DISCUSSION

The incidence of thyroid disorders is increasing all over the world. As many as 50% of people in the community have microscopic nodules, 3.5% have occult papillary carcinoma, 15% have palpable goiters, 10% demonstrate an abnormal thyroid-stimulating hormone level, and 5% of women have overt hypothyroidism or hyperthyroidism.[17]

This high incidence of thyroid disorders suggested that there are hidden factors of thyroid disorders. Exposure to certain toxic chemicals may be one of these factors.[17] Over the last several decades, evidence has begun to emerge suggesting that there may be a connection between occupational exposure to certain toxic substances and thyroid diseases, including cancer and autoimmune thyroid disorder. [18]

In 2005, researchers at the Institute of Epidemiology and Social Medicine in Greifswald, Germany published the results of a study that found a connection between exposure to occupational hazards and thyroid autoimmune disorders. In that research, it was found that workers whose jobs involved a risk of exposure to ionizing radiation were at higher risk of developing autoimmune thyroid disease. Especially female workers who reported a history of on-the-job exposure to ionizing radiation were at particularly high risk of developing signs of thyroid autoimmunity. The researchers also suggested that these results may be an indication that occupational exposure may be the "missing link" that explains the sharp increase in the prevalence of thyroid autoimmune disorders over the last several decades. [19]

Another study identified that occupational risk factors are associated with thyroid cancer. Like thyroid autoimmune disorder, the incidence of thyroid cancer cases have skyrocketed in recent years, prompting some scientists to surmise that environmental factors -- including exposure to dangerous substances in the workplace -- may be to blame[18].

After analyzing the health data and work histories of a number of thyroid cancer patients, the researchers identified a number of risk factors that seemed to place workers at greater risk of developing the disease. Chief among these risk factors were occupational exposure to electromagnetic fields and industrial chemicals. [19]

Among these toxic substances that affect thyroid functions are perchlorate[20], thiocyanate[21], DDT[22] and lead. [23]

Thyroid hormone kinetics, are affected by lead toxicity. Central defect of the thyroid axis or an alteration in T4 metabolism or binding to proteins may be involved in derangements in thyroid hormone action. [84]

Moreover, it has been suggested that the nonspecific symptoms of inorganic lead intoxication are related to the effects of the blood lead on thyroid function. [86]

Our study aimed to explore the effect of lead exposure on thyroid functions in Alexandria occupationally exposed workers, and consisted of 100 male subjects from a factory for bullets and shots.

They were classified to 3 groups according to blood lead level:

Group I: 10-25 micrograms/dl

Group II: 26-40 micrograms/dl

Group III: 41-60 micrograms/dl

The results of this study revealed that the mean TSH level was higher in group III than in the other two groups and there was a significant difference between group I and III and between group II and III regarding it, and there was a significant positive correlation between BLL and serum TSH. Ft3, Ft4 and ATPO were normal in all groups and there was no significant difference between the three groups regarding them.

Our study was in accord with Singh, et al 2000[108] who investigated Fifty-eight men exposed to lead in petrol filling and automobile repair jobs in the city of Chandigarh, India aiming to evaluate the potential effect of blood lead levels on thyroid indices (T3, T4, and TSH) in workers from petrol filling stations and automobile repair market. He classified the exposed workers into tow groups; the first with BLL less than 41µg /dl and the second with BLL of40-70µg/dl. He found that no significant alteration was observed in the mean T3 and T4 levels of exposed workers. On the other hand, there was a rise in TSH associated with increasing levels of blood lead. This rise in TSH was independent of duration of lead exposure, the increase being more pronounced with mean BLL of 40-70µg/dl when compared with the group having mean levels of less than 41µg /dl. The similarities between our study and Singh's study may be attributed to the near ranges of BLL of both study subjects.

Pekcici, et al. 2009[109] who retrospectively examined the records of 65 men who had been exposed to lead while working as automotive mechanics or in battery factories, classified the lead-exposed workers into three groups according to their blood lead levels, as follows: 40 - 59 µg/dl, 60 - 79 µg/dl, or 80 µg/ dl and above. TSH levels were high in all three groups having different blood lead levels despite normal fT3 and fT4 levels. Raised TSH levels in the three groups may be due to the higher levels of BLL in Pekcici's study in comparison to our study.

Lopez CM, et al 2000[110] investigated a total of 75 males working in a factory making lead batteries that were exposed to lead for over 2 and up to 8 years. There was no statistically significant correlation between BLL and thyroid hormones and TSH in the whole population examined (BLL range 8–98 µg/ dl). These discrepancies between our present study and Lopez could be due to the fact that he studied exclusively and globally the total BLL-hormone ranges of the populations without classification, while in our study we classified and investigated every group according to BLL.

Cynthia Schumacher á C, et al 1998[111] used a cross-sectional design, assessing serum parameters of thyroid function in relation to the lead burden. T4, Ft4, and TSH were assessed for internal comparison of groups did not demonstrate evidence of altered pituitary-thyroid axis activity. Low to moderately exposed workers in this study (BLL

less than 60 µg/ dl) had generally normal FT4 and TSH levels, with no evidence being seen of exposure-dose-related alterations in thyroid function. Differences between our study results and those of Cynthia Schumacher may be attributed to different natures of both study subjects. In Cynthia Schumacher, 14% of the participants were current smokers and 82% reported current alcohol consumption. While our study subjects were neither smoker, nor alcohol consumer.

L IANG Qi-rong et al. 2003[113] investigated 157 workers occupationally exposed to lead in a smelting factory to explore the effects of lead on the thyroid function of occupationally exposed workers. The concentration of lead in air at workshop was measured by flame atomic absorption spectrophotometry (FAAS) and the levels of blood lead (BLL) by atomic absorption spectrophotometry (AAS), as well as TSH, T3, T4, FT3 and FT4 in serum by radioimmunoassay. The workers with higher level of blood lead showed lower levels of T3 and FT3 than those with lower blood lead level while TSH T4 and FT4 were normal in all workers. This study supports the idea that higher level of blood lead may cause certain damage to thyroid function by inhibiting de-iodination of T4.

Shahin soltani et al 2012, [115] Presented a cross-sectional study which investigated 195 male workers in a battery recycling factory in Iran. Thyroid function parameters were evaluated in relation to Blood Lead Level (BLL) then compared in two subgroups of blood lead level (<40 and ≥40 µg dL). Mean of BLL in study subjects was 43.44 µg / dL. There was no statistically significant difference in thyroid indices between workers with BLL<40 and workers with BLL ≥40. No evidence of linear correlation between blood lead level, and thyroid function parameters was observed after adjustment for potential confounders (age, BMI, cigarette smoking, duration of exposure). In contrast to our study, this study showed no thyroid dysfunction in different levels of blood lead level up to 85 µg dL. The limitation of Shahin study was using self reports of workers and lack of recent thyroid function estimation in contrary to our present study which used both laboratory and radiological tools for thyroid function assessment.

Regarding thyroid U/S in the present study, all the 3 groups showed many abnormalities regarding size and texture with the presence of multiple or solitary thyroid nodules. Group III had the highest percent of U/S abnormalities and there was significant statistical difference between group I&II, II&III and I&III.

Bumin Dundar, et al. 2006[112] conducted a study on 42 lead exposed adolescents and 55 healthy control subjects matched for demographic properties with the study group. The two groups have been living in the rural area. The study group consisted of randomly selected adolescent males trained by the National Education Ministry Apprenticeship Education Centers and working (5 days per week) in the auto repair workshops in the same city.Lead exposed adolescent workers were divided into three subgroups (A, B, C) according to the BLL: group A; 5 µg/ dl, group B; 5–10 µg/ dl, group C; 10 µg/ dl and above. FT4, FT3 and TSH were measured to evaluate thyroid functions. Thyroid ultrasounds have also been performed to assess thyroid volumes. FT4 levels were found to be significantly lower in the lead-exposed group than in the controls. There was no significant difference between the two groups in FT3 and TSH levels. U/S didn't reveal any thyroid abnormalities. This study supports the idea, that lead causes secondary hypothyroidism in contrary to our study. Differences between our present study and that one may be due to

different age of the study subjects and very low level of BLL in Dundar study in relation to our study subjects.

These laboratory and radiological changes in our study suggest that lead causes primary sub-clinical hypothyroidism due to direct damage to the thyroid gland without an auto immune evidence.

The present study revealed no significant difference between the three groups regarding duration of exposure and there was no significant correlation between BLL and duration of exposure of the study subjects. So, these laboratory and radiological changes in our study were independent of the duration of lead exposure.

When Singh[108] compared subjects according to duration of exposure, T3 was significantly low with the longer lead exposure time of 17.5 years in comparison with the group having lower mean exposure time of 2.4 years and this was in contrary to our results. The difference between the tow studies in T3 may be caused by the longer duration of exposure of Singh's study subjects"13.075 years" than the present study" 7.68years" or because that our study measured Ft3 while Singh measured total T3 and this is likely explainable by variations in thyroid-binding capacity.

Michael L. et al 2011 [114], recruited137 lead-exposed workers and 83 non-exposed workers to explore the effects of lead on the thyroid function of occupationally exposed workers. T4 was evaluated among all the study subjects, while FT4was evaluated among a subset of these workers. Exposure metrics included blood lead level (BLL), which reflects recent exposure, zinc protoporphyrin (ZPP), a marker of intermediate-duration lead exposure, exposure duration, and estimated cumulative exposure. Mean BLLs were 38.9 μg/dL in lead exposed workers and 2.1 μg/dL in non-exposed workers. While T4 was not significantly related to any of the exposure metrics, FT4 was inversely related to the logged values of both exposure duration and cumulative exposure, but not to ZPP or BLL. These findings suggest that FT4 levels may be related to long-term lead exposure. These results are in contrary with our present study which revealed no relation between any of thyroid hormone indices and duration of exposure to lead. This may be attributed to lack of information about cumulative effects of lead in our study.

Regarding blood pressure measurement, our study results revealed higher blood pressure measurements in group III than in the other 2 groups and there was a significant positive correlation between both systolic and diastolic Bp and lead. This was in agreement with Telisman S, 2004[116] who investigated 100 lead exposed workers and found that long-term cumulative lead exposure, which is reflected by ZZP, can significantly increase blood pressure in moderately lead exposed male workers.

Regarding lipid profile in our study, there was significant difference between group I and group III and between group II and group III regarding serum cholesterol level, and there was significant difference between group I and group II and between group II and group III regarding serum TG level. This was in agreement with Shyam Vinay Sharma,et al 2012[117] who investigated battery workers in order to discover the effects of lead exposure on risk of cardiovascular disease and he revealed that lead causes increase in serum cholesterol, triglyceride and LDL cholesterol with a decrease in HDL cholesterol.

SUMMARY

The incidence of thyroid disorders is increasing all over the world. As many as 50% of people in the community have microscopic nodules, 3.5% have occult papillary carcinoma, 15% have palpable goiters, 10% demonstrate an abnormal thyroid-stimulating hormone level, and 5% of women have overt hypothyroidism or hyperthyroidism. This high incidence of thyroid disorders suggested that there are hidden factors of thyroid disorders. Exposure to certain toxic chemicals may be one of these factors. Over the last several decades, evidence has begun to emerge suggesting that there may be a connection between occupational exposure to certain toxic substances and thyroid diseases, including cancer and autoimmune thyroid disorder.

Among these toxic substances that affect thyroid functions are Perchlorate, Thiocyanate, DDT and lead.

Lead is a chemical element in the carbon group with symbol Pb 2. Lead is a soft and malleable metal, which is regarded as a heavy and poor metal.

Lead is a health risk factor leading after high-grade exposure to poisoning. It is rapidly absorbed into the bloodstream then accumulates in the body and exerts toxic effects especially on the central nervous system, the cardiovascular system, kidneys and the endocrine system.

The action of lead includes damage to cell membranes and disorders of the oxido-reductive processes in the cells because it interferes with a variety of enzymes as it binds to sulfhydryl groups found on many enzymes. Part of lead's toxicity results from its ability to mimic other metals like calcium, iron and zinc that take part in biological processes, which act as cofactors in many enzymatic reactions thus interfering with the enzyme's ability to catalyze its normal reaction.

Thyroid hormone kinetics, are affected by lead toxicity. Central defect of the thyroid axis or an alteration in T4 metabolism or binding to proteins may be involved in derangements in thyroid hormone action. Moreover, it has been suggested that the nonspecific symptoms of inorganic lead intoxication are related to the effects of the blood lead on thyroid function.

Our study aimed to explore the effect of lead exposure on thyroid functions in Alexandria occupationally exposed workers, and consisted of 100 male subjects from a factory for bullets and shots and exclusion criteria were past history or family history of thyroid disorders, diabetes mellitus, drugs that affect thyroid function and smoking. Investigation done included: CBC FBS AST ALT urea acreatinine Cholesterol, TG, Ft3, Ft4, TSH, ATPO, BLL and thyroid U/S.

Study subjects were classified to 3 groups according to blood lead level:

Group I: 10-25 micrograms/dl
Group II: 26-40 micrograms/dl
Group III: 41-60 micrograms/dl

The results of our study revealed that:

There was significant difference between group I and III and between group II and III with a significant positive correlation between blood lead level and serum TSH level.

No significant difference between the three groups regarding Ft3, Ft4or ATPO.

Regarding thyroid U/S, all the 3 groups showed many abnormalities regarding size and texture with the presence of multiple or solitary thyroid nodules. Group III had the highest percent of U/S abnormalities and there was significant statistical difference between group I&II, II&III and I&III.

There was significant difference between group I and group II, between group I and group III and between group II and group III regarding systolic and diastolic Bp with a significant positive correlation between blood lead level and Bp measurements.

There was significant difference between group I and group III and between group II and group III regarding serum cholesterol level. No significant correlation between BLL and serum cholesterol level.

There was significant difference between group I and group II and between group II and group III regarding serum TG level. No significant correlation between BLL and serum TG level.

In conclusion; Lead causes abnormal changes in thyroid gland structure "subclinical hypothyroidism " without an autoimmune evidence, in occupationally exposed workers, Mild to moderate hypertension and hyperlipedemia, manifested by increase in serum cholesterol and triglyceride levels. All the previously mentioned effects of lead are not related to the duration of exposure.

CONCLUSIONS

1. Lead causes abnormal changes in thyroid gland structure in occupationally exposed workers.

2. Subclinical hypothyroidism is the most common abnormal thyroid function found in lead exposed workers.

3. Mild to moderate hypertension is a common cardiovascular effect of lead.

4. Hyperlipedemia, manifested by increase in serum cholesterol and triglyceride levels in exposed workers, is one of the commonest lead effects.

5. All the previously mentioned effects of lead are not related to the duration of exposure.