Advances in Life Science and Technology
ISSN 2224-7181 (Paper) ISSN 2225-062X (Online)
Vol.38, 2015

Hepatic Functions of Persons Occupationally Exposed To Formaldehyde in Calabar, Nigeria

Euphoria C. Akwiwu* Chinyere A.O. Usoro Josephine O. Akpotuzor Maisie H. Etukudo

Department of Medical Laboratory Science, University of Calabar, PO box 1115, Calabar, Cross River State, Nigeria

Abstract

Dependence on formaldehyde as a biological preservative has remained a common practice in most developing countries, particularly in Nigeria where regulation and enforcement of labour guidelines are at its lowest ebb compared to developed populations. This research was carried out to investigate hepatic functions in persons occupationally exposed to formaldehyde in Calabar metropolis. Eighty eight male and female subjects comprising anatomists, medical laboratory attendants, medical laboratory scientists and morticians occupationally exposed to formaldehyde in this locality were enrolled in the study. Another group of eighty eight age and sex-matched individuals without formaldehyde exposure served as control subjects. Participants were between 24-52 years of age. Informed consent was obtained from all enrolled subjects. A structured questionnaire was utilized to capture the bio-data and other pertinent information on work place exposure. Hepatic function was assessed by measuring; Aspartate Transaminase (AST), Alanine Transaminase (ALT), Bilirubin, Total Protein (TP), Albumin and Alpha-Fetoprotein (AFP). These were assayed by colourimetric methods with the exception of AFP that was measured using enzyme-linked immunosorbent assay. While AFP and ALT were significantly increased ($p<0.05$), TP and Albumin were significantly reduced ($p<0.05$) in persons occupationally exposed to formaldehyde compared to control subjects. Furthermore, morticians (embalmers) had significantly ($p<0.05$) increased levels of AFP and Bilirubin but lower TP and Albumin levels compared to medical laboratory staff. Moreover, AFP correlated negatively with TP and Albumin ($r = -0.476$ and -0.602 and respectively). Findings from this study point towards possible formaldehyde toxicity among exposed persons particularly embalmers.

Keywords: Formaldehyde, exposure, toxicity

1. Introduction

The use of formaldehyde solutions as fixative for biological specimens is a common practice across the globe. Particularly for the developing countries where infrastructure is often inadequate, the unstable supply of electricity has also reduced the options for preservative techniques. In Nigeria, this is most evident in mortuaries as well as some medical laboratories. Workers and students in such settings have been identified to be at risk because of the possibility of chronic formaldehyde inhalation (Ahmed, 2011; Costa *et al.,* 2008; Ghasemkhani *et al.,* 2005; Raja and Sultana, 2012). The metabolism of formaldehyde in the human body is carried out by the liver, which incidentally plays a central role in the body for intermediary metabolism including that of carbohydrates, proteins and lipids. The consideration that chronic exposure to formaldehyde with the attendant metabolic demands on the liver could affect general hepatic functions has incited a number of research works. Derangement in hepatic functions has been suggested following observed toxicity to the liver in several species of experimental animals (Teng *et al.,* 2001; Cikmaz *et al.,* 2010). More precisely though, it has been recorded that formaldehyde inhalation in different doses and time intervals affect the metabolic pathway of the liver in exposed rats (Yilmaz *et al*., 2004).

Along this line of research interest, the present study was embarked on to assess hepatic functions using Aspartate Transaminase (AST), Alanine Transaminase (ALT), Bilirubin, Total Protein (TP), Albumin and Alpha-Fetoprotein (AFP) among occupationally exposed persons in Calabar Cross River State of Nigeria.

2. Methods

The present research study was conducted in Calabar, Cross River State of Nigeria. Case-control experimental study design was employed in this research. Exposed Subjects comprised eighty eight male and female workers, while, another eighty eight age and sex-matched civil servants and self-employed adults who had no history of formaldehyde exposure as at the time of the study served as control subjects. Bio-data and occupation-related information was obtained using questionnaire. Five milliliters (5mL) of venous blood was collected aseptically from each subject into a plain sample bottle and subsequently separated. Serum samples obtained for measurement of biochemical parameters were stored at -80ºC until the time of analysis.

Quantitative determination of Alpha Feto-Protein (AFP) was carried out by sandwich enzyme immunoassay

technique using ELISA Kit purchased from Pishtaz Teb Diagnostics, Germany (reference range of 0.2 – 8.5 ng/mL). Aspartate Transaminase (AST) and Alanine Transaminase (ALT) were analyzed by Dinitrophenylhydrazone Method using colorimetric kit purchased from Randox Laboratories, United Kingdom (reference range of up to 12 U/L). Total Protein was measured by the Biuret Method (reference range of 66 – 83 g/L), Albumin by Dye-binding Method (reference range of 35 – 55 g/L) and Total Bilirubin by Diazo Method (0.2 – 1.2 mg/dl of reference range). The last three parameters were analyzed using colorimetric Giesse Diagnostics Kits from Italy. SPSS 19.0 was used for the statistical analyses of data. Pearson's correlation coefficient (r) was used to express relationship between two variables. A two tailed P-value of <0.05 was considered indicative of a statistically significant difference.

3. Results

A total of 176 male and female subjects between the ages of 24-52 years were enrolled in the study. Out of this total figure, 88 persons were occupationally exposed to formaldehyde while the remaining had no history of exposure. Exposed persons that participated in this study were health professionals and comprised Medical laboratory Scientists and Attendants who worked in routine hospital-based laboratories as well as Morticians and Anatomists actively involved in embalming and demonstration sessions for medical students (Table 1). The results of hepatic function parameters assessed in both exposed and control subjects are shown in Table 2. The mean concentrations of AFP, ALT and Bilirubin were significantly increased ($p<0.05$), while Total protein and Albumin were significantly reduced ($p<0.05$) in persons occupationally exposed to formaldehyde compared to the control subjects. On the basis of occupational settings, AFP was significantly higher ($p<0.05$), while Total protein and Albumin were significantly lower ($p<0.05$) among mortuary staff compared to laboratory staff (Table 3). Moreover, there were moderate negative correlations between alpha fetoprotein and total protein ($r = -0.476$) as well as albumin ($r = -0.602$) (Figures 1 & 2 respectively).

4. Discussion

The values of AFP recorded in this study were below the cut-off point for establishing hepatocellular carcinoma. However, a relatively increased mean value of AFP was observed among persons occupationally exposed to formaldehyde. This finding was more pronounced among the morticians than the laboratory workers. Inversely, TP and Albumin were reduced among these same groups, while, ALT and Bilirubin were only raised in all exposed subjects.

Considering that formaldehyde metabolism is handled by the liver, chronic exposure such as the one that occurs in occupational settings could pose a challenge to the liver possibly resulting in hepatic toxicity. More so, being that intermediary metabolism of the different food classes is essentially dependent on the liver, it is possible for hepatic toxicity from formaldehyde exposure to interfere with this role hence the high levels of AFP, ALT and bilirubin with corresponding low levels of TP and Albumin observed in this study. These apparent changes may have resulted from disturbances in the synthesizing and excretory functions of the liver. However, formaldehyde-albumin adduct formation following formaldehyde exposure has also been reported previously and probably accounts for the lowered albumin levels frequently observed among exposed subjects (Pala *et al*., 2008).

In this study, we observed increased levels of AFP and ALT among exposed workers and such elevations are attributable to hepatic injury. However, the exact mechanism by which formaldehyde inhalation can exert toxicity is yet to be fully understood. Findings from an animal model, as reported by Yilmaz *et al.* (2004) showed that formaldehyde inhalation in different doses and time intervals affect the metabolic pathway of the liver resulting in decreases in G6PD and 6PGD enzymes. The researchers hypothesized that altered pentose phosphate pathway probably affects the oxidant/antioxidant balance of the liver and thus results in lipid peroxidation with the consequence of cellular damage. This view concurs with the report of Skrzydlewska and Farbiszewski (1997) that sub-chronic formaldehyde exposure causes enzyme changes which partly arise as a result of enormous production of free radicals in the system. On a wider perspective of studies from animal models, inhaled formaldehyde has been associated with toxicity to the liver in several species of experimental animals (Teng *et al.,* 2001; Cikmaz *et al.,* 2010). Moreover, the degree of toxicity appears to correspond with loss of basic functions such as protein synthesis as observed in the correlation analyses of the present study.

In spite of the concerns over the effect of occupational exposure to formaldehyde on the liver, considerations over the effectiveness of the chemical as a good fixative remain; hence it's continued use in tissue processing and embalming. The apparent vulnerability of morticians to increased health risks has been highlighted in recent times (Olooto, 2010). Some of the identified factors that militate against occupational health and safety of this group among developing countries include the continued use of outdated and often unsuitable infrastructure as well as overextending the capacity of existing facilities. The net effect appears to be the compromise of proper ventilation among other challenges (Ogunnowo *et al.,* 2010; Okoth-Okelloh, *et al., 2013).* In addition, job

security remains a sensitive issue in the face of high level of unemployment and economic instability. It is against this backdrop that the enforcement of regulatory laws is being advocated for in addition to sustaining enlightenment campaigns.

References

Ahmed, H.O. (2011). Preliminary study: Formaldehyde exposure in laboratories of Sharjah University in UAE. *Indian Journal of Occupational and Environmental Medicine*, *15*(1),33–37.

Cikmaz, S., Kutoglu, T., Kanter, M. & Mesut, R. (2010). Effect of formaldehyde inhalation on rat livers: a light and electron microscopic study. *Toxicology and Industrial Health*, *26*(2),113-119.

Costa, S., Coelho, P., Costa, C., Silva, S., Mayan, O., Santos, L.S., Gaspar, J. & Teixeira, J.P. (2008) Genotoxic damage in pathology anatomy laboratory workers exposed to formaldehyde. *Toxicology, 252 (1-3)*,40-48.

Ghasemkhani, M., Jahanpeyma, F. & Azam, K. (2005). Formaldehyde exposure in some educational hospitals of Tehran. *Industrial Health, 43 (4),*703–707.

Ogunnowo, B.E., Anunobi, C.C., Onajole, A.T. & Odeyemi, K.A. (2010). Awareness of occupational health hazards and the practice of universal safety precautions among mortuary workers in South West Nigeria. *Nigerian Quarterly Journal of Hospital Medicine, 20*(4),192-196.

Okoth-Okelloh, A.M., Ogonda, B. A., Ogolla, S., Tonui, W.K. & Onyango R. (2013). Quality Assurance for Occupational Health and Safety Administration (OSHA) In the Morgue: The Impact of SOP Domestication on Implementation and Practice of Universal Safety Precautions in Kenya. *Journal of Biology, Agriculture and Healthcare*, 19 (3) 1-10

Olooto, W.E. (2010). Assessment of The Effect of Formaldehyde Exposure on The Liver in Mortuaty Workers in South Western Nigeria. *Nigerian Medical Practitioner*, *http:/dx.doi.org/10.4314/nmp.v57i4.57941*

Pala, M., Ugolini, D., Ceppi, M., Rizzo, F., Maiorana, L., Bolognesi, C., Schilirò, T., Gilli, G., Bigatti, P., Bono, R. & Vecchio, D. (2008). Occupational exposure to formaldehyde and biological monitoring of Research Institute workers. *Cancer Detection and Prevention, 32*(2),121-126.

Raja, D.S. & Sultana, B. (2012). Potential health hazards for students exposed to formaldehyde in the gross anatomy laboratory. *Journal of Environmental Health*, *74*(6),36-40.

Skrzydlewska, E. & Farbiszewski, R. (1997). Decreased antioxidant defense mechanisms in rat liver after methanol intoxication. *Free Radical Res*earch, *27 (4),*369-375.

Teng, S., Beard, K., Pourahmad, J., Moridani, M., Easson, E., Poon, R. & O'Brien, P.J. (2001). The formaldehyde metabolic detoxification enzyme systems and molecular cytotoxic mechanism in isolated rat hepatocytes. *Chemico-Biological Interactions, 130-132(1-3),* 285-296.

Yilmaz, H.R., Ozen, O.A., Ozyurt, H., Songur, A., Sahin, S. & Sarsilmaz, M. (2004). The effect of inhaled formaldehyde on the activities of some metabolic enzymes in the liver of male rats: subchronic (13-weeks) effect. *Eastern Journal of Medicine*, *9* 47-50.

Table1. Demography of study participants with occupational exposure to formaldehyde

Professionals	Number	Percentage	Exposure setting
Medical Laboratory Scientists	38	43	Laboratory
Laboratory Attendants	15	17	Laboratory
Anatomists	14	16	Mortuary
Morticians	21	24	Mortuary

Table2. Hepatic function parameters of persons occupationally-exposed to formaldehyde versus those of control subjects

Parameter	Test Subjects n=88	Control Subjects n=88	p-Value
AFP (ng/mL)	2.66±1.76	1.58±0.84	p=0.00
AST (U/L)	12.36±4.03	11.44±3.41	p>0.05
ALT (U/L)	7.68±3.57	5.66±2.29	p=0.00
Total Protein (g/L)	64.30±8.00	68.30±7.70	p=0.00
Albumin (g/L)	30.80±5.50	35.10±4.60	p=0.00
Bilirubin (mg/dL)	1.08±0.31	0.98±0.31	p=0.03

Table3. Hepatic function parameters of persons occupationally-exposed to formaldehyde based on occupational settings

Parameter	Laboratory Staff n=53	Mortuary Staff n=35	p-Value
AFP (ng/mL)	1.98±1.39	3.69±1.78	p=0.00
AST (U/L)	11.87±4.19	13.11±3.72	p>0.05
ALT (U/L)	7.75±3.55	7.57±3.66	p>0.05
Total Protein (g/L)	66.60±7.70	60.90±7.50	p=0.00
Albumin (g/L)	32.30±5.40	28.50±4.90	p=0.00
Bilirubin (mg/dL)	1.06±0.30	1.12±0.34	p>0.05

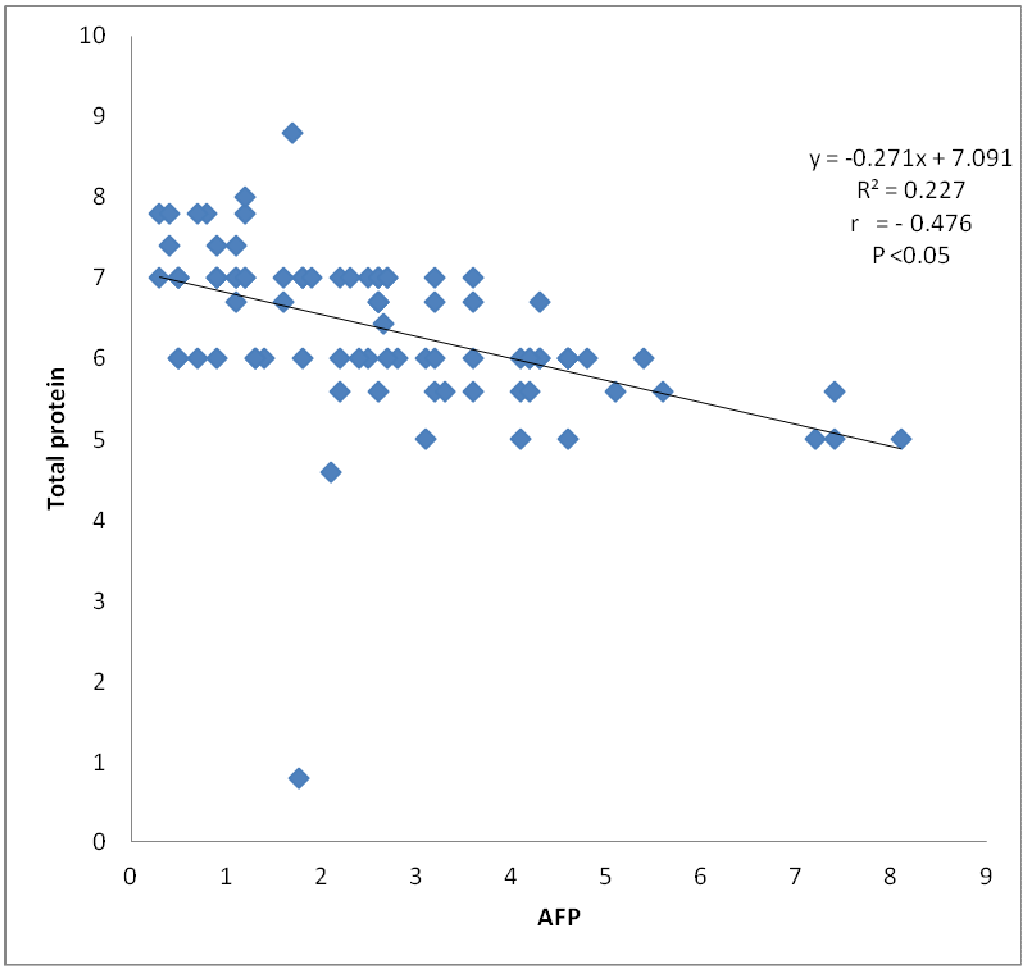

Figure1. Correlation between Alpha Fetoprotein and Total Protein of Occupationally exposed subjects

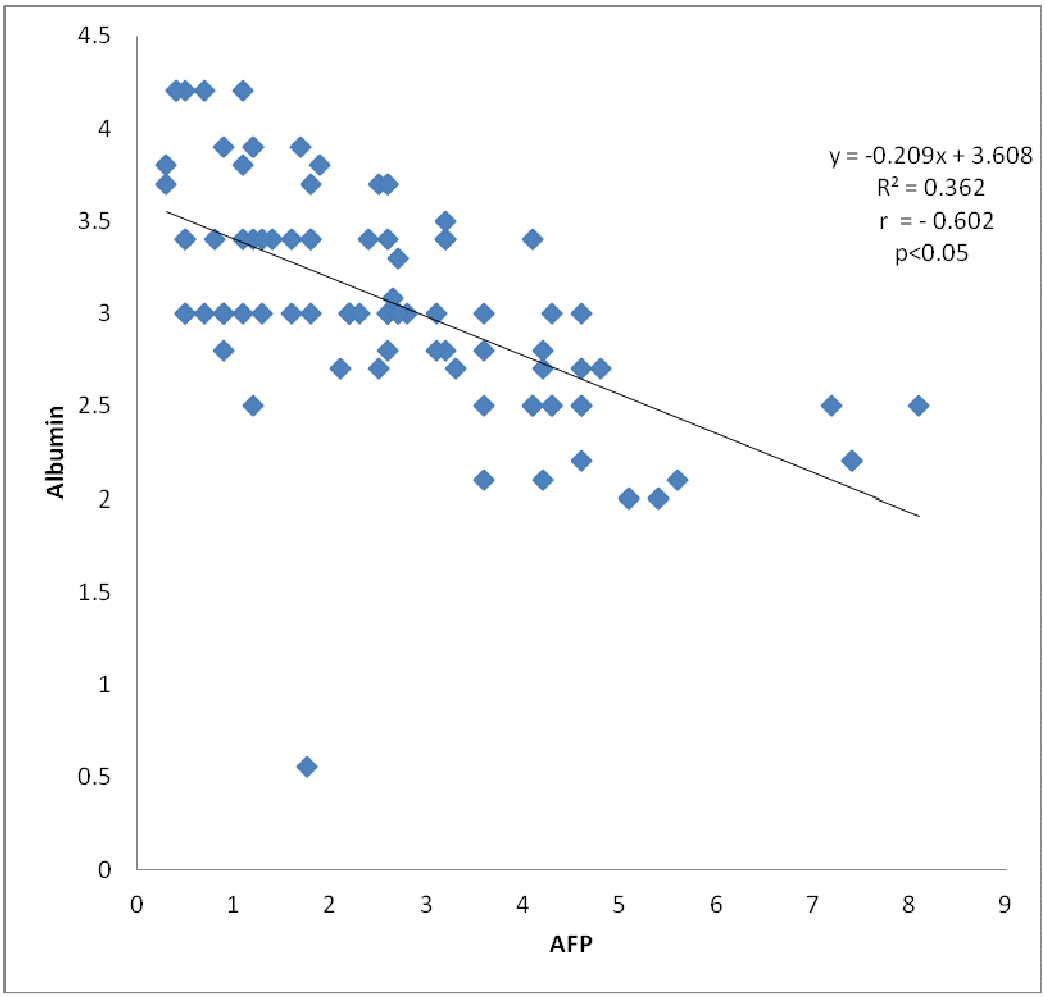

Figure2. Correlation between Alpha Fetoprotein and Albumin of Occupationally exposed subjects