cells in blood are both complicated and time consuming procedures and do not offer any particular advantages in detection or evaluation of lead poisoning.
4. No specific salivary cytological findings present in subjects with lead levels examined in this study.
5. The result of this study remark that lymphocytes count decrease in salivary smear in patients with lead exposure.

5.2. Suggestions:

1. Assessment the effect of other pollutants of car exhausted such as carbon mono-oxide.
2. Compare the lead levels and its effect on oral cavity between urbanized and sub-urbanized rural area.
3. Study the effect of lead poisoning on oral mucosa in histopathological level through mucosal biopsy.
4. Collect pure saliva from parotid gland for lead level examination.
5. Measure the levels of minerals or electrolytes in saliva of subjects with lead poisoning to find out whether significant changes could occur.

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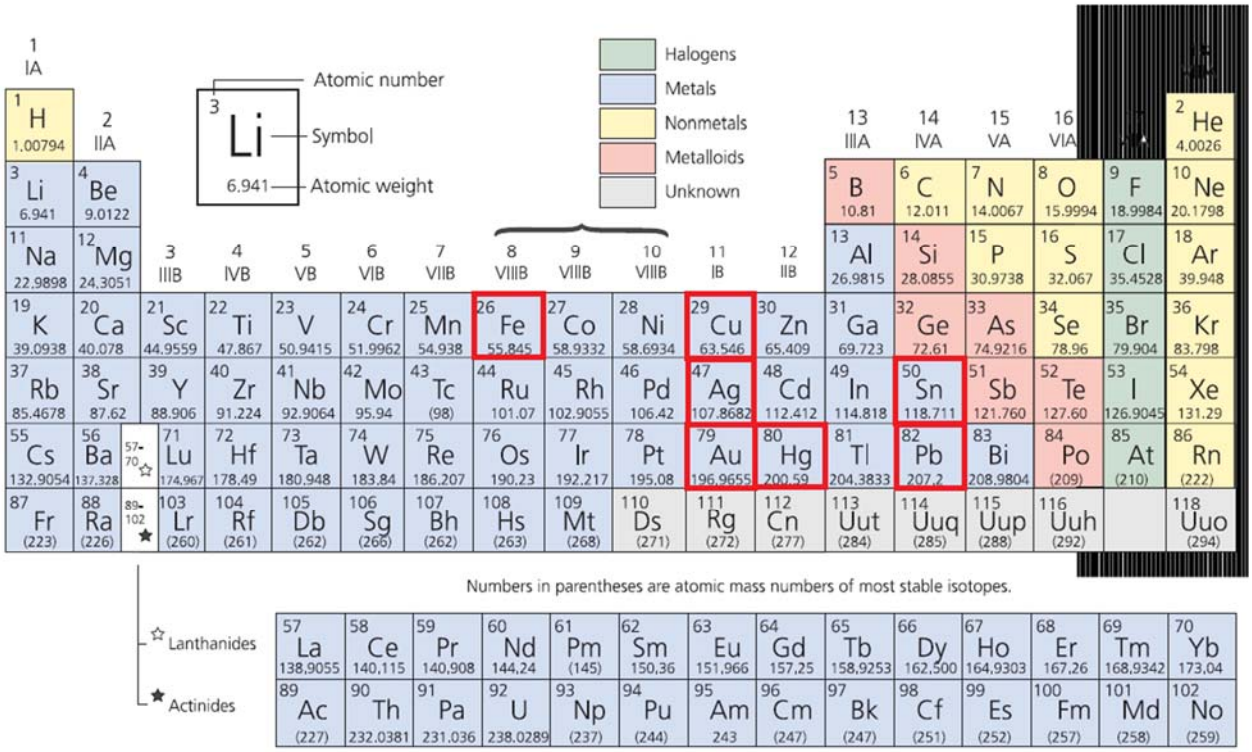


Appendix I: periodic table (Halka and Nordstrom, 2010)

Appendix II

Case sheet

Sample No.

Rank:
Name:
Location of service:
Age:
History of systemic diseases:

ORAL EXAMINATION:

Lead line:	□ present	□absent
Ulcerations:	□ present	□absent
Tongue coating:	□ present	□absent
Other findings:		

SALIVARY EXAMINATION:

- Flow rate:
- pH:
- salivary lead level:
- cytopathological effects of lead:

BLOOD EXAMINATION:

- blood lead level:
- morphological changes:
- CBC sheet *No.* :

مواقفة اجراء البحث

اوافق على المشاركة بالبحث و اعطاء نماذج اللعاب و الدم و فحص الفم و تصويره ولاجل ذلك وقعت .....

الاسم: التوقيع: التاريخ:

Appendix III samples of CBC results:

BPb 13
0.7
52

OK

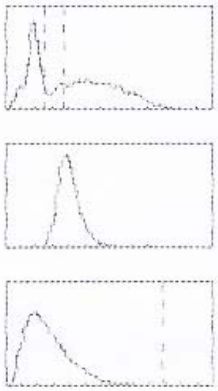
MEDICAL CITY, TEACHING LABS.
HEAMATOLOGY DEPARTMENT

Name :
Comments :

Patient ID :
Sample ID : 011
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 01:03:44PM Seq : 00115

	Results	Flags	Unit	Expected values
WBC	7.1		10^3/µL	4.0 - 10.0
LYM	2.5	*	10^3/µL	1.6 - 3.0
MID	0.7	*L	10^3/µL	4.8 - 11.0
GRA	3.9	*	10^3/µL	2.0 - 7.0
LYM%	34.8	*	%	20.0 - 40.0
MID%	10.2	*H	%	2.5 - 5.5
GRA%	55.0	*	%	40.0 - 80.0
RBC	4.99		10^6/µL	3.95 - 5.00
HGB	14.7		g/dL	12.2 - 16.5
HCT	42.5		%	30.0 - 60.0
MCV	85.3		fL	83.0 - 101.0
MCH	29.6		pg	27.0 - 32.0
MCHC	34.6	H	g/dL	31.5 - 34.5
RDW	13.6		%	11.6 - 14.0
PLT	357		10^3/µL	150 - 400
MPV	8.2		fL	3.0 - 9.0



N 55
L 35
M 7
E 2
B 1

Rc Normochromic normocytic

WBC Normal count no immature cells seen

PLT Normal

د بخاري خوري مجيد

BPP 19
3.6
45

OK

MEDICAL CITY. TEACHING LABS.
HEAMATOLOGY DEPARTMENT

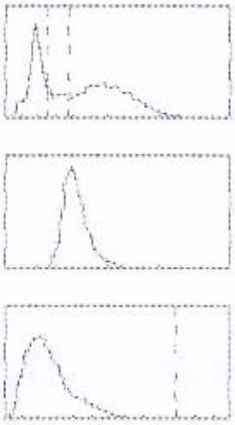
Study

Name :
Comments :

Patient ID :
Sample ID : 000039
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 12:52:39PM Seq : 0010

	Result	Flags	Units	Expected values
WBC	7.3		10^3/µL	4.0 / 10.0
LYM	2.4	*	10^3/µL	1.0 / 3.0
MID	0.8	*L	10^3/µL	4.5 / 11.0
GRA	4.1	*	10^3/µL	2.0 / 7.0
LYM%	32.7	*	%	20.0 / 40.0
MID%	11.1	*H	%	2.5 / 5.5
GRA%	56.2	*	%	40.0 / 80.0
RBC	4.53		10^6/µL	3.95 / 5.00
HGB	13.6		g/dL	12.2 / 16.5
HCT	39.5		%	38.0 / 50.0
MCV	87.3		fL	83.0 / 101.0
MCH	30.0		pg	27.0 / 32.0
MCHC	34.4		g/dL	31.5 / 34.5
RDW	12.8		%	11.6 / 14.0
PLT	261		10^3/µL	150 / 400
MPV	7.8		fL	3.6 / 9.0



N 64
L 25
M 7
E 4

RC Normochromic normocytic

WBC Normal count no primitive cells

PLT Normal

دكتور نورة حسين

19
2.6
43

OR

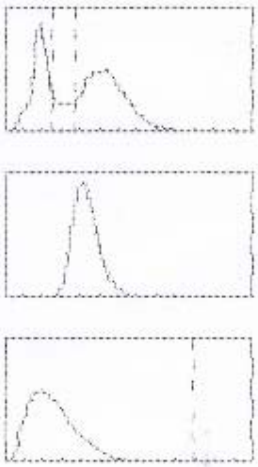
MEDICAL CITY, TEACHING LABS.
HAEMATOLOGY DEPARTMENT

Stat

Name :	Patient ID :
Comments :	Sample ID : 000033
	Type : STANDARD

Operator ID : 123 Date : 20/02/2014 12:47:23PM Seq : 00101

	Result	Flags	Unit	Expected values
WBC	6.5		10^3/µL	4.0 / 10.0
LYM	2.1	*	10^3/µL	1.0 / 3.0
MID	0.7	*L	10^3/µL	4.5 / 11.0
GRA	3.7	*	10^3/µL	2.0 / 7.0
LYM%	32.4	*	%	20.0 / 40.0
MID%	11.2	*H	%	2.5 / 5.5
GRA%	56.5	*	%	40.0 / 80.0
RBC	4.82		10^6/µL	3.95 / 5.00
HGB	16.0		g/dL	12.2 / 16.5
HCT	43.6		%	38.0 / 50.0
MCV	90.5		fL	83.0 / 101.0
MCH	31.1		pg	27.0 / 32.0
MCHC	34.4		g/dL	31.5 / 34.5
RDW	13.5		%	11.5 / 14.6
PLT	258		10^3/µL	150 / 400
MPV	7.7		fL	3.0 / 9.0



N 56 %
L 40
M 3
E 1

RBC : Normocromic with anisocytosis, No basophillic stippling
WBC : No abnormal cells seen
Platelets within normal range

BBb 21

ds

51

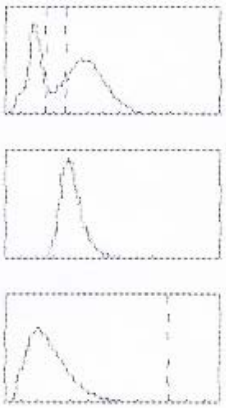
MEDICAL CITY, TEACHING LABS,
HEAMATOLOGY DEPARTMENT

Study

Name :	Patient ID :
Comments :	Sample ID : 000042
	Type : STANDARD

Operator ID : 123 Date : 20/02/2014 12:56:27PM Seq : 00109

	Result	Flags	Units	Expected values
WBC	8.2		10^3/µL	4.0 / 10.0
LYM	3.7	*	10^3/µL	1.0 / 3.0
MID	1.0	*L	10^3/µL	4.5 / 11.0
GRA	4.5	*	10^3/µL	2.0 / 7.0
LYM%	33.2	*	%	20.0 / 40.0
MID%	11.7	*H	%	2.5 / 5.5
GRA%	55.1	*	%	40.0 / 60.0
RBC	5.00	H	10^6/µL	3.95 / 5.00
HGB	15.4		g/dL	12.2 / 16.5
HCT	43.7		%	30.0 / 50.0
MCV	86.6		fL	83.0 / 101.0
MCH	30.3		pg	27.0 / 32.0
MCHC	35.2	H	g/dL	31.5 / 34.5
RDW	13.2		%	11.6 / 14.0
PLT	229		10^3/µL	150 / 400
MPV	8.1		fL	3.0 / 9.0



N 58
L 35
M 3
E 4

ERYTHROCYTOSIS

RBCL normochromic with anisocytosis no basophilic stippling

WBCL normal count, no abnormal cells seen

plat ↓ within normal

BPb 29

ok

in S2

MEDICAL CITY, TEACHING LABS.
HEAMATOLOGY DEPARTMENT

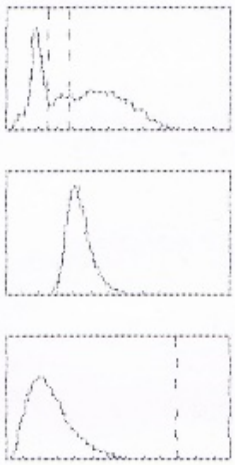
c/o

Name :
Comments :

Patient ID :
Sample ID : 000040
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 12:53:39PM Seq : 00107

	Result	Flags	Unit	Expected values
WBC	9.4		10^3/µL	4.0 / 10.0
LYM	2.9	#	10^3/µL	1.8 / 3.0
MID	1.2	#L	10^3/µL	4.6 / 11.0
GRA	5.3	#	10^3/µL	2.0 / 7.0
LYM%	30.4	#	%	20.0 / 40.0
MID%	12.7	#H	%	2.5 / 5.5
GRA%	56.9	#	%	40.0 / 80.0
RBC	5.08	H	10^6/µL	3.95 / 5.00
HGB	15.8		g/dL	12.2 / 16.5
HCT	46.4		%	30.0 / 50.0
MCV	91.3		fL	83.0 / 101.0
MCH	31.1		pg	27.0 / 32.0
MCHC	34.1		g/dL	31.5 / 34.5
RDW	12.6		%	11.6 / 14.0
PLT	296		10^3/µL	150 / 400
MPV	7.9		fL	3.0 / 9.0



N 61
L 29
M 8
E 2

ERYTHROCYTOSIS

RC Normochromic normocytic

WBC Normal count, neprimitive cells

PLT Normal

د. زكاوري

BPP 26
3.6
43

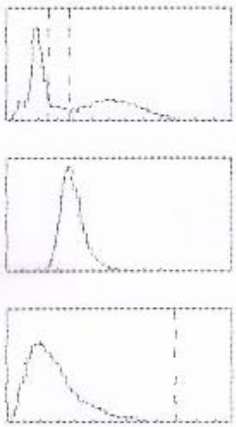
MEDICAL CITY. TEACHING LABS.
HEAMATOLOGY DEPARTMENT

Name :
Comments :

Patient ID :
Sample ID : 0000041
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 12:54:41PM Seq : 00108

	Result	Flags	Unit	Expected values
WBC	6.3		10^3/µL	4.0 - 10.0
LYM	3.5	H	10^3/µL	1.0 - 3.0
MID	0.6	L	10^3/µL	4.5 - 11.0
GRA	4.0		10^3/µL	2.0 - 7.0
LYM%	48.7	H	%	20.0 - 40.0
MID%	9.4	H	%	2.5 - 5.5
GRA%	48.2		%	40.0 - 80.0
RBC	6.09	H	10^6/µL	3.95 - 5.00
HGB	17.2	H	g/dL	12.2 - 16.6
HCT	49.3		%	30.0 - 50.0
MCV	99.9	L	fL	83.0 - 101.0
MCH	28.2		pg	27.0 - 32.0
MCHC	34.9	H	g/dL	31.5 - 34.5
RDW	14.0		%	11.6 - 14.0
PLT	184		10^3/µL	150 - 400
MPV	8.5		fL	3.0 - 9.0



N 60
L 31
M 5
E 4

LYMPHOCYTOSIS
ERYTHROCYTOSIS MICROCYTOSIS

RC Normochromic normocytic
Nobasophilic stippling
WBC Normal Count. no immature cells
Plt Normal

BB 14
1.3

DG

MEDICAL CITY, TEACHING LABS.
HEMATOLOGY DEPARTMENT

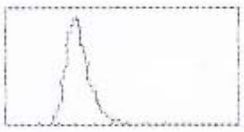
Study

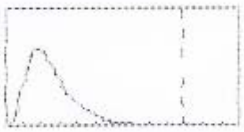
Name :
Comments Fig 42

Patient ID :
Sample ID : 024
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 01:09:25PM Seq : 00119

	Result	Flags	Unit	Expected values
WBC	8.1		10^3/uL	4.0 - 10.0
LYM	2.8		10^3/uL	1.0 - 3.0
MID	0.8	L	10^3/uL	4.5 - 11.0
GRA	4.6		10^3/uL	2.0 - 7.0
LYM%	34.5		%	20.0 - 40.0
MID%	9.3	N	%	2.5 - 5.5
GRA%	56.2		%	40.0 - 80.0
RBC	5.24	H	10^6/uL	3.35 - 6.00
HGB	16.3		g/dL	12.2 - 16.5
HCT	45.8		%	30.0 - 50.0
MCV	87.4		fL	82.0 - 101.0
MCH	31.1		pg	27.0 - 32.0
MCHC	35.6	H	g/dL	31.5 - 34.5
RDW	13.1		%	11.6 - 14.0
PLT	358		10^3/uL	150 - 400
MPV	7.6		fL	3.0 - 9.0





ERYTHROCYTOSIS

N 58
L 37
M 5

RC Normochromic normocytic
No basophilic stippling seen

WBC Normal Count, no immature cells

PLT Normal

MEDICAL CITY, TEACHING LABS.
HEMATOLOGY DEPARTMENT

Name :
Comments :
Patient ID :
Sample ID : 027
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 01:07:15PM Seq : 00118

	Result	Flags	Unit	Expected values
WBC	7.4		10^3/uL	4.0 - 10.0
LYM	3.8	*	10^3/uL	1.0 - 3.0
MID	0.8	*L	10^3/uL	4.5 - 11.0
GRA	3.8	*	10^3/uL	2.0 - 7.0
LYM%	37.7	*	%	20.0 - 40.0
MID%	11.1	*H	%	2.5 - 5.5
GRA%	51.2	*	%	40.0 - 80.0
RBC	4.64		10^6/uL	3.96 - 5.00
HGB	14.2		g/dL	12.2 - 16.5
HCT	41.2		%	30.0 - 50.0
MCV	88.9		fL	83.0 - 101.0
MCH	30.6		pg	27.0 - 32.0
MCHC	34.5		g/dL	31.5 - 34.5
RDW	12.0		%	11.5 - 14.0
PLT	245		10^3/uL	150 - 400
MPV	7.9		fL	3.0 - 9.0

N 54
L 36
M 5
E 3
B 2

RC Normochromic normocytic
WBC No basophilic stippling seen
Normal count, no immature cells seen
PLT Normal.

MEDICAL CITY, TEACHING LABS.
HEMATOLOGY DEPARTMENT

Name :
Comments :
Patient ID :
Sample ID : 030
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 01:02:31PM Seq : 00114

	Result	Flags	Unit	Expected values
WBC	9.2		10^3/uL	4.0 - 10.0
LYM	3.1	*L	10^3/uL	1.0 - 3.0
MID	0.5	*L	10^3/uL	4.5 - 11.0
GRA	5.2	*	10^3/uL	2.0 - 7.0
LYM%	33.5	*	%	20.0 - 40.0
MID%	5.6	*H	%	2.5 - 5.5
GRA%	56.9	*	%	40.0 - 80.0
RBC	5.54	H	10^6/uL	3.96 - 5.00
HGB	17.1	H	g/dL	12.2 - 16.5
HCT	50.7	H	%	30.0 - 50.0
MCV	92.0		fL	83.0 - 101.0
MCH	31.0		pg	27.0 - 32.0
MCHC	33.7		g/dL	31.5 - 34.5
RDW	13.7		%	11.5 - 14.0
PLT	296		10^3/uL	150 - 400
MPV	8.2		fL	3.0 - 9.0

LYMPHOCYTOSIS
ERYTHROCYTOSIS

N 53
L 37
M 7
E 3

RC Normochromic normocytic
WBC No immature cells seen.
PLT Normal

High pcv, close follow up please

MEDICAL CITY, TEACHING LABS.
HEMATOLOGY DEPARTMENT

Name :
Comments :
Patient ID :
Sample ID : 025
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 01:05:12PM Seq : 00115

	Result	Flags	Unit	Expected values
WBC	9.9		10^3/uL	4.0 - 10.0
LYM	3.5	*H	10^3/uL	1.0 - 3.0
MID	1.2	*L	10^3/uL	4.5 - 11.0
GRA	5.2	*	10^3/uL	2.0 - 7.0
LYM%	35.8	*	%	20.0 - 40.0
MID%	12.1	*H	%	2.5 - 5.5
GRA%	52.1	*	%	40.0 - 80.0
RBC	5.45	H	10^6/uL	3.96 - 5.00
HGB	17.0	H	g/dL	12.2 - 16.5
HCT	47.5		%	30.0 - 50.0
MCV	87.2		fL	83.0 - 101.0
MCH	31.2		pg	27.0 - 32.0
MCHC	35.8	H	g/dL	31.5 - 34.5
RDW	12.8		%	11.5 - 14.0
PLT	263		10^3/uL	150 - 400
MPV	8.1		fL	3.0 - 9.0

LYMPHOCYTOSIS
ERYTHROCYTOSIS

N 53
L 37
M 5
E 3
B 2

RC Normochromic normocytic
WBC Normal count no primitive cells seen
PLT Normal

MINISTRY OF HEALTH
MEDICAL CITY
TEACHING LABORATORIES
ABBOTT DIAGNOSTIC
Chartable Page
Spec ID 067
Pat Name
Pat ID
Doctor
Comment

RRTT R6 T6
Spec Type Patient
DOB
Sex Unknown
Draw Date/Time
User Field 1
User Field 2

SEQ# 7436 OPID Group
Run 22/1/2014 11:13
Test CBC
Mode Closed Param 1
Limits Default (1)

WBC	7.35	10e3/uL
NEU	4.03	54.8 %
LYM	2.38	32.4 %
MONO	.639	8.69 %
EOS	.244	3.33 %
BASO	.058	.796 %
RBC	5.58	10e6/uL
HGB	15.3	g/dL
HCT	49.5	%
MCV	88.7	fL
MCH	29.6	pg
MCHC	33.4	g/dL
RDW	11.1	%
PLT	308.	10e3/uL
MPV	6.79	fL

LIMIT SET					
WBC	3.70-10.1		RBC	4.06-4.69	PLT 150.-450.
NEU	1.63-6.96	39.3-73.7 %	HGB	12.8-14.2	MPV 6.90-10.6
LYM	1.09-2.99	18.0-48.3 %	HCT	37.7-63.7	
MONO	.240-.790	4.40-12.7 %	MCV	81.1-98.0	
EOS	.030-.440	.600-7.38 %	MCH	27.0-31.2	
BASO	0.00-.080	0.00-1.70 %	MCHC	31.8-35.4	
			RDW	11.6-14.5	

BPb 22
2.3
ii 49

OK

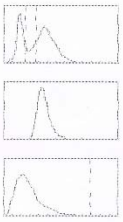
MEDICAL CITY, TEACHING LABS.
HEMATOLOGY DEPARTMENT

Study

Name :
Comments :
Patient ID :
Sample ID : 000043
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 12:57:27PM Seq : 00110

	Result	Flags	Units	Expected values
WBC	6.3		10^3/uL	4.0 - 10.0
LYM	1.3	*	10^3/uL	1.0 - 3.0
MID	0.8	*L	10^3/uL	4.5 - 11.0
GRA	3.7	#	10^3/uL	2.0 - 7.0
LYM%	20.4	*	%	20.0 - 40.0
MID%	12.2	#H	%	2.5 - 5.5
GRA%	58.4	*	%	40.0 - 80.0
RBC	4.29		10^6/uL	3.95 - 5.00
HGB	14.6		g/dL	12.2 - 16.5
HCT	42.0		%	38.0 - 50.0
MCV	98.0		fL	83.0 - 101.0
MCH	34.0	H	pg	27.0 - 32.0
MCHC	34.8	H	g/dL	31.5 - 34.5
RDW	11.7		%	11.6 - 14.0
PLT	243		10^3/uL	150 - 400
MPV	9.5		fL	3.0 - 9.0



N 62
L 26
M 7
E 5

Rc normochromic normocytic
WBC Normal count, no immature cells seen
Plt Normal

BPb 15

OK

ii 30

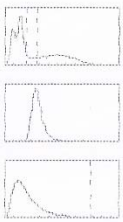
MEDICAL CITY, TEACHING LABS.
HEMATOLOGY DEPARTMENT

Study

Name :
Comments :
Patient ID :
Sample ID : 000018
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 12:59:48PM Seq : 00112

	Result	Flags	Units	Expected values
WBC	8.8	#	10^3/uL	4.0 - 10.0
LYM	4.5	#H	10^3/uL	1.0 - 3.0
MID	0.7	#L	10^3/uL	4.5 - 11.0
GRA	3.6	#	10^3/uL	2.0 - 7.0
LYM%	51.1	#H	%	20.0 - 40.0
MID%	7.9	#H	%	2.5 - 5.5
GRA%	41.0	#	%	40.0 - 80.0
RBC	5.30	H	10^6/uL	3.95 - 5.00
HGB	14.7		g/dL	12.2 - 16.5
HCT	42.5		%	38.0 - 50.0
MCV	80.1	L	fL	83.0 - 101.0
MCH	27.7		pg	27.0 - 32.0
MCHC	34.5	H	g/dL	31.5 - 34.5
RDW	13.3		%	11.6 - 14.0
PLT	[illegible]	L	10^3/uL	150 - 400
MPV	7.9		fL	3.0 - 9.0



LYMPHOCYTOSIS
ERYTHROCYTOSIS MICROCYTOSIS
THROMBOPENIA PLATELET AGGREGATES

N 55
L 38
M 5
E 2

RBC : normochromic with anisocytosis, no basophilic stippling seen
WBC : normal count, no abnormal cells seen
plat : seen in aggregates

BPb 26
4
ii 38

OK

38

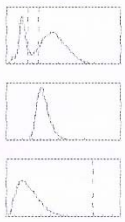
MEDICAL CITY, TEACHING LABS.
HEMATOLOGY DEPARTMENT

Study

Name :
Comments :
Patient ID :
Sample ID : 000038
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 12:51:38PM Seq : 00105

	Result	Flags	Units	Expected values
WBC	9.2		10^3/uL	4.0 - 10.0
LYM	2.4	*	10^3/uL	1.0 - 3.0
MID	0.8	*L	10^3/uL	4.5 - 11.0
GRA	5.9	#	10^3/uL	2.0 - 7.0
LYM%	26.5	*	%	20.0 - 40.0
MID%	8.9	#H	%	2.5 - 5.5
GRA%	64.6	*	%	40.0 - 80.0
RBC	5.24	H	10^6/uL	3.95 - 5.00
HGB	16.5		g/dL	12.2 - 16.5
HCT	47.2		%	38.0 - 50.0
MCV	90.5		fL	83.0 - 101.0
MCH	31.7		pg	27.0 - 32.0
MCHC	35.0	H	g/dL	31.5 - 34.5
RDW	13.9		%	11.6 - 14.0
PLT	293		10^3/uL	150 - 400
MPV	7.8		fL	3.0 - 9.0



N 69
L 24
M 5
E 2

ERYTHROCYTOSIS

Rc normochromic normocytic with basophilic stippling
WBC Normal count, no immature cells seen
Plt Normal

BP 24
26
ii 30

OK

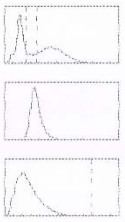
MEDICAL CITY, TEACHING LABS.
HEMATOLOGY DEPARTMENT

Study

Name :
Comments :
Patient ID :
Sample ID : 000032
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 12:46:22PM Seq : 00100

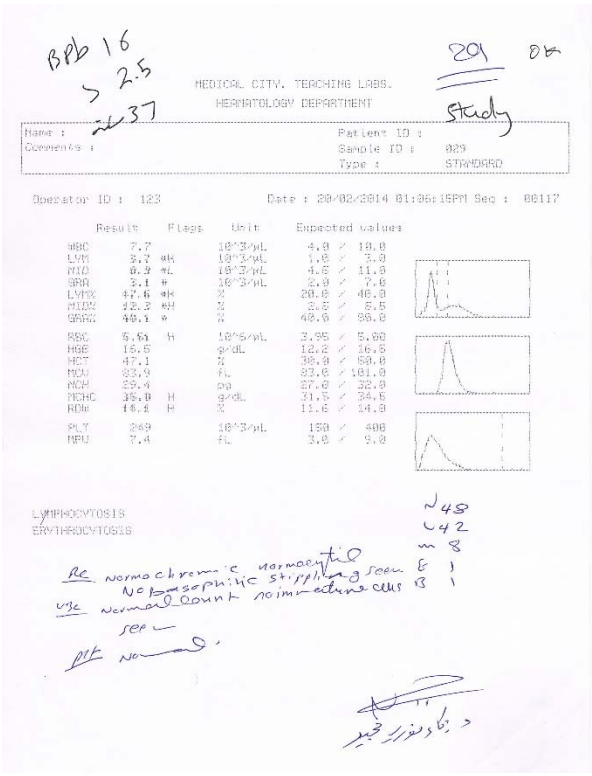
	Result	Flags	Units	Expected values
WBC	7.9		10^3/uL	4.0 - 10.0
LYM	3.0	#	10^3/uL	1.0 - 3.0
MID	0.6	#L	10^3/uL	4.5 - 11.0
GRA	4.1	#	10^3/uL	2.0 - 7.0
LYM%	38.5	#	%	20.0 - 40.0
MID%	10.0	#H	%	2.5 - 5.5
GRA%	51.5	*	%	40.0 - 80.0
RBC	5.51	H	10^6/uL	3.95 - 5.00
HGB	14.7		g/dL	12.2 - 16.5
HCT	42.2		%	38.0 - 50.0
MCV	76.5	L	fL	83.0 - 101.0
MCH	26.7	L	pg	27.0 - 32.0
MCHC	34.8	H	g/dL	31.5 - 34.5
RDW	13.3		%	11.6 - 14.0
PLT	241		10^3/uL	150 - 400
MPV	8.2		fL	3.0 - 9.0



ERYTHROCYTOSIS MICROCYTOSIS

RBC : Normochromic, Normocytic
WBC : Normal leukocyte Count,
Normal differential Count,
No immature cells are seen
Plt : within normal range

N 51
L 39
M 5
E 4.
B 1



MEDICAL CITY. TEACHING LABS.
HEMATOLOGY DEPARTMENT

Name :
Comments :
Patient ID :
Sample ID : 029
Type : STANDARD

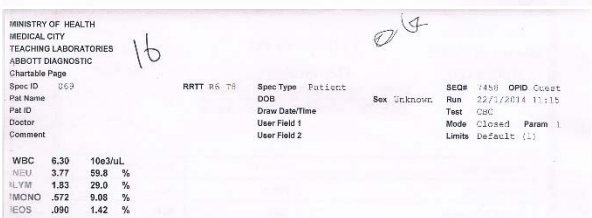
Operator ID : 123 Date : 20/02/2014 01:06:15PM Seq : 00117

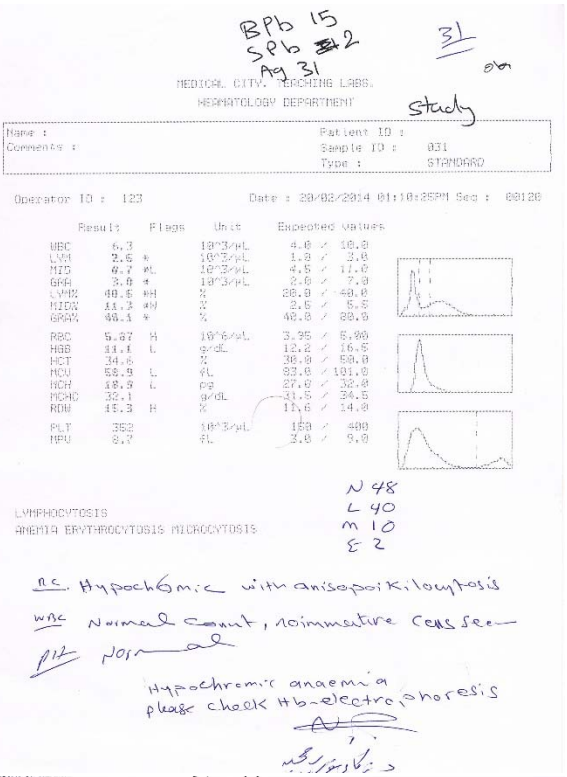
	Results	Flags	Unit	Expected values
WBC	7.7		10^3/uL	4.0 - 10.0
LYM	3.7	ok	10^3/uL	1.0 - 3.0
MID	0.9	WL	10^3/uL	4.5 - 11.0
GRA	3.1	#	10^3/uL	2.0 - 7.0
LYM%	47.6	ok	%	20.0 - 40.0
MID%	12.2	eH	%	2.5 - 6.5
GRA%	40.1	*	%	40.0 - 80.0
RBC	5.45	H	10^6/uL	3.95 - 5.00
HGB	15.5		g/dL	12.2 - 16.5
HCT	47.1		%	38.0 - 50.0
MCV	83.9		fL	83.0 - 101.0
MCH	28.4		pg	27.0 - 32.0
MCHC	33.0	H	g/dL	31.5 - 34.5
RDW	14.1	H	%	11.6 - 14.0
PLT	269		10^3/uL	150 - 400
MPV	7.4		fL	3.0 - 9.0

LYMPHOCYTOSIS
ERYTHROCYTOSIS

N 48
L 42
M 8
E 1
B 1

Rc Normochromic normacytic
No basophilic stippling seen
WBC Normal count no immature cells seen
Plt Normal.





MEDICAL CITY. TEACHING LABS.
HEMATOLOGY DEPARTMENT

Name :
Comments :
Patient ID :
Sample ID : 031
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 01:10:25PM Seq : 00120

	Results	Flags	Unit	Expected values
WBC	6.3		10^3/uL	4.0 - 10.0
LYM	2.6	*	10^3/uL	1.0 - 3.0
MID	0.7	WL	10^3/uL	4.5 - 11.0
GRA	3.0	*	10^3/uL	2.0 - 7.0
LYM%	40.5	eH	%	20.0 - 40.0
MID%	11.3	eW	%	2.5 - 6.5
GRA%	46.1	*	%	40.0 - 80.0
RBC	5.67	H	10^6/uL	3.95 - 5.00
HGB	11.1	L	g/dL	12.2 - 16.5
HCT	34.6		%	38.0 - 50.0
MCV	58.5	L	fL	83.0 - 101.0
MCH	18.9	L	pg	27.0 - 32.0
MCHC	32.1		g/dL	31.5 - 34.5
RDW	15.3	H	%	11.6 - 14.0
PLT	352		10^3/uL	150 - 400
MPV	8.7		fL	3.0 - 9.0

LYMPHOCYTOSIS
ANAEMIA ERYTHROCYTOSIS MICROCYTOSIS

N 48
L 40
M 10
E 2

Rc. Hypochromic with anisopoikilocytosis
WBC Normal count, no immature cells seen
Plt Normal

Hypochromic anaemia
please check Hb-electrophoresis

MINISTRY OF HEALTH
MEDICAL CITY
TEACHING LABORATORIES
ABBOTT DIAGNOSTIC
Charitable Page

Spec ID 069 RRTT R6 T8
Pat Name
Pat ID
Doctor
Comment

Spec Type Patient
DOB Sex Unknown
Draw Date/Time
User Field 1
User Field 2

SEQ# 7458 OPID Guest
Run 22/1/2014 11:15
Test CBC
Mode Closed Param 1
Limits Default (1)

WBC	6.30	10e3/uL
NEU	3.77	59.8 %
LYM	1.83	29.0 %
MONO	.572	9.08 %
EOS	.090	1.42 %
BASO	.046	.730 %
RBC	4.38	10e6/uL
HGB	13.5	g/dL
HCT	39.3	%
MCV	89.8	fL
MCH	30.8	pg
MCHC	34.3	g/dL
RDW	11.2	%
PLT	305.	10e3/uL
MPV	6.60	fL

LIMIT SET					
WBC	3.70-10.1		RBC	4.06-4.69	PLT 150.-450.
NEU	1.63-6.96	39.3-73.7 %	HGB	12.9-14.2	MPV 6.90-10.6
LYM	1.09-2.99	18.0-48.3 %	HCT	37.7-53.7	
MONO	.240-.790	4.40-12.7 %	MCV	81.1-98.0	
EOS	.030-.440	.600-7.30 %	MCH	27.0-31.2	
BASO	0.00-.080	0.00-1.70 %	MCHC	31.8-35.4	
			RDW	11.5-14.5	

MEDICAL CITY
TEACHING LABORATORIES
ABBOTT DIAGNOSTIC
Charitable Page

Spec ID 000006
Pat Name
Pat ID
Doctor
Comment

Spec Type Patient
DOB Sex Unknown
Draw Date/Time
User Field 1
User Field 2

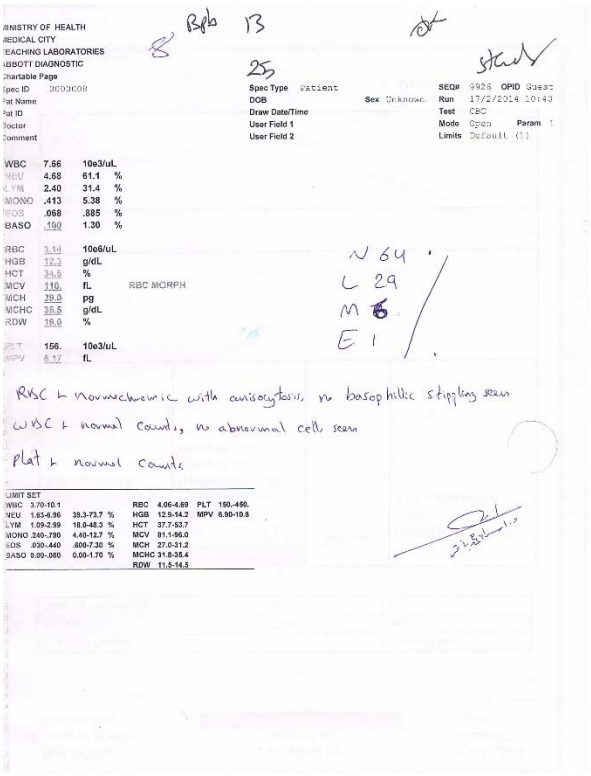
SEQ# 9924 OPID Guest
Run 17/2/2014 10:38
Test CBC
Mode Open Param 1
Limits Default (1)

WBC	9.29	10e3/uL
NEU	6.16	66.2 %
LYM	2.24	24.1 %
MONO	.719	7.74 %
EOS	.110	1.19 %
BASO	.071	.762 %
RBC	5.13	10e6/uL
HGB	14.8	g/dL
HCT	43.1	%
MCV	84.0	fL
MCH	28.9	pg
MCHC	34.4	g/dL
RDW	11.7	%
PLT	221.	10e3/uL
MPV	6.70	fL

LIMIT SET					
WBC	3.70-10.1		RBC	4.06-4.69	PLT 150.-450.
NEU	1.63-6.96	39.3-73.7 %	HGB	12.9-14.2	MPV 6.90-10.6
LYM	1.09-2.99	18.0-48.3 %	HCT	37.7-53.7	
MONO	.240-.790	4.40-12.7 %	MCV	81.1-98.0	
EOS	.030-.440	.600-7.30 %	MCH	27.0-31.2	
BASO	0.00-.080	0.00-1.70 %	MCHC	31.8-35.4	
			RDW	11.5-14.5	

N 65
L 26
M 7
E 2

RBC : normochromic with anisocytosis, , no basophilling stipling seen
WBC : normal count, no abnormal cells seen
Platt : with in normal range



MINISTRY OF HEALTH
MEDICAL CITY
TEACHING LABORATORIES
ABBOTT DIAGNOSTIC
Chartable Page

Spec ID 3003008
Pat Name
Pat ID
Doctor
Comment

Spec Type Patient
DOB
Draw Date/Time
User Field 1
User Field 2
Sex Unknown

SEQ# 9926 OPID Guest
Run 17/2/2014 10:40
Test CBC
Mode Open Param 1
Limits Default (1)

WBC	7.66	10e3/uL	
NEU	4.68	61.1	%
LYM	2.40	31.4	%
MONO	.413	5.38	%
EOS	.068	.885	%
BASO	.100	1.30	%
RBC	3.14	10e6/uL	
HGB	12.2	g/dL	
HCT	34.6	%	
MCV	110.	fL	RBC MORPH
MCH	39.0	pg	
MCHC	35.5	g/dL	
RDW	19.0	%	
PLT	156.	10e3/uL	
MPV	8.17	fL	

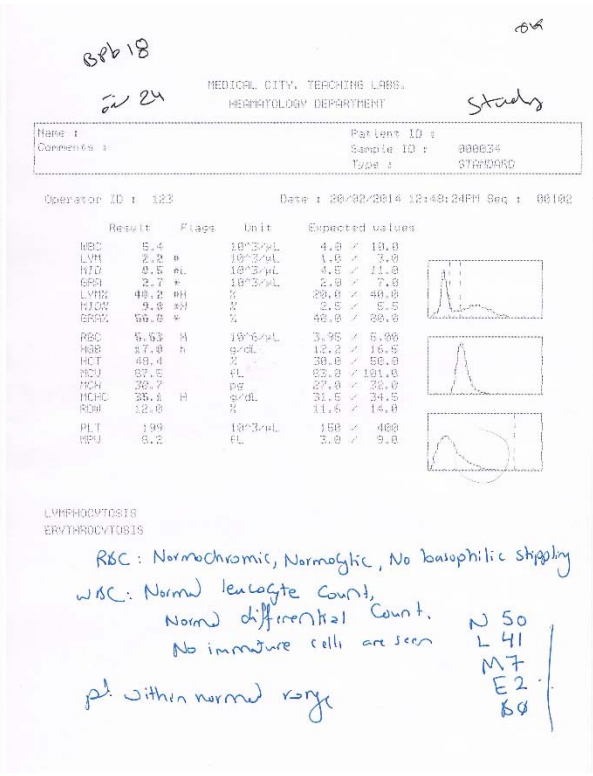
LIMIT SET
WBC 3.70-10.1
NEU 1.63-6.96 39.3-73.7 %
LYM 1.09-2.99 18.0-48.3 %
MONO .240-.730 4.40-12.7 %
EOS .030-.440 .600-7.30 %
BASO 0.00-.080 0.00-1.70 %

RBC 4.06-4.69 PLT 150.-450.
HGB 12.9-14.2 MPV 6.90-10.5
HCT 37.7-53.7
MCV 81.1-96.0
MCH 27.0-31.2
MCHC 31.8-35.4
RDW 11.5-14.5

BPb 13

N 64
L 29
M 6
E 1

RBC : normochromic with anisocytosis, no basophilic stippling seen
WBC : normal count, no abnormal cell seen
Plat : normal counts



BPb 18

MEDICAL CITY, TEACHING LABS.
HEAMATOLOGY DEPARTMENT

Study

Name :
Comments :

Patient ID :
Sample ID : 000034
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 12:48:24PM Seq : 00102

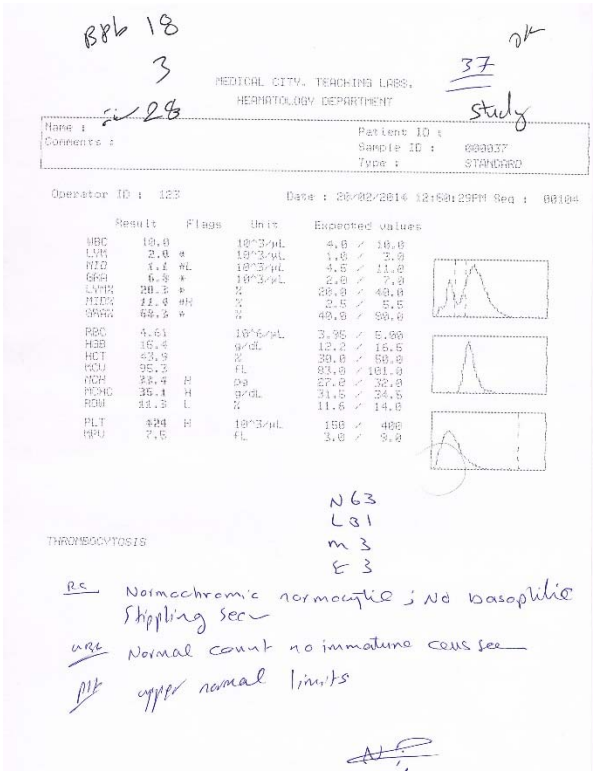
	Result	Flags	Unit	Expected values
WBC	5.4		10^3/uL	4.0 - 10.0
LYM	2.2	a	10^3/uL	1.0 - 3.0
MID	0.5	aL	10^3/uL	0.5 - 1.0
GRA	2.7	*	10^3/uL	2.0 - 7.0
LYMX	40.2	aH	%	20.0 - 40.0
MIDX	9.8	aN	%	2.5 - 5.5
GRAX	50.0	*	%	40.0 - 80.0
RBC	5.63	H	10^6/uL	3.95 - 5.00
HGB	17.0	h	g/dL	12.2 - 16.5
HCT	48.4		%	36.0 - 50.0
MCV	87.6		fL	83.0 - 101.0
MCH	30.2		pg	27.0 - 32.0
MCHC	35.1	H	g/dL	31.5 - 34.5
RDW	12.0		%	11.5 - 14.0
PLT	199		10^3/uL	150 - 400
MPV	8.2		fL	3.0 - 9.0

LYMPHOCYTOSIS
ERYTHROCYTOSIS

RBC : Normochromic, Normocytic, No basophilic stippling
WBC : Normal leucocyte count,
Normal differential count.
No immature cells are seen

Plt within normal range

N 50
L 41
M 7
E 2
B 0



BPb 18

3

MEDICAL CITY, TEACHING LABS.
HEAMATOLOGY DEPARTMENT

37

Study

Name :
Comments :

Patient ID :
Sample ID : 000037
Type : STANDARD

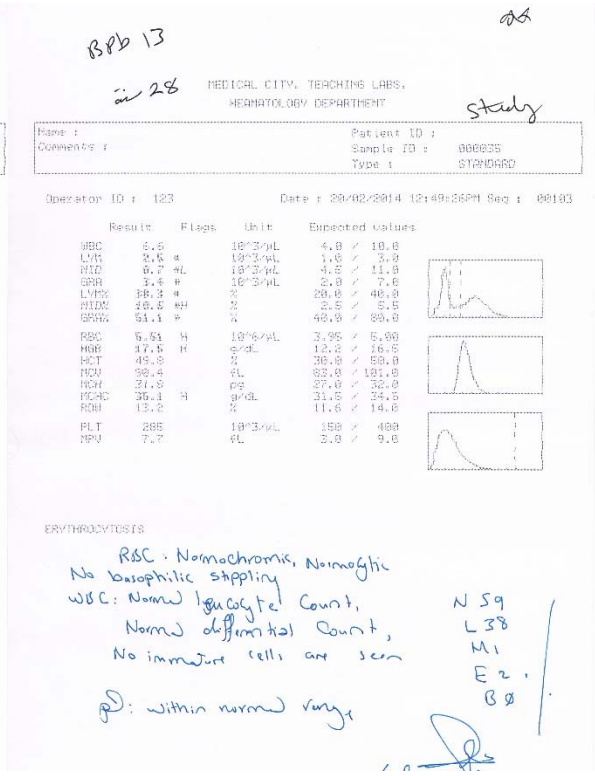
Operator ID : 123 Date : 20/02/2014 12:50:29PM Seq : 00104

	Result	Flags	Unit	Expected values
WBC	10.0		10^3/uL	4.0 - 10.0
LYM	2.0	a	10^3/uL	1.0 - 3.0
MID	1.1	aL	10^3/uL	0.5 - 1.0
GRA	6.9	*	10^3/uL	2.0 - 7.0
LYMX	20.3	*	%	20.0 - 40.0
MIDX	11.0	aN	%	2.5 - 5.5
GRAX	68.5	*	%	40.0 - 80.0
RBC	4.61		10^6/uL	3.95 - 5.00
HGB	15.4		g/dL	12.2 - 16.5
HCT	43.9		%	36.0 - 50.0
MCV	95.3		fL	83.0 - 101.0
MCH	33.4	H	pg	27.0 - 32.0
MCHC	35.1	H	g/dL	31.5 - 34.5
RDW	11.3	L	%	11.6 - 14.0
PLT	424	H	10^3/uL	150 - 400
MPV	7.5		fL	3.0 - 9.0

N 63
L 31
M 3
E 3

THROMBOCYTOSIS

RBC : Normochromic normocytic ; No basophilic stippling seen
WBC : Normal count no immature cells seen
Plt : upper normal limits



BPb 13

MEDICAL CITY, TEACHING LABS.
HEAMATOLOGY DEPARTMENT

Study

Name :
Comments :

Patient ID :
Sample ID : 000035
Type : STANDARD

Operator ID : 123 Date : 20/02/2014 12:49:26PM Seq : 00103

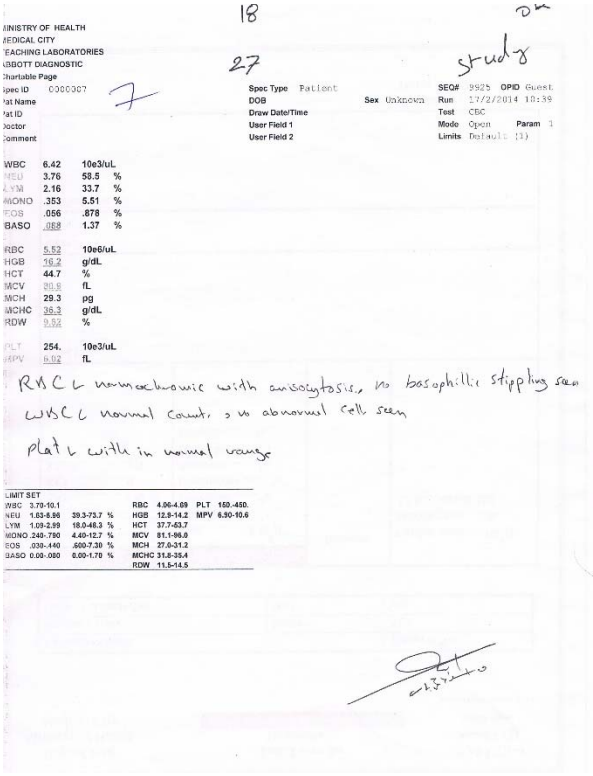
	Result	Flags	Unit	Expected values
WBC	6.8		10^3/uL	4.0 - 10.0
LYM	2.5	a	10^3/uL	1.0 - 3.0
MID	0.7	aL	10^3/uL	0.5 - 1.0
GRA	3.6	*	10^3/uL	2.0 - 7.0
LYMX	38.3	a	%	20.0 - 40.0
MIDX	10.5	aN	%	2.5 - 5.5
GRAX	51.1	*	%	40.0 - 80.0
RBC	5.51	H	10^6/uL	3.95 - 5.00
HGB	17.5	H	g/dL	12.2 - 16.5
HCT	49.8		%	36.0 - 50.0
MCV	90.4		fL	83.0 - 101.0
MCH	31.9		pg	27.0 - 32.0
MCHC	35.1	H	g/dL	31.5 - 34.5
RDW	13.2		%	11.6 - 14.0
PLT	285		10^3/uL	150 - 400
MPV	7.7		fL	3.0 - 9.0

ERYTHROCYTOSIS

RBC : Normochromic, Normocytic
No basophilic stippling
WBC : Normal leucocyte Count,
Normal differential Count,
No immature cells are seen

Plt : within normal range

N 59
L 38
M 1
E 2
B 0



MINISTRY OF HEALTH
MEDICAL CITY
TEACHING LABORATORIES
ABBOTT DIAGNOSTIC
Charitable Page

18
27
study

Spec ID 0000007
Pat Name
Pat ID
Doctor
Comment

Spec Type Patient
DOB
Draw Date/Time
User Field 1
User Field 2
Sex Unknown

SEQ# 9925 OPID Guest
Run 12/2/2014 10:39
Test CBC
Mode Open Param 1
Limits Default (1)

WBC	6.42	10e3/uL	
NEU	3.76	58.5	%
LYM	2.16	33.7	%
MONO	.353	5.51	%
EOS	.056	.878	%
BASO	.088	1.37	%
RBC	5.52	10e6/uL	
HGB	16.2	g/dL	
HCT	44.7	%	
MCV	80.9	fL	
MCH	29.3	pg	
MCHC	36.3	g/dL	
RDW	9.52	%	
PLT	254.	10e3/uL	
MPV	9.02	fL	

RBC ↓ normocytic with anisocytosis, no basophilic stippling seen
WBC ↓ normal count, no abnormal cell seen
Plat ↓ with in normal range

LIMIT SET

WBC	3.70-10.1			RBC	4.06-4.69	PLT	150.-450.
NEU	1.83-8.86	39.3-73.7	%	HGB	12.8-14.2	MPV	6.50-10.6
LYM	1.09-2.99	18.0-48.3	%	HCT	37.7-53.7		
MONO	.240-.790	4.40-12.7	%	MCV	81.1-96.0		
EOS	.030-.440	.500-7.30	%	MCH	27.0-31.2		
BASO	0.00-.080	0.00-1.70	%	MCHC	31.8-35.4		
				RDW	11.5-14.5		

دراسة تجويف الفمي بحثا عن علامات التسمم بالرصاص. ونصح االمشاركون بعدم التدخين، وتناول الطعام، أو شرب (ما عدا الماء) لمدة ساعة واحدة قبل جمع اللعاب. بعد شطف الفم بالماء جيدا، ثم جمع اللعاب غير المحفز في انبوب زجاجي مدرج لمدة خمسة دقائق . تم استخدام مقياس الطيف الامتصاص الذري للتحليل الكمي من الرصاص، وتحليل عينة من الدم عن طريق استخدام محلل الدم، تم اختبار الدم عن طريق فحص عينة الدم بالمجهر و فحص الترسبات اللعابية بعد تثبتها على شرائح من قبل اختصاصي بامراض الخلايا، وقد تم تحليل البيانات باستخدام برنامج الاحصاء IBM® SPSS® .

النتائج:

أظهرت نتائج هذه الدراسة فرق كبير بين مجموعة الدراسة (19 ميكروغرام / ديسيلتر) والمجموعة الضابطة (14.1 ميكروغرام / ديسيلتر) تشير إلى تعرض كبير لعوادم السيارات، ومستوى التلوث هو فوق المستوى الحرج من الرصاص (10 ميكروغرام / ديسيلتر) والتي قد تمثل زيادة في تلوث البيئة بالرصاص .

وكشفت هذه الدراسة ارتباط كبير جدا بين مستوى الرصاص في الدم ومستوى الرصاص في اللعاب في مجموعة دراسة والمجموعة الضابطة $P = 0.001$ و 0.018 على التوالي؛ كذلك لوحظ ارتباط كبير بين مستوى الرصاص في الدم مع المعلمات السريرية والخلوية الأخرى ، ولكن شوهد ارتباط ضعيف غير مهم بين هذه المعايير ومستوى الرصاص في اللعاب .

الاستنتاجات:

على الرغم من أن فكرة قياس مستوى الرصاص في اللعاب للرصد البيولوجي جذابة، النتائج التي توصلنا إليها لا تدعم استخدامه لهذا الغرض.

الخلاصة

خلفية الدراسة:

الرصاص هو من المعادن السامة واسعة الاستخدام التي خلفت مشاكل صحية كبيرة و سببت تلوث بيئي في أجزاء كثيرة من العالم. رجال شرطة المرور من السكان الأكثر تعرضا للرصاص من عوادم السيارات. هناك قلق متزايد بشأن الآثار الضارة المحتملة من الرصاص من عوادم السيارات على صحة رجال شرطة المرور .

في الوقت الراهن فان تقييم التعرض للرصاص بواسطة المختبرات يتم بالاعتماد على قياس مسوى الرصاص في الدم في المقام الأول. رغم أن عددا من الأنسجة والسوائل البشرية الأخرى، مثل اللعاب والأسنان والشعر والعظام و البول كلها تعكس التعرض للرصاص، اكتسب تركيز الرصاص في الدم كله قبولا واسعا باعتبارها أداة مفيدة للغاية للفحص والاختبارات التشخيصية، على الرغم من ذلك فقد اقترح اللعاب كبديل للدم لتقييم التعرض للرصاص باعتباره وسط بايولوجي غير غازي .

الهدف من الدراسة:

لدراسة إمكانية استخدام تركيز الرصاص في اللعاب كبديل لتركيز الرصاص في الدم وتقدير التاثيرات (السريرية, الدموية و الخلوية) التي يتعرض لها الفرد المتعرض الى الرصاص و تقييم تأثير عوادم السيارات على الصحة العامة .

الاشخاص, المواد وطرق العمل:

اجريت هذه الدراسة في الفترة المتدة من شهر كانون الثاني 2014 الى شهر نيسان من العام نفسه, تم فحص 53 شرطي مرور يعمل في مناطق الازدحام مدينة بغداد و 38 شخص من غير المعرضين بحكم المهنة للرصاص كمجموعة ضابطة. وافق مجلس الكلية على اجراء الدراسة، و قد أعطى المشاركون في البحث موافقات خطية للاشترك بالبحث و توفير المعلومات الشخصية و اعطاء العينات من اللعاب و الدم و استخدام الصور الشخصية لاغراض البحث ،تمت


وقل رب زدني علما
سورة طه : من الآية 114

جمهورية العراق
وزارة التعليم العالي و البحث العلمي
جامعة بغداد
كلية طب الاسنان

تقييم مستوى الرصاص في اللعاب وعلاقته مع الاعراض الفموية و القراءات الخلوية و الدموية في أفراد شرطة المرور في بغداد

رسالة مقدمة الى
كلية طب الأسنان
جامعة بغداد
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درجة الماجستير في
علم طب الفم

من قبل
علي عماد عبد الله
بكلوريوس طب و جراحة الفم و الاسنان
دبلوم عالي في التشخيص الفمي

باشراف
أستاذ مساعد
الدكتورة سحر حمدان

2014 م 1436 هـ