Hematological Indices of Patients with Retained Lead Pellets in the Craniomaxillofacial Region Following Gunshot Wounds

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Abstract

Background: Acute and chronic environmental lead exposures are associated with alteration of hematological parameters. It is not known whether retained lead pellets have similar effects on hematological variables to environmental exposures. **Objective:** The objective of this study is to assess the effects of retained lead pellets on hematological indices in patients that sustained gunshot injuries to the craniomaxillofacial region. **Patients and Methods:** We examined individuals with retained pellets following gunshot injuries to the craniomaxillofacial region using a prospective cohort study design in a tertiary health center, Nigeria. **Results:** A total of 54 male individuals (27 in each group) enlisted in the study. The age of the patients and control subjects ranges from 20 to 58 years, with a mean age of 40.3 years. The mean blood lead levels (BLLs) of the exposed group were lower than the unexposed ($P = 0.03$). There were statistically significant ($P < 0.05$) variations in the hematological indices between the exposed and the unexposed groups. There was a significant association ($P < 0.001$) between the hematological indices assessed and the BLLs, number of retained pellets, and duration of retention. No basophilic stippling was observed in the red cell morphology of the individuals. **Conclusion:** Retained lead pellets cause significant elevated BLL and associated higher hematocrit, hemoglobin concentration, and mean cell volume.

Keywords: Blood lead levels, craniomaxillofacial region, gunshot wounds, hematological indices, lead pellets

Introduction

The effect of lead exposure on the hematological parameters has recently received a great deal of attention because of the implication that mortality from hematological disease might be reduced by preventing lead exposure of any source.[1]

Various experts have reported the effect of lead on oral tissues and nervous, cardiovascular, renal, gastrointestinal, hematological, and reproductive systems.[2,3] Hematological disturbances are seen early before other clinical manifestations.[4] Erythroid alterations are present before the development of clinical symptoms of lead intoxication. The functional hematological alteration from long-term exposure to lead is the reduction in white blood cell count, erythrocyte count, platelet count, hemoglobin (Hb), and hematocrit (Hct) while the morphological alterations are reduced mean cell volume (MCV), mean cell Hb hemoglobin (MCH), and MCH concentration.[3] Other reported alterations are basophilic stippling, microcytosis, and elevated levels of δ-aminolevulinic acid and free erythrocyte protoporphyrin.[4] The anemia is due to lead inhibition of aminolevulinate dehydratase and ferrochelatase, preventing both porphorbilinogen formation and incorporation of iron into protoporphyrin IX; the final step is hem synthesis.[1]

Several occupational-based[5-7] and environmental-based[8-11] studies had demonstrated a relationship between lead exposure and hematological alterations in developed and developing countries. Although several case reports[12,13] have demonstrated a relationship between missile-related lead exposure and hematological changes, they neither uniformly quantify the hematological alterations from report to report nor do they give indication of risk factors. To date, there are no large quantitative controlled studies to guide clinicians as to whether patients with retained lead missiles should be evaluated for hematological changes.

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The prevention of hematological alteration in patients with retained lead missiles requires the development of criteria that will identify individuals at risk of hematological changes. We therefore undertook this cohort study to determine whether there will be alteration in the hematological indices of patients with retained lead missile.

Patients and Methods

Study samples

This study was a case–control research approved by the institution's ethics and research committee. The sample size was extrapolated from the work of previous study.[14] All participants signed the informed consent form and were enrolled simultaneously based on convenience sampling. The recruited test subjects were individuals who had treatment in the Department of Oral and Maxillofacial Surgery of the University of Benin Teaching Hospital, Southern Nigeria, following gunshot injuries to the craniomaxillofacial region with retained lead pellets for not <3 months' duration. They were recalled from the hospital's registry using their names, home addresses, telephone numbers, and e-mail addresses. The participants were matched individually with a control group for age, weight, gender, and socioeconomic status.[14] The controls were individuals treated for craniomaxillofacial fracture(s) with trans-osseous wires or plates and screws based on different etiology other than gunshot injuries. The wires, plates, and screws were retained for not <3 years. Both groups were excluded to control for predictive factors, if there were history of lead exposure from environmental and/or occupational sources, history of chronic disease, and history of hematological diseases, ferritin level <20 ng/ml or >500 ng/ml, and serum iron <50 μg/dl.

Blood lead determination

The sample collection was strictly based on the Centers for Disease Control and Prevention (CDC) guidelines for collecting and handling blood lead samples.[15] About 5 ml of whole blood was obtained by venipuncture from the cubital vein with a sterile 10 ml syringe and subsequently transferred to a heparin-containing test tube. It was transported to a laboratory of the Nigerian Institute for Oil Palm Research where lead analysis was done with atomic absorption spectrophotometry with graphite furnace using the Model 210, Graphite Furnace Atomic Absorption Spectrometer. Readings were recorded after the instrument was the adjustment to wavelength of 217 nm, bandpass of 1.0 mm, detection limit of 0.001 g/dl, optimum working range 2.5, and hollow cathode lamp. Two analytical chemists were instructed to each perform single measurement for standardization. An average of the two measurements was considered for analysis.

Hematological measurement

The blood obtained was analyzed for blood lead levels (BLLs), Hct, hemoglobin (Hb), MCV, and basophilic stippling. All hematological parameters except basophilic stippling were determined with an automated hematology analyzer. For certainty, micro-Hct and cyanmethemoglobin methods were also used for Hct and hemoglobin, respectively. Information on all measurements has been published elsewhere.[16]

Radiographic measurements

The posteroanterior radiographs of the head and necks of the participants were reviewed to verify the presence and approximate estimation of the number of retained pellets. Where there were limitations with the plain radiographs, computed tomography scan was used for pellets dose assessment.

Health and risk questionnaires

These were used to exclude history of previous occupational and/or environmental lead exposure in both the control and test subjects.[17] It was also used to determine the duration of lead pellets retention.

Serum ferritin and iron determination

These estimations were done for both groups to rule out anemia due to iron deficiency. The method of determination was previously described.[6]

Data management

The data collected were age, gender, number of retained pellets, duration of retention, BLL, Hct, and MCV. In univariate analysis, the continuous data were summarized in means and standard deviations and the categorical data were in proportions and percentages. In bivariate analysis, mean difference of continuous variables was tested with two-sampled *t*-tests. In multivariate statistics, the predictor variables were the age, gender, BLL, duration of pellets retention, and number of retained pellets, while the outcome variables were the Hct, Hgb, and MCV. The relationship between these variables was analyzed using Pearson's correlation coefficient after controlling for cofounders. Statistical tests were subjected to assumption testing to determine their data fitness. Using a two-tailed test, a $P < 0.05$ and 95% confidence level were considered statistically significant. Statistical analysis was performed using an SPSS, Version 17 (SPSS, Inc., Chicago, USA).

Results

Of the 32 patients contacted, only 27 agreed to participate and duly gave their consent, thus giving a response rate of 84.4%. This made up the total participants of 54 (27 cases and controls) with age ranging from 20 to 58 years, with a mean of 40.3 years [Table 1]. All enlisted participants were males. The minimum and maximum numbers of 6 and 35 lead pellets were observed, respectively, while the minimum and maximum duration of retention were 5.3 months and 13.8 years, respectively.

The minimum and maximum BLL seen in the test group was 1.13 and 7.58 μg/dl while that of the control group was 0.82 and 2.83 μg/dl, respectively. The difference between their means was statistically significant [Table 2]. There was a variation in all the hematological parameters between the test and the control groups as shown in Table 2, except in the basophilic stippling where no difference was seen. They were all statistically significant ($P < 0.005$) [Table 2].

When adjustment for cofounders in the multivariable analysis was done, there was statistically significant association between the number of retained pellets, duration of retention, and BLL with Hct, Hb, and MCV [Table 3]. There was a stronger association between BLL and MCV followed by Hct and least association with Hb which was the most statistically significant ($P < 0.001$) [Table 3].

Discussion

This study shows that there were significantly higher BLLs in the test group than in the control group. This finding is in agreement with previous studies[18,19] where comparison of BLLs was done between those with and without retained lead missiles (pellets, bullets, and shrapnel) where higher BLL was seen in those with retained missiles in their bodies. This is expected since, in most developed and developing countries such as Nigeria, there is a reduction in environmental and occupational lead exposures due to the ban in leaded gasoline and the reduction in the use of lead in plumbing.[20] However, most countries still use lead in ammunition production making missile-related lead exposure unabated.[21] Although higher levels were seen in these groups, they were lower than the threshold value of 10 µg/dl. This cutoff value as defined by the CDC as a limit for an elevated BLL is primarily based on neurological toxicity.[19] Recent work has shown that there is no level <10 µg/dl that is considered safe.[22]

Table 1: Age distribution of subjects

Age	Number of patients	Number of controls
11-20	2	2
21-30	8	9
31-40	8	9
41-50	6	5
51-60	3	2
61-70	0	0
Total	27	27

There were variations in the hematological parameters between the exposed and the unexposed individuals in this study. However, the lower level of Hct, Hb, and MCV seen in our exposed subjects was not clinically, statistically significant. Thus, the higher BLL is likely implicated for the observed variations [Table 2]. Several occupational[5-7] and/or environmental studies[8-11] have reported similar findings in the exposed compared to the unexposed. However, in a well-controlled occupational study done by Ukaejiofo *et al*.,[23] they reported a mean BLL of 7.00 and 2.00 µg/dl in the exposed and unexposed, respectively, while the value of Hb and Hct in the exposed and unexposed was 12.05 g/dl and 37.97% and 13.25 g/dl and 40.63%, respectively. Khatib *et al*.,[24] when comparing the haematological parameters of prisoners and their control group from the general populations, reported a mean BLL of 0.924 µg/dl in the prisoners and 0.57 µg/dl in the control group while the effects of BLLs on hematological parameters including the Hb of the prisoners were 14.87% in the test group and 16.5% in the control, respectively. The result of our study agrees with previous studies[5,6] but disagrees with the findings from other studies[8,10] that reported lower Hb, Hct, and MCV in the population with lower BLL. In a population-based study conducted by Alsaeed *et al*.,[25] the authors categorized the population based on BLLs and reported that the mean Hb, Hct, and MCV in those with BLL >10 µg/dl were 14.8 µg/dl, 14.6 g/dl, 44.6%, and 82.2 fl, respectively, while that of the group with <10 µg/dl were 4.61 µg/dl, 13.6 g/dl, 43.6%, and 81.5 fl in the same order. The possible reason for these contrary findings is not readily discernible. Literature has shown that there are several case reports that documented hematological alterations following missile-related lead exposure.[12,13] Marc *et al*.[12] reported male patients who had BLL of 201.9 µg/dl and Hb of 7.6 g/dl after 15 years of missile retention. Linden *et al*.[13] reported a female patient who had missile retention for 5 months presenting with BLL, Hct, and Hb of 525 µg/dl, 23.9%, and 7.6 g/dl, respectively. In addition, the patient had reticulocytosis and marked basophilic stippling, which could all probably be due to the high level of lead causing acute toxicity. In contrast, basophilic stippling was not the observation in our study likely because we did not record such high level of BLL [Figure 1].

Table 2: Characteristics of the study participants (*n*=45)

Variables	Measurement	Case	Control	Mean difference	95% CI	*P*
BLL (µg/dl)	Range	1.13-7.58	0.82-2.83	2.74 (0.70)	2.31-2.95	0.03
	Mean (SD)	4.38 (1.60)	1.64 (0.90)			
Hct (%)	Range	30.5-45.8	41.4-43.3	4.90 (0.70)	3.81-5.21	0.01
	Mean (SD)	38.6 (4.50)	43.5 (3.80)			
Hb (mg/dl)	Range	10.1-15.3	11.2-15.4	0.60 (2.1)	0.41-1.58	0.04
	Mean (SD)	12.9 (1.50)	13.5 (3.60)			
MCV (Fl)	Range	79.0-89.0	83.1-93.0			
	Mean (SD)	84.0 (15.2)	88.1 (14.4)	4.1 (0.80)	3.51-6.21	<0.01
Basophilic stippling	*n* (%)	0.00	0.00			

SD – Standard deviation; CI – Confidence interval; BLL – Blood lead levels; Hct – Hematocrit; Hb – Hemoglobin; MCV – Mean cell volume

Table 3: Correlation of hematological parameters, exposures, and risk factor (n=45)

	Hct	Hb	MCV	BLL	Number of pellets	Duration of retention
Hct (%)	1*					
Hb (mg/dl)	0.17¥					
MCV (fl)	0.12¥	0.34¥				
BLL (µg/dl)	0.48**	0.36**	0.62**			
Number of pellets	0.15¥	0.06**	0.32**	0.07**		
Duration of retention	0.26**	0.24**	0.14**	0.19**	0.34¥	1*

*No correlation; **P<0.001; ¥Statistically nonsignificant. Hct – Hematocrit; Hb – Hemoglobin; BLL – Blood lead level; MCV – Mean cell volume

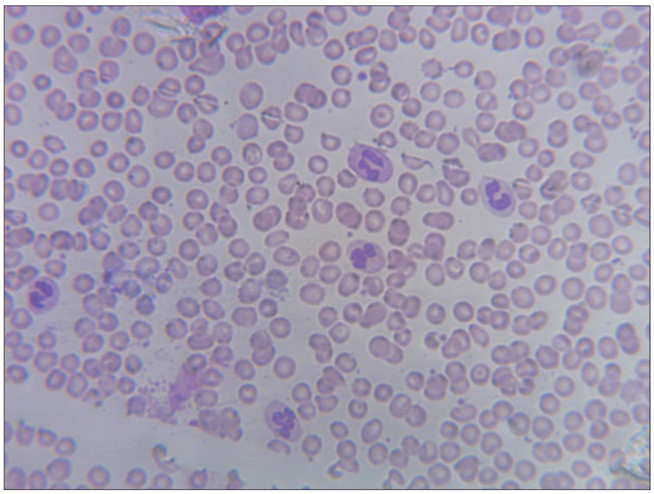

Figure 1: A photomicrograph showing blood film of patients having lead pellets in the body

There was a positive and strong association between BLLs, number of retained pellets, and duration of retention with Hct, Hb, and MCV, which was statistically significant [Table 3]. Although, clinically, all parameters were not significant, they were statistically significant. It would therefore be fair to assume that BLL, number of retained pellets, and duration of retention are related, are associated with hematological parameters, and could be responsible for the deviations in the hematological parameters of our patients. Similar findings were observed by Chalkley *et al*.,[26] who reported a relationship between blood lead and MCV in the London schoolchildren (r = 0.1809, P < 0.001) investigated. A contrasting finding was reported by Hegazy *et al*.,[27] who recorded a significant (P < 0.001) negative correlation between lead level and Hb (r = −0.461), Hct (r = −0.484), and MCV (r = −0.2670) in their investigation of the relationship between anemia and blood levels of lead, copper, zinc, and iron among children. The possible explanation for these differences could be errors in measurements methodology, sample size, or duration of exposure.

Our study was limited by lack of Nigeria's cohort studies in the literature for comparison as regard missile-related lead exposure and hematological parameters.

Conclusion

We conclude from this study that Hct, Hb, and MCV could be lower in individuals with retained pellets in the body than those without. The extent of these hematologic abnormalities is related to the concentration of BLL, number of retained pellets, and duration of body exposure.

Ethics statement/confirmation of patients' permission

The institution's Ethics and Research Committee approval was obtained and informed consent was obtained from each participants.

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Conflicts of interest

There are no conflicts of interest.

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