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Formaldehyde-Associated Immunologic Responses among Exposed Nigerian Health Professionals

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Abstract

Immunologic involvements have been reported over the years in association with formaldehyde exposure both in humans and animal models. This study was aimed at investigating immunologic responses among health professionals with occupational exposure to formaldehyde in Calabar, Nigeria. Eighty eight male and female subjects comprising anatomists, medical laboratory attendants, medical laboratory scientists and morticians occupationally exposed to formaldehyde in Calabar 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 as well as allergic reactions experienced during working periods. Circulating immune cells were measured as neutrophil , lymphocyte, eosinophil and monocyte using automation. The total white cell count was also enumerated by automation. Itching, watery eyes and sneezing were part of the allergic reactions experienced by exposed persons. Total white blood cell (WBC), neutrophil and lymphocyte counts were significantly reduced ($p<0.05$), whereas eosinophil and monocyte counts increased significantly ($p<0.05$) among exposed persons. When viewed from the perspective of exposure setting, morticians (embalmers) had significantly ($p<0.05$) increased eosinophil count but reduced WBC, neutrophil and lymphocyte counts compared to medical laboratory staff. Findings from this study point towards formaldehyde possible impact on immune responses from skin, mucous membrane and even circulating immune cells among exposed persons particularly morticians.

Keywords: Formaldehyde, exposure, immune responses

1. Introduction

Formaldehyde exposure in occupational setting often occurs by inhalation, and is thought to be rapidly metabolized after absorption. Over the years though, findings that suggest immunologic involvements have been reported both in experimental animal models and exposed human populations (Pyatt et al., 2008; Beane-Freeman et al., 2009). Quite disturbing is the inferred risk of lymphohaematopoietic malignancies among workers with history of formaldehyde exposure (Hauptmann et al., 2003; Jakab et al., 2010).

The search for the exact mechanism by which formaldehyde exposure results in systemic abnormalities has yielded quite a few hypothetical thoughts. In a broad manner of consideration, these proposed mechanisms rely on the possible distribution of formaldehyde to distal sites or cancer-initiating processes that could occur in circulation (Murrell et al., 2005; Murgia et al., 2008; Zhang *et al.,* 2009). An interesting observation about formaldehyde has been its identification as an electrophile that reacts with a variety of endogenous molecules, including glutathione, proteins, nucleic acids, and folic acid. Possible effects of such wide scale reactivity include genotoxic damage as well as escape from the natural apoptic signaling pathway (Costa et al., 2008; Thompson*,* 2009).

Some studies have demonstrated increased levels of formaldehyde adducts in exposed persons. More specifically, serum levels of formaldehyde-albumin adducts were found to be significantly higher in laboratory workers exposed to high levels of formaldehyde than in workers exposed at lower levels (Pala et al., 2008). Perhaps, continuous exposure as well as overwhelming endogenous concentrations makes way for competitive binding and transportation of formaldehyde by plasma proteins. In any case, diverse immune response in association with formaldehyde exposure continues to be an area of interest in the evaluation of formaldehyde toxicity. Hence the assessment of formaldehyde-associated immunologic responses among exposed health workers using total white cell, neutrophil, lymphocyte, eosinophil and monocyte counts.

2. Methods

This case-control study was carried out in Calabar, Cross River State of Nigeria. There were 88 persons of both

genders with history of occupational exposure to formaldehyde who participated in the study. An equal number of age and sex-matched subjects with no history of similar exposure were enrolled as control subjects. A structured questionnaire was used to capture individual bio-data and occupation-related information, especially as it concerns allergic reactions to formaldehyde exposure. Two milliliters (2mL) of venous blood was collected aseptically from each subject into an ethylene di-amine tetra acetic acid sample bottle at a concentration of 2mg/mL of blood. Samples were transported to the laboratory and analyzed within two hours of collection. Total white blood cell (WBC), neutrophil, lymphocyte, eosinophil and monocyte counts were performed by automation using Sysmex Kx-2IN from Sysmex Corporation, Japan. SPSS 19.0 was used for the statistical analyses of data. A two tailed P-value of <0.05 was considered indicative of a statistically significant difference.

3. Results

Eighty eight occupationally-exposed persons including Medical laboratory Scientists, Laboratory Attendants, Anatomists and Morticians (Figure 1) were enrolled in the present study. These professionals were further categorized on the basis of the different occupational settings with risk of exposure as Laboratory and Mortuary staff (Figure 2). The common allergic reactions suffered by the exposed persons during work hours as retrieved from the administered structured questionnaire were itching, watery eyes sneezing and airways-related symptoms as shown in Figure 3. Total white blood cell count (WBC), neutrophil, lymphocyte, eosinophil and monocyte counts of both exposed and unexposed subjects are recorded in Table 1. The Total white blood cell count (WBC), neutrophil and lymphocyte counts were significantly reduced ($p<0.05$), where as eosinophil and monocyte counts increased significantly among the exposed subjects compared to control subjects. Furthermore, these parameters were considered among exposed subjects on the basis of place of exposure. The study observed that total white blood cell (WBC), neutrophil and lymphocyte counts of those working in mortuaries were significantly lower ($p<0.05$), whereas eosinophil count was significantly higher when compared to the laboratory staff.

4. Discussion

The circulating immune cells measured as neutrophil, lymphocyte, eosinophil and monocytes counts in this study, revealed significantly lower neutrophil and lymphocyte counts, but higher eosinophil and monocyte counts among professionals occupationally-exposed to formaldehyde in comparison to unexposed persons. Moreover, these relative differences in the measured parameters, with the exception of monocyte count, were even more pronounced for workers whose exposure occurred at the mortuaries as against those working in medical laboratories. In the former group, decline in the lymphocyte count to (0.98×10^9/L) as recorded in this study was actually below the lower border of its reference range ($1.0\text{-}3.0 \times 10^9$/L) as reported by Lewis (2006). Lymphocytes as we know are the major cells that mediate cytotoxic attack, and more precisely antibody secretion. As such, reduced counts may imply reduced antibody production, reduced T cells and it subset production and therefore increased risk of infection for the affected persons. On the other hand, the present study observed reduced total white blood cell count among workers with formaldehyde exposure. Similar finding was reported by Kuo and co-workers (1997), whose study was among nurses with long term exposure to formaldehyde. However, this observed tendency towards reduced WBC count and lympho-suppression may represent the initial direct stages of formaldehyde toxicity to the bone marrow which may evolve with time into more complicated aberrations that mark leukaemogenesis as the body mounts compensatory response. This is even more likely the case, considering that total T cells and more specifically T-suppressor cells are reportedly reduced following formaldehyde exposure (Ye et al., 2005). Ineffective suppression of abnormal cellular clones could thus be one of the consequences of such exposure-related cytotoxicity. To this end, the possibility of a link between formaldehyde exposure and leukaemia has remained a subject of no small controversy, largely due to inconclusive biological evidence on the toxicity of formaldehyde at distal sites including the bone marrow (Heck and Casanova, 2004; Pyatt et al., 2008). Perhaps, immune cells cytoxicity is an important aspect of formaldehyde-associated lymphohaematopoietic disorders. Again, the observed rise in eosinophil count probably represents an aspect of immune response to the allergic effect of formaldehyde on the body. Other allergic reactions to formaldehyde that were recorded in the study include sneezing, itching and tears secretion. Inhalation of formaldehyde obviously is adversely affecting the exposed workers. Such widespread involvement could over time trigger neoplastic development within the naso-pharyngeal compartment, dermatitis and sight deterioration among these exposed workers.

Even with the seemingly impaired marrow production, different circulating immune cells are distinctly affected in the body's response to formaldehyde toxicity. Allergic response appears to be sustained where as humoral immunity and cytotoxic immune surveillance may be dwindling with continued exposure among morticians. The current occupational safety measures in these facilities have to be reviewed in line with current international

labour guidelines on safety with the intent of addressing lapses so as to forestall further deterioration in the health of professionals with risk of exposure.

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Table1. Circulating immune cell counts of persons occupationally exposed to formaldehyde versus those of control subjects

Parameter	Exposed Subjects n=88	Control Subjects n=88	p-Value
WBC (10^9/L)	4.71±1.03	6.23±1.56	p=0.00
Neutrophils (10^9/L)	3.14±0.06	4.13±0.09	p=0.00
Lymphocytes (10^9/L)	1.26±0.08	2.03±0.1	p=0.00
Eosinophils (10^9/L)	0.23±0.03	0.08±0.02	p=0.00
Monocytes (10^9/L)	0.08±0.01	0.06±0.02	p=0.00

Table2. Circulating immune cell counts of persons occupationally exposed to formaldehyde based on setting of exposure

Parameter	Laboratory Staff n=53	Mortuary Staff n=35	p-Value
WBC (10^9/L)	5.04±0.95	4.22±0.96	p=0.00
Neutrophils (10^9/L)	3.27±0.06	2.93±0.04	p=0.00
Lymphocytes (10^9/L)	1.46±0.08	0.98±0.06	p=0.00
Eosinophils (10^9/L)	0.22±0.03	0.24±0.03	p=0.03
Monocytes (10^9/L)	0.08±0.01	0.07±0.01	p>0.05

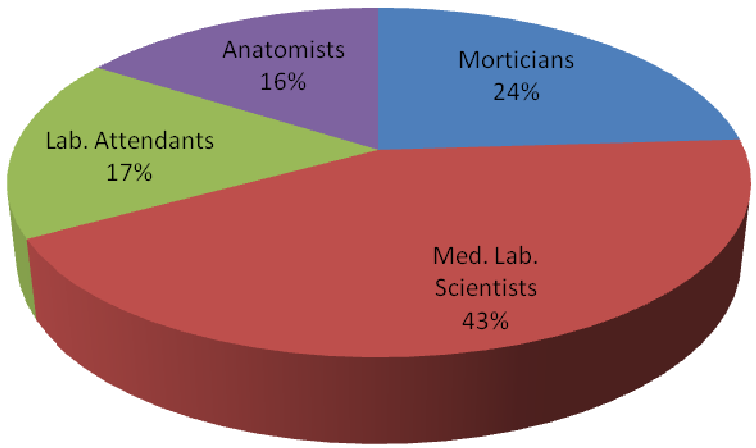

Figure1. Distribution of formaldehyde-exposed persons based on occupation

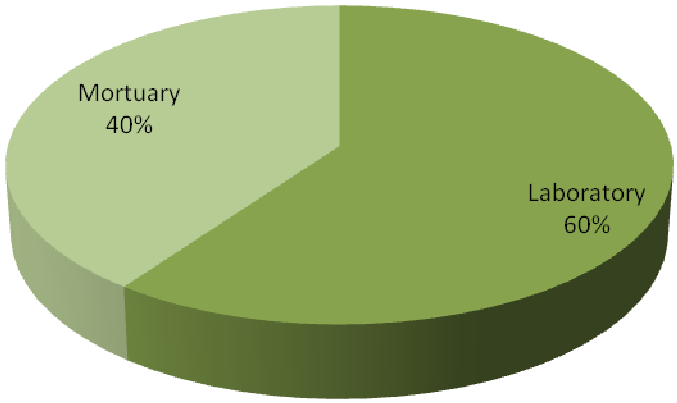

Figure2. Distribution of formaldehyde-exposed persons based on exposure setting

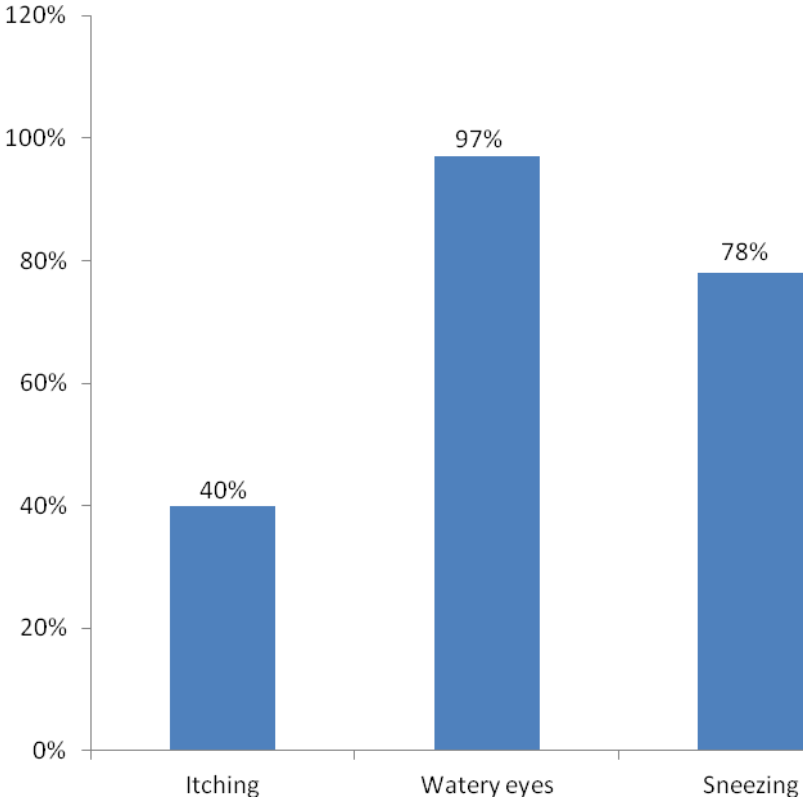

Figure3. Noticeable reactions to formaldehyde among exposed persons