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Alterations in Hepatorenal Profile of Occupationally Exposed Workers to Welding Fumes

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ABSTRACT

Welding fumes contain enormous harmful toxicants including Cadmium (Cd^{2+}), iron (Fe^{2+}), aluminium (Al^{3+}), manganese (Mn^{2+}), zinc (Zn^{2+}) and their derivatives that can give rise to multiple chronic ailments in individuals exposed to them. Present investigation was designed to estimate the harmful effects of welding environments on hepatic and renal profile of welders. Blood samples of welders (n=30) and controls (n=30) were collected from Shakargarh-Punjab. Hepatorenal parameters were assessed by the medical chemistry analyser using commercially available diagnostic kits for each parameter. At confidence interval (CI) of 95% ($P \leq 0.05$), independent sample t-test was applied for statistical analysis. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) and showed non-significant decrease in welders as compared to controls. While, Alkaline phosphatase (ALP) and bilirubin exhibited highly significant increase ($P \leq 0.0001$ and $P \leq 0.01$, respectively) in welders as compared to controls, respectively. A prominent decrease was observed in creatinine ($P \leq 0.02$) and urea ($P \leq 0.0004$) in labours of the welding industry as compared to controls. Whereas, in serum electrolytes; K^+ ($P \leq 0.005$) and Cl^- ($P \leq 0.002$) demonstrated a considerable elevation, while Na^+ showed a non-significant difference in welders when compared to controls. Thus, our investigation showed that welding fumes and its related constituent's exposure bring disturbance in hepatic and renal physiology due to variations in respective parameters in welders. Therefore, welders are recommended to use safe techniques such as masks on face to prevent inspiration of harmful gases and related toxic compounds, glasses on eyes, gloves on hands for good health.

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NR: Supervision of the investigation
FL: Biochemical analysis
HA: Acquisition of data from participants

Key words
ALT, AST, ALP, Creatinine, Liver function enzymes, Heavy Metals, Renal function test

INTRODUCTION

Welding is an industrial practice in which joining of metallic objects is performed by using metal as a filler. The filler, in turn, is created from a wire of electrode utilized during the welding fusion method (Antonini, 2003). Workers in the welding industry are exposed to fumes, primarily through skin contact and inhalation. These fumes are chief contributors to deviations in various bodily mechanisms that could ultimately lead to the manifestation of different ailments (Liden and Surakka, 2009) Welders can also get a considerable quantity of these toxicants, while, eating or drinking with dirty hands through contaminating their food or liquid.

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The materials typically found in welding fumes include chromium (Cr), aluminium (Al), nickel (Ni), copper (Cu), beryllium (Be), lead (Pb), manganese (Mn), molybdenum (Mo), vanadium (V), fluoride (F^-), oxides of cadmium (CdO), iron oxides (FeO) and zinc oxides (ZnO). Gases are also produced during the welding process. Main gases are hydrogen fluoride (HF), nitrogen oxides (NO_x), carbon monoxide (CO), fluorine (F) and ozone (O_3) (Liu *et al*., 2007).

A variety of mechanisms could be involved in generating welding fumes. More than 90% of the particles of fumes in welding are produced by the electrode filling metal vaporization, core and coatings as in arc welding and to a lesser degree, in laser beam welding (Schnick *et al*., 2010). Welding fumes can be of various forms. Particulates in the welding fumes can be classified into three groups based on their sizes: coarse (d > 2.5µm), fine (0.1 < d < 2.5µm) and ultrafine (0.01 < d < 0.1µm) (Jenkins, 2003). Overall, exposure of these environmental toxicants can induce epigenetic changes in these occupationally exposed subjects (Feinberg, 2018). Pathological symptoms that appear due to an exposure to welding fumes have been associated with systemic and respiratory health effects, such as a decline in the lung function, enlarged air passage sensitivity, bronchitis, lung cirrhosis, fibrosis, and a large number of pulmonary disorders including emphysema, chronic bronchitis and asthma (Antonini *et al*., 2013; Kim *et al*., 2005). These systemic conditions are produced by inspiration of oxides of zinc (Draznin and Epstein, 2011) in fumes and are categorized by onset of acute flu-like sickness with dry cough, muscle aches, headaches, dyspnea and fever (McHugh, 2010).

Additionally, several respiratory dysfunctions such as asthma, bronchitis, changes in the lung function as well as cardiovascular complications have been attributed to the chronic exposure to welding fumes (Leso *et al*., 2019). Welding fumes including Be and Cr may get absorbed by the skin causing allergy and irritation. Absorption by skin is further boosted by ultrafine particles and via cuts or other injuries to the skin (Nygren, 2006). Welding fumes are also linked to the metal fume fever (MFF), inflamed oral and nasal cavity (El-Zain *et al*., 2003; Greenberg and Vearrier, 2015) and cardiovascular abnormalities. Many investigations have also demonstrated an increased mortality due to ischemic heart disease in the welders, who have had a prolonged exposure to welding fumes (Ibfelt *et al*., 2010; Fan *et al*., 2014; Li *et al*., 2015).

Biomonitoring of blood is essential to assess the level of toxicity in exposed workers. This study was designed to evaluate sickness pattern, attentiveness of work-related threats such as the effects of long-term welding fume exposure on hepatorenal profile of the welders working in such environment.

MATERIALS AND METHODS

A case-control study was designed for the welding fume workers. For this purpose, blood samples of age matched (20-45) welders (N=30) and controls (N=30) were collected from Shakargarh, Punjab, Pakistan. It was assured that samples were collected after 8-12 h of fasting with their consent. Only male workers were recruited for the present investigation as in Pakistan welding process is specifically associated with males.

A systemised proforma was made to document demographic variables of both groups. Participants noticeables such as sex, height, weight, waist, blood pressure, hip circumference, drug usage, family history of illness, smoking history, working experience were documented. Parameters regarding the health perspective of all individuals were attained before phlebotomy. Reliable and sanitized syringes of Becton Dickinson (BD) Pakistan were utilised for withdrawing the blood from all participants. For this purpose a registered medical laboratory technician was hired.

Blood samples were centrifuged (Model; Hettich, Zentrifugein D-7200 Tuttligen, Germany) at 2500-3000 rpm for about 10 min, for separation of blood serum which was stored at -80 ºC for future biochemical investigations.

Commercially available kits of Beckman Coulter USA, were used for determination of hepatic and renal metabolites through Chemistry analyser (Beckman Coulter USA, Model AU480).

Two tailed independent sample t-test at Confidence Interval (CI): 95%; $P \leq 0.05$, was applied for statistical analysis. All Statistical exploration was performed on GraphPad Prism 6.00 software.

RESULTS

Body mass index expressed highly significant ($P \leq 0.0005$) decrease of 17 % in welders as compared to control group. In hepatic profile, alanine aminotransferase (ALT) presented a non-significant decrease of 15% in welders as compared to controls. Moreover, the same trend was witnessed in the aspartate aminotransferase (AST) levels in comparison of welders and control group. The level of alkaline phosphatase (ALP) was significantly ($P \leq 0.0001$) increased in welders as compared to control group. Similarly, concentration of bilirubin expressed a significant ($P \leq 0.01$) increase of 37% in welders as compared to control group (Table I). In renal metabolites, creatinine levels demonstrated significant ($P \leq 0.02$) decrease of 20% in welders as compared to control group. Moreover, serum concentration of urea depicted a prominent ($P \leq 0.0004$) decrease of 32% in welders as compared to control group. In serum electrloytes, workers of welding industry presented slight increase of 1% of Na^+ concentration as compared to control group. In addition to that, K^+ expressed significant ($P \leq 0.005$) increase of 8% in welders' group as compared to healthy controls. Comparing serum chloride Cl^- levels indicated a considerable ($P \leq 0.002$) elevation of 8% in welders when compared to controls (Table I).

DISCUSSION

Liver diseases are the most common health conditions in all over the world. A massive diversity of chemicals, microbes and especially viruses are renowned liver damaging agents (Stankova *et al*., 2010).

Under occupationally exposed conditions, inhalation of certain hazardous substances cause damage to the hepatic lobules that contain parenchymal cells which ultimately are unable to perform vital roles, resulting in distressed and unprovoked intermediate metabolism. It can lead to cellular destruction and tissue necrosis. These substances enhance the permeability of hepatic bio-membranes,

Table I. Effect of metal welding funes on hepatorenal profile concentrations in blood samples of control and welders.

Parameters	Control (N=30)	Welders (N=30)	t value	p value	Difference %
ALT (U/L)	50.62±9.96	43.23±3.93	0.80	0.4	15 ↓
AST (U/L)	37.31±4.65	35.45±2.47	0.38	0.7	5 ↓
ALP (U/L)	103.20±6.41	215.10±7.20	10.54	< 0.0001***	108 ↑
Bilirubin (mg/dL)	0.63±0.04	0.86±0.06	2.53	0.01**	37 ↑
BMI (kg/m^2)	25.13±1.00	20.92±0.59	3.85	0.0005***	17 ↓
Creatinine (mg/dL)	0.79±0.08	0.63±0.01	2.37	0.02*	20 ↓
Urea (mg/dL)	30.54±2.74	20.91±0.99	3.91	0.0004***	32 ↓
Na^+ (mmol/L)	139.5±0.64	141.1±0.61	1.70	0.09	1 ↑
K^+ (mmol/L)	3.73±0.09	4.02±0.04	3.01	0.005**	8 ↑
Cl^- (mmol/L)	98.08±0.78	100.8±0.43	3.25	0.002**	8 ↑

↑ and ↓ represents increase and decrease, respectively, mmol/L = millimole per litre, mg/dL = milligram per decilitre. ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; BMI, body mass index.

ultimately leading to elevated levels of hepatocellular enzymes in plasma (Center, 2007). Elevation of these enzymes in serum above a normal range presents degree of destruction in liver morphology as well as hepatocytes malfunction (Louvet and Mathurim, 2015).

Both ALT and AST are related to the transaminase group of enzymes. The main sites for the production of ALT is generally are hepatocytes. It is also produced in minute quantity in extrahepatic tissue comprising kidney, heart and muscle mass. While, AST is generally produced in several body organs such as kidney, lungs, heart, muscle and brain (Louvet and Mathurim, 2015; Afalobi *et al*., 2018, 2020). Estimation of the activity of ALT, AST, ALP as well as total bilirubin are renowned markers for assessment of liver function (Adaramoye *et al*., 2008). Current study was intended to analyse the effect of welding fumes exposure on hepatic and renal profile of experienced welders in comparison with controls. In our study, ALT and AST of welders showed non-significant decrease as compared with control. However, ALP level of welders demonstrated highly significant increase as compared with control, which may indicate the presence of hepatocyte injury.

In an investigation, workers facing metal fumes showed significant increase in biomarkers of liver physiology (Orisakwe and Nduka, 2009) similar to the contaminated metallic fumes of welding exposure. Heme-oxygenase metabolic activity in our body yields a natural product known as bilirubin, which has been documented as an effective antioxidant, whether it is unconjugated or conjugated, free or albumin bound (Neuzil and Stocken, 1994; Wu *et al*. 1996).

In our study, bilirubin of welders depicted prominent increase as compared with controls. This increase of total bilirubin level may indicate the chances of haemolytic jaundice, cardiovascular diseases and malaria. Gul *et al*. (2013) presented that high bilirubin concentration in serum can independently results in acute myocardial infarction in patients having ST-segment elevation in hospital, who undergo primary percutaneous coronary interference.

Welding fumes containing diverse chemical constituent have been revealed to bring DNA destruction through ROS generation in animals as well as in humans (Antonini *et al*., 2005; Singh and Chadha, 2016). Another research revealed that inspiration of Mn present in welding fumes result in higher brain Mn concentration which causes oxidative stress and neurodegeneration in rats (Erikson *et al*., 2004; Sriram *et al*., 2010). Overall welding fumes can be regarded as oxidative contaminants and can bring detrimental effects on liver profile of welders through increased oxidative stress (Bagchi *et al*., 2002).

Welding fumes are composed of numerous fine and ultrafine metallic particles and a variety of gases. Inspiration of these particles and gases bring alternations in the respiratory, hepatic and renal physiology (Dumkova *et al*., 2016). As far as renal profile is concerned both urea and creatinine were assessed in present investigation. These metabolites play an important role in several mechanisms, such as, urea metabolism, oxidation and/or reduction pathways, carbohydrate and amino acid metabolism (Kuo *et al*., 2012). Renal function analysis demonstrated a significant decrease in creatinine and urea levels in welders as compared to healthy individuals, which could be an indication of a possibly disturbed renal functioning.

Several studies revealed significant urea concentration in serum of occupationally exposed subjects of different industrial units as compared with healthy controls (Wang *et al*., 2002). Patil *et al*. (2007) have reported marked elevation of blood urea concentration in workers of battery manufacturing sector having an exposure of fumes containing toxicants. Main cause of reduced creatinine and urea level in our study could be attributed to lean body mass as welders depicted reduced body mass index (BMI) possibly due to occupational stress (Fohr *et al*., 2016). So, it is conceivable that reduced creatinine and urea may be associated with lower BMI. Previous investigations have documented renal tubular epithelial damage and proximal tubular defects that occurs via the exposure to ferrochromium particles, bringing variations in the renal functions of workers in the welding industry (Lee *et al*., 2016). Moreover, Casalegono *et al*. (2015) have documented association of nickel and chromium fumes exposure with renal defects and immunosuppression activities in experimentally exposed animals. Hence, this phenomenon advocates the possibility of renal defects in workers of welding industry.

A significant decline in creatinine level of workers was observed in an investigation where workers had an exposure to air borne toxicants during their job activities parallel to those who didn't face toxicants (Ehrlich, 1998). Welding fumes have also been demonstrated to increase lipid peroxidation in plasma, lungs and liver tissue in rats (Chuang *et al*., 2010). Because welding fumes produce oxidative stress, we suspect that ROS decreased creatine kinase and therefore caused a decrease in creatinine concentration (Chuang *et al*., 2010).

Serum electrolyte analysis revealed that Na^+ level of welders showed non-significant increase, while, K^+ and Cl^- levels of welders depicted a significant increase as compared with controls. The electrolyte disturbances should be monitored and treated appropriately to avoid ill effects e.g., prolonged diarrhoea or vomiting, increased secretion of mineralocorticosteroids and urinary obstruction etc (Wu *et al*., 2012).

An earlier investigation revealed non-significant differences in Na^+ and K^+ concentration of blood among designated industrial employees of Ewekoro, Abeokuta and Ogun states in Nigeria. The study further suggested it to be a consequence of an exposure to similar kind of metals as found in welding fumes (Babalola and Babejide, 2009).

Due to high Cd exposure, primarily through respiratory pathways, decline in the efficacy of the kidneys to eliminate acids from the blood due to dysfunction in proximal renal tubule have been reported (Vallero, 2011).

Previous investigations have described high blood Cd levels in battery recyclers, welders and spray painters due to Cd being a joint constituent of Cd-batteries, welding fumes and spray paint pigments.

Another report exhibit that exposure to welding fumes can lead to enhanced Cd concentration in urine and indicates renal tubular dysfunction (Ding *et al*., 2011). It is worth mentioning that higher levels of electrolytes in blood are symbol of gradual progression to kidney disorders (Pachal *et al*., 2000). Overall, welding fumes can be regarded as oxidative contaminants and can bring detrimental effects on kidney profile of welders through increased oxidative stress (Bagchi *et al*., 2002).

Based on above findings, we suggest that both hepatic and renal injury can be a manifestation of welding fume exposure.

In conclusion, the statistics which were obtained during our study entirely suggest hepatocyte injury and oxidative stress production in hepatocytes in response to welding fume exposure.

Specially, indication of highly increased ALP level reflected a hepatic injury, rickets or renal tubular dystrophies. Increased bilirubin concentration may be the sign of hemolytic jaundice, internal haemorrhage, acute hemolytic anemia, malaria and septicaemia.

Precautionary measure such as use of masks on face to prevent inspiration of poisonous fumes, glasses on eyes and gloves on hands are suggested to welders for maintenance of appropriate health. A well-managed ventilation system and methods to dispose off wastes must be necessary during welding operations to prevent health related complications.

More investigations are necessary to evaluate other health vulnerabilities occurring because of exposure to welding fumes and related toxic species on multiple organs, because this kind of exposure may bring huge hazards to the human organs particularly those which are related with manufacturing and removal of waste such as the liver and kidney.

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IRB approval

Institutional ethical review committee of the Institute of Zoology, University of the Punjab, Lahore, endorsed the study plan.

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The authors have declared that no generative AI or AI-assisted technologies were used to create this manuscript.

Statement of conflict of interest

The authors have declared no conflict of interest.

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