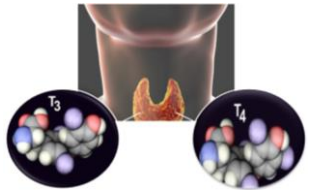

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Deviations in Thyroid and its Regulatory Hormone Profile in Workers Exposed to Welding Fumes

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ABSTRACT: *This study evaluates health risks manifested by the exposure of welding fumes to the labourers working in welding environments. Welding fumes, are the complexes of fluorides, silicates and metal oxides, cause burns, eye damage, hormonal imbalance, organ damage and cataracts. In order to check the changes caused by fumes on thyroid gland, a study was planned to evaluate the variations in thyroid regulatory hormone levels in workers occupationally exposed to welding fumes. For this purpose, blood sampling of the welders (n=24) having exposure to welding fumes was done from different sites in city Lahore, whereas, blood samples of healthy controls (n=24) were collected from University of the Punjab, Lahore. Thyroid (T3 and T4) and its regulatory hormone (TSH) assessment was executed by ELISA. Independent student "t" test at confidence interval of 95% and $P < 0.05$ was applied. A non-significant decrease of both hormones i.e. T3 and T4 was found in the subjects under study as compared to controls. Levels of TSH in blood serum of workers showed a non-significant increase than healthy controls. Elevated TSH and reduced T3 and T4, although, statistically non-significant, predict chances of hypothyroidism due to chronic exposure to welding fumes. Welders are, therefore, recommended to adopt prophylactic measures and safer techniques in order to avoid direct hazardous exposure to welding fumes.*

Keyword: *TSH, T3, T4, ELISA, Welding Fumes, Thyroid*

INTRODUCTION

The environment at the occupational site is of prime importance. This environment serves for the health and working capabilities of workers (Kumara, 2001). Each occupation possesses some degree of risk to the workers and expresses some sort of disease. The risk may be due to physical, or chemical exposure (Gulani, 2008).

The thyroid gland, a vital endocrine gland responsible for producing thyroid hormones (T_3

and T_4) which regulates growth, development and basal metabolic rate (Sarkar, 2015). Thyroid is a butterfly shaped gland, has two lobes; one left and the other right separated by isthmus (Marshall and Bangert, 2008). The gland has thousands of follicles made of thyrocytes with colloid lumen on adjacent sites. This acts as precursor site for thyroglobulin storage. The recommended dose for iodine is 150 µg a day, 1mg per week or 50 mg per year (Triggiani, 2009).

The World Health Organization (WHO) reports an estimated 250 million injuries posed yearly due to work hazards. Out of these the development countries are faced with welding related risks (Sabitu et al., 2009).

In welding, metal objects are joined by means of another metal that acts as filler. The filler is an electrode wire utilized in joining. High level of temperature serves for welding purpose that resultantly produce fumes by welding along with sheer noise and radiation (Antonini, 2003).

Evidences pertaining to toxic fine and ultrafine particles in welding fumes has been reported (McNeilly et al., 2004; Dybdahl et al., 2004; Hirano et al., 2003). Welding, a common indispensable procedure in industry has wide ranging health hazards that include ultraviolet (UV), infrared radiation (IR) exposure. It also includes electrocution, thermal burns, electromagnetic exposure and heat stress (Chauhan et al., 2014).

Retinal damage due to excessive exposure to arc welding can result (Park et al., 2021). Metal fume fever (MFF) can result due to excessive fumigation of various metal atoms involved. This results in influenza like conditions and another respiratory dysfunctions (Ashby, 2002).

MFF largely due to excessive exposure to fumes induces cancer of lungs and larynx to welders (Taylor et al., 2003; ATSDR, 2008). However, the duration of exposure, welding type, the environment and protective equipment can determine the health risk of welders (Palmer et al., 2009).

Thyroid gland plays a vital role in controlling the development and metabolism. Thyroid function is affected by metals due to occupational exposure (Benvenga et al., 2020). Environmental chemicals play vital role in this

regard (Pearce and Braverman, 2009; Boas et al., 2009; Blount et al., 2006; Zoeller, 2005). Polychlorinated biphenyls (PCBs), phthalates, per fluorinated compounds along with metals have relations to thyroid functioning (Pearce and Braverman, 2009; Kashiwagi et al., 2009)

A number of processes generate welding fumes resulting oxidative stress. In welding above 90% of particulates are by electrode filling metal vaporization, core and coating like in arc welding and least to laser beam welding (Shoham et al., 2008). Transformed nanoparticles of metal oxides are formed (about 1%) by condensation of metallic vapors and these nanoparticles after association form particle agglomerates (Sengul et al., 2020).

In children and adults, thyroid hormones have a crucial role in functioning of cardiovascular, nervous and reproductive system (Williams 2008; Danzi and Klein, 2012; Yazbeck and Sullivan, 2012). The main hormones are thyroid stimulating hormone (TSH), tri-iodothyronine (T_3) and thyroxine (T_4). A very small portion of free form of T_3andT_4 enter the cells (<1%). There is negative feedback mechanism between these hormone (Holt and Hanley, 2021). T_3 and T_4 synthesis is by stimulation of TSH. For homeostasis purpose in body, high T_3 levels suppress TSH production while low T_3 andT_4 stimulate the production. Anomaly in thyroid function is usual. A study in US proposed 4.6% of the population faced with hypothyroidism while 1.3% suffers from hyperthyroidism (Hollowell et al., 2002).

Several anomalies are there because of exposure of workers to welding fumes. The current study is aimed to access thyroid and its regulatory hormone levels (T_3 and T_4 and TSH, respectively) among the workers occupationally exposed to welding fumes.

MATERIALS AND METHODS

Experimental Design

Institutional ethical review committee, Institute of Zoology, University of the Punjab Lahore, endorsed the study plan. Welders (n=24) from welding sites of Lahore and healthy controls (n=24) from University of The Punjab were engaged for current case-control investigation.

A comprehensive, self-explanatory proforma was prepared. Information from every participant of both groups was filled in this predesigned proforma. This proforma included information like sample id, name, gender, body mass index (kg/m^2), incidence of any disease, medication, drug addiction and smoking.

Exclusion and inclusion

Individuals not having any history of ailment were included in this study. However, any individual having hepatic, diabetic, renal or any other viral infection were excluded from the investigation. As diseased condition can have impact on outcomes of the study.

Blood Sampling and Processing

Blood samples from all the subjects of both groups were collected after 12 hours overnight fast. Since human were the participants of the study, hence, all precautionary measures were taken. A registered technician was engaged for the purpose of phlebotomy.

Becton and Dickinson (B.D) syringes having sound reliability, originality, in terms of proper sterilization were employed. Also, an expert technician was hired to take the blood from peripheral vein of subjects. During sampling, the part of skin facing peripheral vein was disinfected by rectified spirit. B.D syringe was injected in persons' vein at approximate 45° angle prudently and 5ml of blood was withdrawn, keeping the person sitting and then drained in vaccutainer tubes. After 30-40 minutes, subject's samples were centrifuged (3,000 rpm) for about 10 minutes and serum (supernatant) was separated. The Eppendorf tubes that contained serum was labelled and stored at -80°C. Serum samples were thawed appropriately at room temperature of lab before biochemical analyses.

Hormonal Analyses

The concentration of the tri-iodothyronine (T_3), thyroxine (T_4) and thyroid stimulating hormone (TSH) in controls and welders blood serum were estimated by commercially available ELISA (Enzyme-Linked Immunosorbent Assay) kits in Physiology/Endocrinology laboratory, University of the Punjab, Lahore.

Statistical Analysis

Statistical analysis was done using latest version of Graph Pad Prism version 6.00 software. Results were demonstrated as Mean ± SEM. Un-paired student T test with 95% confidence intervals and $P< 0.05$ was applied to determine variations among the studied groups.

RESULTS

The levels of TSH in controls and welders compared and a non-significant increase of 47.48% was recorded in the blood samples of workers as compared to healthy controls (Fig. 1). An average value of TSH in controls and welders was found to 0.94 ± 0.18 and 1.33 ±0.20 µIU/mL, respectively (Table 1).

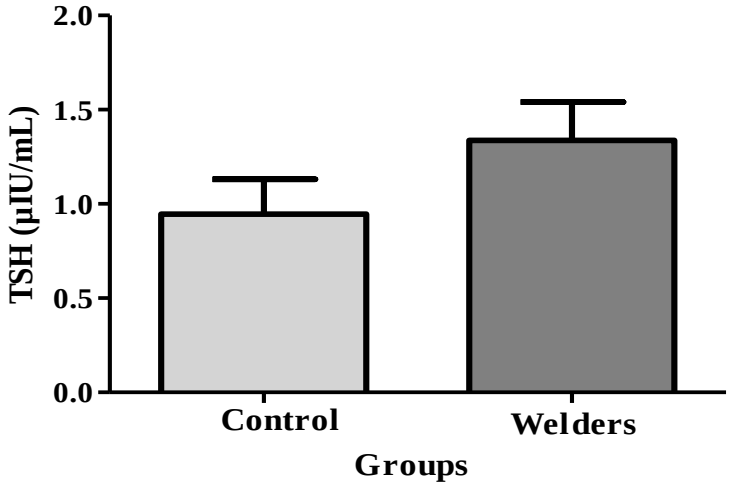

Fig. 1. Levels of serum TSH (µIU/mL) in control and welders

In controls, the approximate mean value of T_3 was 1.47 ± 0.052 (ng/mL) and among the workers it was found to be 1.41 ± 0.057 (ng/mL). The decrease in serum T_3 concentration for workers was a non-significant (Confidence level; 95%, *P* =0.79) (Table 1).

Table 1: An overall comparison of serum thyroid and its regulatory hormone in controls and welders (Mean ± SEM)

Parameters	Control	Welders	t value	P-value	Difference
TSH (µIU/mL)	0.94 ± 0.18	1.33 ± 0.20	t=1.41	0.16	47.48↑%
T_3 (ng/mL)	1.47 ± 0.05	1.41 ± 0.05	0.25	0.79	4.08↓%
T_4 (µg/mL)	41.87 ± 2.51	39.74 ± 2.46	1.10	0.54	5.08↓%

TSH: Thyroid Stimulating Hormone, **T_3:** Tri-iodothyronine, **T_4:** Tetra-iodothyronine, **↓:** decrease, **↑:** increase, **µIU/mL:** micro international unit per milliliter, **ng/mL:** nanogram per milliliter, **µg/mL:** microgram per milliliter

It was noticed the levels of T_3 hormone higher in controls as compared to workers (Fig. 2).

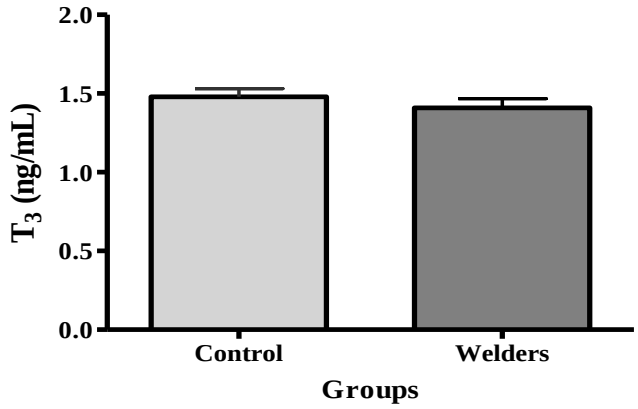

Fig. 2. Levels of serum of Tri-iodothyronine (ng/mL) in control and welders

In controls, the approximate mean value of T_4 was found to be 41.87 ± 2.51 (ng/mL). Among the workers it was calculated as 39.74 ± 2.46 (ng/mL). The decrease in serum levels for T_4 in workers was found non-significant (Confidence level; 95%, *P* value=0.27) (Table 1). The levels of T_4 was noticed higher in controls as compared to workers (Fig. 3).

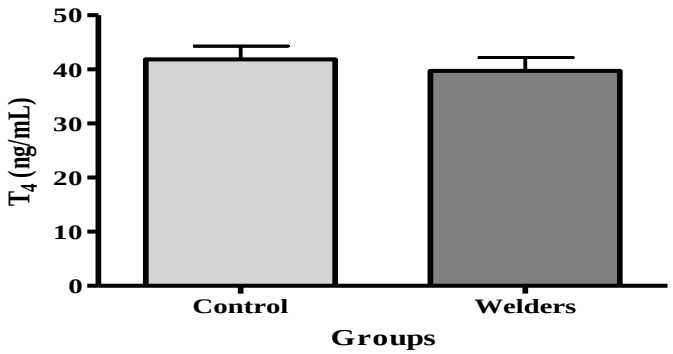

Fig. 3. Levels of serum of Thyroxin (ng/mL) in control and welders

DISCUSSION

Thirteen types of metals are associated with welding fumes that include vanadium (V), manganese (Mn), lead (Pb), chromium (Cr), molybdenum (Mo), zinc (Zn),cobalt (Co), beryllium (Be), mercury (Hg), antimony (Sb), nickel (Ni), cadmium (Cd), copper (Cu) and iron (Fe). Due to chronic Mn exposure particularly to welders cause health risks. Exposure to Mn can also promote the spread of Parkinson's disease that may be a risk factor among welders. While, neurogenic disorders may be caused due to change in the homeostasis of Mn and Fe (Li et al., 2004).

Main constituent of welding fumes includes Mn, Fe and Zn. Whereas, Pb, Cr, and Ni serve as trace elements and can cause change in functioning of thyroid gland. High temperature and exposure to radiations also have an impact on functioning of thyroid (Shakeel et al., 2022).

Welding fumes are formed by complex binding of metal oxides with gases. Metal oxides are the result of oxidation of metal alongside vaporization during welding (McNeilly et al., 2004). Nano particles found in fumes are produced by welding. These fumes pass into blood stream from respiratory tract and in meantime result

in toxic outcomes if they are accumulated in extra pulmonary organs (Roth, 2006). These are accompanied with occupational disorders in welders. Change in functioning of kidney and liver are a result of their inhalation (Antonini, 2003). Inspiration of these particles and gases bring alternations in the kidney and liver physiology (Dumkova et al., 2016).

The disorder of thyroid gland is quite common in Pakistan and hence public's major health burden. Causes are still not understood but considerable findings accomplish chemical exposure in the environment (Iqbal et al., 2016).

The hormones of thyroid are pivotal to regulation of metabolism, differentiation and development. Any amelioration associated with the thyroid biology disrupts whole metabolic machinery in human (Heussen et al., 1993).

Thyroid functioning is properly managed by the levels of T_3, T_4 and TSH that indicate normality in of the gland. Any anomaly in functioning can affect metabolism of thyroid. Calibrating thyroid hormones level in blood can account for proper thyroid working (Yousif and Ahmed, 2009).

The current study highlights evaluates alterations in the levels of TSH, T_3 and T_4 due to welding fume exposure. The blood serum levels for TSH, T_3 and T_4 were analyzed and compared to normal healthy persons.

On the basis of this investigation, abnormal levels of TSH alongside lesser deviations of T_3 and T_4 levels were found. Thyroid dysfunction resulting from compensatory increase in TSH levels have been observed previously by Mortavazi et al. (2009). Consequently, hypothyroidism accompanied with increased risk for coronary artery disease can be anticipated in these workers. Hypothyroidism whether primary or secondary is associated with hyperlipidemia. Thus, decreasing the levels of circulating lipids is the treatment to reduce cardiovascular risks (O'brien et al., 1993).

Thyroid hormones play a major role in spermatogenesis (contrary to previous findings). Evidences of thyroid receptors on nurturing cells for sperms in testis and sertoli cells has accounted research for hormones of thyroid in male reproduction. As sertoli cells back spermatogenesis therefore significant regularity role is played on part of thyroid gland in sperm production. Hence, male fertility alongside spermatogenesis is affected by thyroid malfunctioning (Singh et al., 2011).

In females no significant influence on ovulation rate resulted due to hypothyroidism rather lesser number per litter of implantation sites were reported (Hapon et al., 2010).

Acquired and congenital hypothyroidism can also result in loss of hearing, evidenced both in clinical and laboratory studies (morphological, biochemical, and electrophysiological findings) testify the hypothesis that cochlea is harmed owing to sensory neural loss of hearing in hypothyroidism. Hence, change in middle ear is responsible for conductive component (Villaume et al., 1978).

Clinical hypothyroidism present increased cardiovascular risk and also the patients with sub clinical hypothyroidism exhibit several potential cardiovascular risk factors. Recently, more data has become available indicating mild hypothyroidism affecting cardiovascular system. In patients with mild deficiency of thyroid hormone caused by impairment in function of left ventricular diastole, consistency in cardiac abnormality has been observed (Biondi, 2008).

Involvement in production and regulation of thyroid hormones by contaminants of environment are immense (Zoeller, 2005; Boas et al., 2006; Pearce and Braverman, 2009). Like in T_4 to T_3 conversion, selenium ion accepts the iodine atom released by deiodinase enzyme (Holt and Hanley, 2021). Both selenium and methyl-mercury hold high affinity for each other. Hence, increase in concentration of methylmercury holds selenium, making the thyroid conversions impossible (Soldin et al., 2008; Ursinyova et al., 2012). Substances having percholate and nitrate cause decrease in thyroid's iodine concentration through competitively inhibiting symporter for sodium/iodine leading decreased T_3 and T_4 (Leung et al., 2010; Pearce and Braverman, 2009). Polychlorinated biphenyls and polybrominated diphenyl ethers, that serve as environmental chemicals become structurally similar to thyroid hormones and directly bind to their receptor sites or transporters (Pearce and Braverman, 2009). After binding they can act as agonists or like antagonists.

Certain exposures cause a dysfunction in the thyroid gland secretion that may include hypothyroidism and hyperthyroidism accompanied by abnormality in other organs and systems.

CONCLUSION

The present investigation concluded that welders have chances of manifesting hypothyroid conditions due to the hazardous fumes associated with the welding procedure. Hence,

hypothyroid conditions in these laborers can prognosticate cardiovascular risks, fertility problems in males and associated ailments. Moreover, appropriate personal protective equipment's and prophylactic measures at site of work must be addressed in this sect of workers. There is also need for ample research by quantifying the effects and duration of exposure on health of these welders. As such exposure may have chronic effects on human beings.

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