LUNG FUNCTION AND CARDIOVASCULAR RISK FACTORS IN OCCUPATIONAL EXPOSURE TO POLYCYCLIC AROMATIC HYDROCARBONS.

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ABSTRACT

Dyslipidemia, hypertension, and lung function impairment leading to cardiopulmonary disorders has been associated with chronic exposure to chemical toxicants including polycyclic aromatic hydrocarbons (PAHs) in automobile workshop. The cardiovascular risk factors, indices of lung function and PAH exposure in relation to duration of years at occupation were assessed in automobile workers. This comparative cross-sectional study enrolled one hundred men comprising 50 automobile workers and 50 non-automobile workers (controls). The peak expiratory flow rate was estimated using the peak flow meter, PAH metabolite (urine 1-hydroxy pyrene (1-HOP) by high-performance liquid chromatography, lipid profile indices (triglycerides (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C)) by colorimetry, very low density lipoprotein cholesterol (VLDL-C) and low density lipoprotein cholesterol (LDL-C) by Friedewal’s formular. Atherogenic index of plasma (AIP) was calculated as a ratio of TG to HDL-C. The Anthropometric indices and blood pressure (systolic (SBP) and diastolic (DBP)) were obtained. Data analysis was done using t-test and correlation at P<0.05. Automobile workers had lower PEFR, HDL-C, and higher SBP, AIP and LDL-C compared to non-automobile workers (P<0.001). PEFR correlated negatively with 1-HOP (r=−0.322, P=0.022) while AIP correlated negatively with HDL (r=−0.307, P=0.030) and positively with TG (r=0.774, P=0.000), TC (r=0.726, P=0.000), LDL (r=0.777, P=0.000) and VLDL (r=0.793, P=0.000) respectively only in automobile workers. Atherogenic dyslipidemia characterized by elevated LDL, AIP, and lower HDL and PEFR observed in automobile workers may suggest an increased risk for cardiopulmonary dysfunctions.

Keywords: Dyslipidemia, Lipid profile, Lung, Polycyclic aromatic hydrocarbons
INTRODUCTION

Myriads of deleterious health effects ranging from genotoxicity, pulmonary, and hepato-renal toxicities leading to chronic obstructive pulmonary disease (COPD), cardiovascular (CVD) and hepatocellular diseases, renal failure, and increased risk of cancer has been associated with occupational exposure to environmental toxicants in the workplace including the automobile workshop (Ataro et al., 2018, Ramdhan et al., 2018). The severity of the health effects has been reported to be a function of the level and duration of exposure to such toxicants (Ramdhan et al., 2018). Automobile workers are routinely involved in the general repair of auto vehicles, battery work, panel beating, spray painting, and electrical work. These activities expose them to diesel and gasoline exhaust gas (DE) and volatile organic compounds (VOC) making them vulnerable to various occupational health hazards associated with their exposure (Kumar & George, 2017). Health effects associated with such exposures have been attributed to the various components of DE and VOC including PAH and their differential effects on biological systems which contribute to unfavorable biochemical and physiological responses with adverse clinical outcomes (Ajani et al., 2011).

Exposure to PAH has been linked to cardio-pulmonary impairment, and the exact causal connection is still uncertain. However, a number of cellular and molecular mechanisms which promote inflammation and induction of systemic oxidative stress (OS) precipitate pathological processes related to cardio-pulmonary disorders such as dyslipidemia, atherosclerosis, endothelial dysfunction, hypercoagulability, thrombosis and bronchoconstriction have been implicated (Chin, 2015). Elevated urine levels of hydroxylated PAH have been positively linked with increased risk of CVD while the prolonged duration of exposure to organic and inorganic pollutants including PAH has been associated with a progressive decline in lung functions among auto mechanics (Alhamdow et al., 2018).

In most developing countries including Nigeria, exposure to DE and VOC as seen in automobile workers is occupationally risky, due to poor implementation of safety measures with minimal monitoring for adherence to these measures by the regulatory authorities (Ataro et al., 2018). As such, most of these workers operate without observing any safety measures and workplace hygiene as most of them are ignorant of the health risks associated with exposure to these common workplace chemicals. Prevention of occupational diseases related to exposure to chemicals in the workplace could be achieved by biological monitoring of exposure levels on regular basis. Therefore, evaluation of lung function indices and cardiovascular risk factors in automobile workers who are routinely exposed to PAH in DE and VOCs may be vital in determining those at increased risk of cardio-pulmonary events and for the adoption of appropriate prophylactic measures. This study assessed the urine levels of PAH metabolite, lipid profile, and peak expiratory flow rate of automobile workers in relation to the duration of years at occupation.

MATERIALS AND METHODS

Study design

This comparative cross-sectional study enrolled healthy adult male automobile workers and age-matched non-automobile workers (controls) living within the Calabar metropolis in Southern Nigeria. The participants in the study were enrolled after obtaining written consent and approval of the study protocol from the Cross River State, Health Research Ethics Committee. The conduct of this study was done in full compliance with the ethical principles guiding research involving humans according to the Helsinki declaration of 1975 and recent modifications.
Selection of subjects
A total number of 50 professional automobile workers (including auto mechanics, spray painters, battery recyclers, and panel beaters) who had been actively working in an automobile workshop for the past year and above were recruited into the study. The control subjects were 50 non-automobile workers, who have never worked or resided in the vicinity of an automobile workshop or been exposed to paint in their environment for the past year. Socio-demographic information including age, marital status, educational qualifications, occupation (number of years at occupation, use of personal protective equipment), social habits (smoking history, alcohol use, and substance abuse), and family and medical history (current health status, previous illness) were obtained using a semi-structured questionnaire. Anthropometric measurements as waist circumference (WC) and body mass index (BMI) were taken and blood pressure taken using standard methods (Nuttal, 2015, Ogedegbe and Pickering, 2010). Individuals that are occupationally exposed to charcoal smoke, volatile organic compounds, and high automobile exposed traffic environment including fuel pomp attendants, traffic police, smokers, and individuals with any form of a chronic organ or systemic illness or on chronic medication were all excluded from the study.

Collection of samples
Whole blood samples (5ml) were collected from all participants in the study into plain sample containers, allowed to clot and retract, and spun at room temperature at 500g for 5 minutes to obtain sera for the estimation of lipid profile indices (TC, TG, LDL-C, VLDL-C and HDL-C). Spot urine samples (10ml) were collected for the estimation of urinary PAH metabolite; 1-hydroxy pyrene (1-HOP) and creatinine after at least 4 hours at the automobile workshop.

Laboratory Methods
Total cholesterol and triglycerides were estimated by enzyme colorimetric methods (Artiss and Zak, 1997, Cole et al., 1997), HDL-C by enzyme colorimetric method after precipitation (Izzo et al., 1981), LDL-C and VLDL-C were derived using Friedewal’s formula (Friedewald et al., 1972) while the atherogenic index of plasma was calculated as a ratio of TG to HDL-C (Dobiasova and Frohlich, 2001). The PEFR was estimated using a peak flow meter (Chan and Wu, 2005), urine 1-hydroxypyrene was estimated by high performance liquid chromatography (Hansen et al., 1993), and urine creatinine by colorimetry (Andersen et al., 2014).

Data analysis
Results were presented as Mean±SD and the statistical package for social sciences (SPSS version 20.0, IBM, USA) was used for data analysis. T-test was used to determine mean differences among groups, while Pearson correlation analysis was employed to determine the level of associations between variables at P<0.05.

RESULTS
The comparison of age, cardiovascular risk factors (WC, BMI, SBP, DBP, TC, TG, HDL-C, LDL-C, VLDL-C, AIP), PEFR, 1-hydroxy pyrene and urine creatinine in automobile and non-automobile workers were depicted in table 1. Automobile workers had significantly higher SBP, AIP and LDL-C and lower PEFR and HDL-C compared to controls (P<0.05). No significant differences were observed in the levels of other indices between the 2 groups studied (P>0.05).
The correlation of PEFR with 1-HOP in automobile workers was shown in figure 1. PEFR correlated negatively (r = -0.322, P=0.022) with 1-HOP in automobile workers.

Figure 2 depicts the correlation of HDL-C with AIP in automobile workers. Negative correlation was seen between HDL-C and AIP (r=-0.307, P=0.030).

The correlations of AIP with TC, TG, LDL-C, and VLDL-C in automobile workers were shown in figure 3. Significant positive correlations were observed between AIP and TC (r=0.726, P=0.000), VLDL-C (r=0.793, P=0.000), LDL-C (r=0.777, P=0.000) and TG (r=0.774, P=0.000) respectively.

Table 1: Comparison of age, BMI, BP, cardiovascular risk factors, PEFR and 1-hydroxy pyrene in automobile workers and non-automobile workers.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Automobile workers n=50</th>
<th>Non-automobile workers n=50</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>36.00±11.02</td>
<td>34.04±6.48</td>
<td>0.281</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>31.36±3.67</td>
<td>32.36±3.10</td>
<td>0.145</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.16±2.83</td>
<td>23.54±2.65</td>
<td>0.261</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>130.72±13.11</td>
<td>123.24±12.44</td>
<td>0.004*</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>79.84±8.94</td>
<td>76.84±8.62</td>
<td>0.091</td>
</tr>
<tr>
<td>TC (mmol/l)</td>
<td>4.69±1.13</td>
<td>4.43±0.88</td>
<td>0.203</td>
</tr>
<tr>
<td>TG (mmol/l)</td>
<td>1.16±0.22</td>
<td>1.10±0.16</td>
<td>0.154</td>
</tr>
<tr>
<td>HDL-C (mmol/l)</td>
<td>1.35±0.16</td>
<td>1.45±0.13</td>
<td>0.003*</td>
</tr>
<tr>
<td>LDL-C (mmol/l)</td>
<td>3.00±0.87</td>
<td>2.46±0.75</td>
<td>0.001*</td>
</tr>
<tr>
<td>VLDL-C (mmol)</td>
<td>0.52±0.10</td>
<td>0.50±0.07</td>
<td>0.215</td>
</tr>
<tr>
<td>AIP</td>
<td>-0.07±0.08</td>
<td>-0.12±0.05</td>
<td>0.001*</td>
</tr>
<tr>
<td>PEFR (L/min)</td>
<td>256.70±46.55</td>
<td>286.60±34.08</td>
<td>0.000*</td>
</tr>
<tr>
<td>1-HOP (µg/g Cr⁻³)</td>
<td>1.51±1.56</td>
<td>1.26±1.07</td>
<td>0.368</td>
</tr>
<tr>
<td>uCr (mg/L)</td>
<td>252.28±26.94</td>
<td>268.49±24.86</td>
<td>0.002*</td>
</tr>
</tbody>
</table>

Values expressed as mean±SD, *=indicate significant at p<0.001, BMI=body mass index, WC=waist circumference, SBP=systolic blood pressure, DBP=diastolic blood pressure, TC=total cholesterol, TG=triglyceride, HDL-C=high density lipoprotein cholesterol, LDL-C=low density lipoprotein cholesterol, VLDL-C=very low density lipoprotein cholesterol, AIP=Atherogenic index of plasma, PEFR=peak expiratory flow rate, 1-HOP=1-hydroxy pyrene, uCr=urine creatinine.

Figure 1: Correlation plot of PEFR against 1-HOP in automobile workers

\[ y = -9.5894x + 271.19 \]
\[ R^2 = 0.1039 \]
\[ r = -0.322 \]
\[ P = 0.022 \]
\[ n = 50 \]
DISCUSSION
Exposure to environmental chemicals including PAHs has been described as risk factor for chronic obstructive lung diseases, atherosclerosis, and various forms of cancers (Ifegwu et al., 2012). The deleterious effects of exposure to PAHs on the physiological functions of vital organs and tissues mediated by their transformation to toxic metabolites...
have been implicated in the development of these disorders. The cardiovascular risk factors and indices of lung function and PAH exposure index with duration of years at occupation were assessed in automobile workers.

In this study, the urine levels of 1-HOP of automobile workers though higher than the control groups, were not statistically significant. Comparable levels of 1-HOP in automobile workers and their control counterparts may be attributed to genetic polymorphism in PAH metabolizing enzymes which modulate the metabolism and excretion of PAH metabolite 1-HOP and inherent individual’s variations in the kinetics of PAH excretion (Jenga and Pan, 2014). Contrary to our findings, mechanics and fuel attendants have been shown to have significantly higher levels of urine 1-HOP when compared to their control counterparts and this was attributed to higher level of exposure to diesel exhaust emissions (Ataro et al., 2018, Ifegwu et al., 2012). Urine levels of 1-HOP have been used as a reliable index of PAH exposure even at very low levels of air pollution since it is the major end product of metabolism of PAH representing 90% of PAH metabolites. Elevated urine levels of 1-HOP have been associated with increased risk of cancer. (Ifegwu et al., 2012, Castan˜o-Vinyals et al., 2004).

The SBP of automobile workers was observed to be significantly higher than those of controls and this may be linked to their exposure to toxic chemicals present in automobile workshop. Previous studies have also reported significantly higher values of SBP and DBP in automobile workers compared to the controls (Obi-Ezeani et al., 2019, Ataro et al., 2018). Increased generation of reactive oxygen species (ROS) and OS associated with phase 1 metabolism of PAHs in humans and consequent decrease in vascular bioavailability of NO, structural and functional changes in vascular smooth muscles, endothelial dysfunction, and vascular damage have been implicated in changes in BP due to exposure to PAH in automobile exhaust gas (Montezano et al., 2015). Increased SBP in automobile workers has also been related to the interaction of the fine particulate matter (PM2.5) present in the exhaust gas with noradrenergic receptors to stimulate the secretion of angiotensin II and increased BP (Cosselman et al., 2012). Increased BP in automobile workers has also been related to exposure to lead present in exhaust particles and spray paints (Vitayavirasuk et al., 2005). However, the SBP of automobile workers (130.72±13.11mmHg) though higher than the controls as observed in this study may not be classified as hypertensive (hypertension is defined as BP ≥140 or ≥90 mm Hg) (ACC/AHA, 2018).

Lower PEFR was observed in automobile workers compared to their control counterparts. Consistency with our findings, less than 80% of expected values of forced expiratory volume (FEV1), forced vital capacity (FVC), and PEFR which represent significant impairment in lung functions has been demonstrated in auto mechanics compared to controls (Alhamdow et al., 2018). The mechanism for the progressive lung function abnormalities have been shown to be related to the direct toxic effects of PAH compounds on the thin alveolar epithelium; chronic inhalation injury which precipitates hypoxic injury to the alveoli; PAH-induced OS and inflammation leading to ischemic changes, increased fibrosis, small airway obstruction, and hence decreased PEFR (Kumar and George 2017, Ana, 2014). A significant negative correlation was observed between PEFR and 1-HOP in automobile workers studied. A similar negative association has been reported between elevated urine levels of PAH metabolites and lung functions in a Chinese population (Zhou et al., 2016). Thus, increased levels of PAH metabolites in automobile workers studied may therefore be a risk index for lung dysfunction (Zhou et al., 2016).

Automobile workers had higher LDL-C, AIP, and lower HDL-C compared to non-automobile workers (p<0.05). Previous studies have reported significantly higher levels of TC, TG, LDL-C, VLDL-C, atherogenic and coronary risk index, and a low serum HDL-C level in automobile mechanics and spray painters compared to controls
(Adejumo et al., 2016, Obi-Ezeani et al., 2019). Higher TG levels in auto mechanics observed in previous studies have been attributed to indicate increased hepatic secretion and a decreased clearance of triglyceride. Repeated exposure to benzo[a]pyrene in mice has been shown to induce dyslipidemia characterized by increased serum triglyceride receptor ligand (TGRL), TG, TC, hepatic TC, and adipose TG concentrations (Layeghkhavidaki et al., 2014). Mechanisms of B[a]p induced dyslipidemia may involve degradation of LSR (lipolysis-stimulated lipoprotein receptor), LDL-R (LDL-receptor), and inhibition of LPL binding to LSR and LDL receptor which may induce observed alterations in lipid profile in mice exposed to B[a]p (Irigaray et al., 2006, Layeghkhavidaki et al., 2014). AIP correlated positively with TC, TG, LDL-C, VLDL-C and negatively with HDL-C in automobile workers studied.

The risk of ischemic heart disease has been positively correlated with increased levels of plasma TC and LDL-C and negatively with increased HDL-C levels in auto mechanics compared to controls. Elevated TC, TG, LDL-C, and HDL-C have been implicated as risk factors for cardiovascular diseases (Ajani et al., 2011). Insulin resistance, adipose dysfunction, dyslipidemia, and vascular inflammation associated with chronic exposure to PAH in particulate matter have been shown to enhance the development of metabolic disorders such as type 2 diabetes and atherosclerosis (Zhang et al., 2017).

The limitations of the study lie on the small sample size and single spot sampling method, larger sample size is required for future studies. The design of the study is cross sectional, it may therefore suggest association but cannot establish causation. The strength of the study lies on its ability to demonstrate unfavourable lipid profile and depressed peak expiratory flow rate among automobile workers in Calabar metropolis.

CONCLUSION

The findings of this study have shown that automobile workers have unfavorable lipid profiles characterized by elevated low-density lipoprotein cholesterol and lower high-density lipoprotein cholesterol. The association of exposure to PAH with decreased peak expiratory flow rate coupled with positive atherogenic risk index observed in automobile workers suggests an increased risk of a future cardio-pulmonary events in the absence of any prophylactic measures. The use of personal protective equipment (PPE) such as goggles, face masks, coverall, hand gloves and safe hygienic practice in the automobile workshop may mitigate the development of adverse health conditions.

Author’s Contribution

All authors contributed to the conception and design of the work, data acquisition, analysis and interpretation of the results, revision, final approval and are accountable for the originality of the work.

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Conflict of interest

We declare no conflict of interest regarding the publication this article.

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