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ORIGINAL ARTICLE

Effects of lead exposure on the status of platelet indices in workers involved in a lead-acid battery manufacturing plant

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This study was carried out to determine the effect of Pb exposure on the status of platelet indices in workers exposed to Pb during lead-acid battery plant process. Platelet indices and blood lead levels (BLLs) were determined in 429 male workers. BLLs were determined by using an atomic absorption spectrophotometer. Platelet indices in the samples were quantified by using the Sysmex KX-21 hematology analyzer. The levels of platelet count (PLT), plateletcrit (PCT) and mean platelet mass (MPM) were significantly decreased and platelet distribution width (PDW), platelet large cell ratio (P-LCR) and mean platelet volume were increased with an increase in BLLs. The results of linear multiple regression analysis showed that the platelet count (β -0.143, $P=0.005$), PCT (β -0.115, $P=0.023$) and MPM (β -0.110, $P=0.030$) were negatively associated with BLLs and P-LCR (β 0.122, $P=0.016$) was positively associated with BLLs. The variable of body mass index showed a positive association with PCT (β 0.105, $P=0.032$) and MPM (β 0.101, $P=0.039$). The results of the study may indicate that lead exposure may impair coagulation function through endothelial tissue injury and reduction of nitric oxide.

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Keywords: platelet indices; blood lead levels; lead-acid battery plant

INTRODUCTION

Lead is a major environmental and occupational pollutant, and its toxicity continues to be a major public health problem.[1] Pb exposure can cause damages to hematopoietic, nervous and renal systems.[2] Workers are exposed to Pb in many occupations including battery manufacturing and recovery, soldering, lead mining and smelting, lead alloy production and in the paint, glass, plastic, printing, ceramic industries, construction and fiber optic technologies.[3] Lead is absorbed through inhalation, ingestion and dermal contact. Inhalation is the primary route of occupational exposure to lead. After absorption into the blood, 99% of Pb is associated with red blood cells.[4] Platelet is small size blood components and they are formed in the bone marrow from large cells called megakaryocytes. These cells are multifunctional and are necessary for homeostasis, thrombosis, clot retraction, vessel constriction, endothelial repair and promotion of atherosclerosis.[5] The normal platelet count in human beings ranges from 150×10^9/l to 400×10^9/l. If platelet counts are less than 150×10^9/l considered as thrombocytopenia and greater than 400×10^9/l considered as thrombocytosis.

Epidemiological studies have reported a positive association between mean platelet volume (MPV) and risk of cardiovascular disease.[6] Occupational exposure, studies have reported higher platelet count (PLT) in pesticide workers,[7,8] firefighters,[9] cement factory workers,[10] taxi drivers[11] and metallic mercury workers,[12] as well as those exposed to noise[13] and diesel exhaust inhalation.[14] Low platelet counts were reported in gasoline filling workers,[15,16] and those exposed to gas flares[17] and benzene,[18] as well as beedi rollers.[19] Lead affects the blood coagulation actions through endothelial tissue injury, reduced nitric oxide, tissue plasminogen activator and an increased production of plasminogen activator inhibitor-1.[20] The chronic Pb intoxication of animals has reported higher levels of PLT, platelet distribution width (PDW) and MPV.[21–23] In lead battery workers, only PLT count was assessed and other platelet indices such as plateletcrit (PCT), MPV, PDW, platelet large cell ratio (P-LCR) and mean platelet mass (MPM) were not determined.[24,25] Therefore, this study was undertaken to investigate the effect of lead exposure on the status of platelet indices in workers exposed to Pb from lead-acid battery plant with lifestyle confounding factors.

Platelets are special blood cells that plug up damaged blood vessels with the help of a blood clot to stop bleeding. The MPV is a measurement of the average size of platelet cells in the blood, and it is used as an indicator of inflammation and thrombosis.[26] PDW quantifies the variability in the platelet size. The increased level of platelet distribution width indicates platelet anisocytosis. It is a specific marker of platelet activation.[27] PCT reflects the proportion % of whole blood occupied by platelets. It is associated with the PLT count and the size of platelets. P-LCR is the ratio of large platelets. It is used to evaluate the differential diagnosis of conditions associated with abnormal platelet counts.[28] MPM is a better predictor of thrombopoietin production and regulation of megakaryocytic cells.

METHODS

This study was a cross-sectional study carried out in 429 male subjects working in a lead-acid battery manufacturing plant located in Tamil Nadu, India. Status of platelet indices among lead-exposed workers was compared with age, body mass index (BMI), experience, alcohol consumption, smoking, blood lead level (BLL) and job categories. Before including them in the study, an informed consent was obtained from each one of them.

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Demographic details, occupational history and habits of subjects (smoking and alcohol consumption) were collected by using pre-designed questionnaire. BMI was calculated by using subjective weight (kg) and height (m) and expressed as kg/m^2.

Blood Lead Level

Three milliliters of venous whole blood was collected in a heparinized vacuette from the workers and stored at $-20\,^{\circ}C$ until it was taken for analysis. Two milliliters of blood was digested by using an ETHOS-D milestone microwave system (Italy) with 2 ml of nitric acid (HNO_3) and 0.2 ml of hydrogen peroxide (H_2O_2) by maintaining power, temperature and duration of time. The digested samples were made up to 5 ml using triple-distilled water and centrifuged. The concentration of lead in blood was measured using an atomic absorption spectrophotometer (GBC-Avanta, Australia). 20 μg/dl of the standard solution was prepared from the lead standard solution of Merck (1.19776.0500) and added to the lowest concentration of the sample, and the analysis found 100% recovery with % relative standard deviation at <0.5 for three replicates. BLLs were expressed as μg/dl.

Platelet Indices

Two milliliters of venous whole blood was collected from each subject in a lavender-colored top vacutainer tube that contains K3-EDTA. The platelet indices such as PLT, PDW, MPV and P-LCR were quantified within 30 min after collection of samples by using the Sysmex KX-21 hematology analyzer. It is a three-part differential and eighteen-parameter analyzer that works on the principle of volumetric impedance. PCT is a product of platelet count multiplied with MPV divided by 10,000. MPM is a product of MPV and PLT count. The instrument was calibrated by using Bio-Rad QC before analysis of the samples.

Statistical Analysis

Statistical Package for the Social Sciences (SPPS) version 7.5 for Windows, was used for the statistical analysis of the data. The data presented in proportions and adjusted mean with standard error. One-way analysis of variance (ANOVA) was used to assess the effect of categorical variables on platelet indices. One-way ANOVA with *post hoc* test was used to compare various categories within the categorical variables on platelet indices. The Spearman correlation coefficient test was used to find out the correlation between BLLs and platelet indices. Multiple linear regression analysis with the above-mentioned method was used to evaluate the association between platelet indices and BLLs by controlling for the influence of age, BMI, smoking, alcohol consumption and experience. Probability <0.05 was considered significant.

RESULTS

Demographic characteristics of the study population are presented in Table 1. The age distribution reveals that the highest percentage of workers were in the age group of 34–39 years and the lowest percentage of workers were in the age group of 22–27 years. BMI of subject indicates that 56.6% of subjects fall within the normal BMI, 38.5% of subjects correspond to overweight and 3.3% of subjects were obese. Only 1.6% of subjects were underweight. Maximum percentage of lead exposed workers had 11–15 years of exposure. Alcohol consumption and smoking habits were recorded in 39.6% and 19.8%, respectively. The frequency distribution of BLL among subjects was 15.2%, 28.4%, 33.6%, 18.6% and 4.2% in 15–20, 21–30, 31–40, 41–50 and >51 μg/dl, respectively. The highest percentage of BLL was noticed in the range of 31–40 μg/dl. The job categories involved in the manufacturing process are casting, pasting, ball mill, plate cutting, formation, acid filling, charging and assembly. The highest percentage of workers was occupied in the assembly.

Table 1. Demographic characteristics of lead-exposed workers.

Variables	N *(429)*	*Percentage (%)*
Age (years)		
22–27	25	5.8
28–33	105	24.5
34–39	226	52.7
$\geq$40	73	17.0
BMI (kg/m^2)		
$\leq$18.5	7	1.6
18.5–24.9	243	56.6
25–29.9	165	38.5
$\geq$30	14	3.3
Experience (years)		
$\leq$5	36	8.4
6–10	103	24.0
11–15	260	60.6
$>$15	30	7.0
Alcohol consumption		
No	259	60.4
Yes	170	39.6
Smoking		
No	344	80.2
Yes	85	19.8
BLL (μg/dl)		
15–20	65	15.2
21–30	122	28.4
31–40	144	33.6
41–50	80	18.6
$>$51	18	4.2
Job categories		
Assembly	211	49.2
Casting	50	11.7
Pasting	46	10.7
Ball mill	6	1.4
Charging	25	5.8
Plate cutting	5	1.2
Formation	6	1.4
Acid filling	13	3.0
Engineer services	47	11.0
Executives	20	4.7

Table 2 shows univariate analysis of variables that affect on the status of platelet indices among lead-exposed workers. One-way ANOVA was used to find out the effect of categorical variables of age, BMI, experience, alcohol consumption, smoking, BLLs and job category on platelet indices (PLT, PCT, PDW, MPV, P-LCR and MPM) among lead-exposed workers. The results of the model were indicating that the age group category was significantly associated with P-LCR ($P=0.012$) and job category groups were associated with PLT ($P=0.003$), PDW ($P=0.006$), MPV ($P=0.010$) and P-LCR ($P=0.002$). The one-way ANOVA *post hoc* comparison method was used to assess the effect of various categories within the categorical variables on the status of platelet indices. The level of P-LCR was significantly reduced in the age group of 34–39 years as compared to age group of 22–27 years. The measurements of PCT and MPM significantly decreased in the experience category of 6–10 and 11–15 years as compared with $\leq$5 years. PLT count reduced in the BLL category from 41 to 50 and >51 μg/dl as a contrast to BLL 15–20 μg/dl. PCT and MPM noticeably reduced in BLL categories from 20–30, 31–40 and 41–50 μg/dl, as evaluated with a BLL of 15–20 μg/dl. The levels of PLT, PCT and MPM were decreased significantly in operators, who are working in assembly, casting, pasting, charging, plate cutting and acid filling, as compared with the executives. The variables of BMI, alcohol consumption and smoking habits shows no significant effect on platelet indices.

The results of Spearman's correlation coefficients (r) between BLL and platelet indices among lead-exposed workers are presented in Table 3. A negative correlation coefficient was noticed between BLL and PLT ($r=-0.117$; $P=0.015$), PCT ($r=-0.080$; $P=0.097$) and MPM ($r=-0.076$; $P=0.114$). A significant correlation was noticed between BLL and PLT. The positive correlation coefficient was noticed between BLL and PDW ($r=0.077$;

Table 2. Univariate analysis of the variables that affect platelet indices among lead-exposed workers.

Variables	N *(429)*	*Percentage (%)*	*PLT (x $10^3/\mu$l)*	*PCT (fL)*	*PDW (fL)*	*MPV (fL)*	*P-LCR (%)*	*MPM (fl/nl)*
Age (years)								
22–27	25	5.8	258 ± 12.1	0.26 ± 0.01	13.0 ± 0.5	10.2 ± 0.22	26.9 ± 1.7	2586 ± 101
28–33	105	24.5	248 ± 6.5	0.23 ± 0.005	12.4 ± 0.3	09.7 ± 0.15	24.4 ± 1.0	2379 ± 55
34–39	226	52.7	262 ± 4.1	0.25 ± 0.003	12.0 ± 0.1	09.5 ± 0.08	23.0 ± 0.6	2480 ± 35
≥40	73	17.0	248 ± 7.8	0.24 ± 0.007	13.0 ± 0.4	09.9 ± 0.20	25.9 ± 1.2	2432 ± 75
P-values for ANOVA test			*P* = 0.178	*P* = 0.239	*P* = 0.054	*P* = 0.088	*P* = 0.012*	*P* = 0.273
BMI (kg/m^2)								
≤18.5	7	1.6	231 ± 26	0.22 ± 0.02	12.8 ± 0.9	10.0 ± 0.44	25.7 ± 3.2	2245 ± 210
18.5–24.9	243	56.6	255 ± 4.2	0.24 ± 0.003	12.2 ± 0.2	9.63 ± 0.10	23.4 ± 0.6	2424 ± 39
25–29.9	165	38.5	259 ± 4.7	0.25 ± 0.004	12.4 ± 0.2	9.80 ± 0.09	24.3 ± 0.7	2499 ± 36
≥30	14	3.3	253 ± 19	0.25 ± 0.02	13.0 ± 0.6	10.0 ± 0.24	26.0 ± 1.7	2518 ± 173
P-values for ANOVA test			*P* = 0.630	*P* = 0.363	*P* = 0.646	*P* = 0.446	*P* = 0.555	*P* = 0.555
Experience (years)								
≤5	36	8.4	268 ± 11	0.26 ± 0.009	12.6 ± 0.4	9.95 ± 0.89	25.4 ± 1.2	2645 ± 93
6–10	103	24.0	252 ± 6.3	0.24 ± 0.005*	12.6 ± 0.3	9.82 ± 1.66	24.7 ± 1.0	2433 ± 56*
11–15	260	60.6	255 ± 4.0	0.24 ± 0.003*	12.1 ± 0.2	9.62 ± 1.46	23.2 ± 0.6	2425 ± 35*
> 15	30	7.0	260 ± 8.9	0.25 ± 0.006	12.7 ± 0.4	9.89 ± 1.04	24.8 ± 1.4	2536 ± 64
P-values for ANOVA test			*P* = 0.605	*P* = 0.139	*P* = 0.301	*P* = 0.390	*P* = 0.342	*P* = 0.124
Alcohol consumption								
No	259	60.4	258 ± 4.0	0.25 ± 0.003	12.2 ± 0.2	09.7 ± 0.09	23.7 ± 0.57	2471 ± 38
Yes	170	39.6	252 ± 4.8	0.24 ± 0.003	12.4 ± 0.2	09.8 ± 0.09	24.1 ± 1.1	2426 ± 39
P-values for ANOVA test			*P* = 0.415	*P* = 0.415	*P* = 0.486	*P* = 0.428	*P* = 0.633	*P* = 0.410
Smoking								
No	344	80.2	256 ± 3.3	0.24 ± 0.003	12.3 ± 0.1	09.7 ± 0.08	23.7 ± 0.48	2459 ± 30
Yes	85	19.8	253 ± 7.6	0.24 ± 0.006	12.6 ± 0.3	09.8 ± 0.15	24.5 ± 1.16	2430 ± 59
P-values for ANOVA test			*P* = 0.685	*P* = 0.687	*P* = 0.331	*P* = 0.401	*P* = 0.507	*P* = 0.672
BLL (μg/dl)								
≤20	65	15.2	272 ± 7.1	0.26 ± 0.006	12.2 ± 0.28	9.68 ± 0.13	22.8 ± 1.07	2608 ± 65
21–30	122	28.4	255 ± 5.9	0.24 ± 0.005*	12.3 ± 0.26	9.61 ± 014	23.2 ± 0.86	2417 ± 52*
31–40	144	33.6	256 ± 5.6	0.24 ± 0.005*	12.2 ± 0.23	9.72 ± 0.12	24.0 ± 0.79	2446 ± 47*
41–50	80	18.6	248 ± 6.8*	0.24 ± 0.006*	12.5 ± 0.33	9.82 ± 0.18	25.0 ± 1.08	2415 ± 61*
> 50	18	4.2	239 ± 12.6*	0.23 ± 0.010	13.0 ± 0.67	10.0 ± 0.24	25.9 ± 1.89	2370 ± 102
P-values for ANOVA test			*P* = 0.178	*P* = 0.158	*P* = 0.792	*P* = 0.494	*P* = 0.494	*P* = 0.179
Job category								
Assembly	211	49.2	250 ± 4.3**	0.24 ± 0.004*	12.5 ± 0.19	9.9 ± 0.10	25.1 ± 0.64	2432 ± 39**
Casting	50	11.7	255 ± 7.9*	0.24 ± 0.003*	12.1 ± 0.35	9.6 ± 0.17	23.0 ± 1.32	2420 ± 61*
Pasting	46	10.7	245 ± 9.6**	0.24 ± 0.007*	13.3 ± 0.55	10.0 ± 0.21	26.4 ± 1.62	2416 ± 76*
Ball mill	6	1.4	266 ± 23.6	0.25 ± 0.019	11.7 ± 0.57	9.5 ± 0.15	21.5 ± 1.44	2509 ± 197
Charging	25	5.8	247 ± 14.3*	0.24 ± 0.0018*	12.4 ± 0.48	9.8 ± 0.25	23.6 ± 2.07	2363 ± 108*
Plate cutting	5	1.2	232 ± 18.8*	0.22 ± 0.019*	12.4 ± 0.65	9.6 ± 0.28	24.0 ± 2.34	2240 ± 197*
Formation	6	1.4	252 ± 14.7	0.23 ± 0.009	11.2 ± 0.31	9.4 ± 0.23	17.5 ± 3.90	2340 ± 90
Acid filling	13	3.0	246 ± 16.2*	0.23 ± 0.010*	12.2 ± 0.57	9.7 ± 0.28	23.6 ± 2.18	2350 ± 107*
Engineer services	47	11.0	290 ± 9.2	0.26 ± 0.009	10.8 ± 0.34*	8.9 ± 0.23*	18.4 ± 1.05*	2590 ± 97
Executives	20	4.7	292 ± 16.9	0.27 ± 0.014	12.4 ± 0.48	9.7 ± 0.21	23.0 ± 1.64	2783 ± 145
P-values for ANOVA test			*P* = 0.003**	*P* = 0.234	*P* = 0.006**	*P* = 0.010*	*P* = 0.0.002**	*P* = 0.179

Values are mean ± standard error. $^*P < 0.05$ and $^{**}P < 0.01$.

$P = 0.113$), MPV ($r = 0.087$; $P = 0.071$) and P-LCR ($r = 0.097$; $P = 0.045$). The correlation coefficient between BLL and P-LCR was significant. Positive correlation coefficients (r) were found between PLT and PCT ($r = 0.884$; $P < 0.01$) and MPM ($r = 0.889$; $P < 0.01$). Negative correlation coefficients (r) were found between PLT and PDW ($r = -0.485$; $P < 0.01$), MPV ($r = -0.515$; $P < 0.01$) and P-LCR ($r = -0.524$; $P < 0.01$).

Linear multiple regression analysis of variables that affect platelet indices among lead-exposed workers were presented in Table 4. In this model, each of the parameters of platelet indices (PLT, PCT, PDW, MPV, P-LCR and MPM) were used as dependent variables, and BLL, age, BMI, alcohol consumption (yes = 1 and no = 0), smoking habits (yes = 1 and no = 0) and experience (years) were used as independent variables. The results of linear multiple regression analysis showed that the platelet count (β -0.143, $P = 0.005$), PCT (β -0.115, $P = 0.023$) and MPM (β -0.110, $P = 0.030$) were negatively associated with BLL and the P-LCR was positively associated with BLL. The variable of BMI showed a positive and significant association with PCT (β 0.105, $P = 0.032$) and MPM (β 0.101, $P = 0.039$). The variables of age, smoking, alcohol consumption and experience were not predicted significantly on platelet indices.

DISCUSSION

The present study assessed the effect of Pb exposure on the status of platelet indices in subjects exposed to Pb during lead-acid battery plant process. Biino et al.[29] has reported decreasing PLT by 35% in male subjects and 25% in female subjects from infancy to adulthood. In this study, age groups showed a significant association with P-LCR. Samocha-Bonet et al.[30] and Farhangi et al.[31] have reported a significant association between obesity and platelet counts in female subjects. During this study, the comparison of univariate analysis did not find any association. However, linear multiple regression analysis indicates that the BMI significantly associated with PCT and MPM. Alcohol consumption causes low platelet counts, impaired platelet function and diminishes fibrinolysis.[32] In the current study, we observed

Table 3. Spearman's correlation coefficient (*r*) between BLLs and platelet indices among lead-exposed workers.

Parameters	*BLL (μg/dl)*	*PLT ($\times 10^3/\mu$l)*	*PCT (%)*	*PDW (fL)*	*MPV (fL)*	*P-LCR (%)*	*MPM (fl/nl)*
BLL (μg/dl)	1.000	–	–	–	–	–	–
PLT($\times 10^3/\mu$l)	− 0.117[a]	1.000	–	–	–	–	–
PCT (%)	− 0.080	0.884[b]	1.000	–	–	–	–
PDW (fL)	0.077	− 0.485[b]	− 0.102[a]	1.000	–	–	–
MPV (fL)	0.087	− 0.515[b]	− 0.110[a]	0.952[b]	1.000	–	–
P-LCR (%)	0.097[a]	− 0.524[b]	− 0.127[b]	0.959[b]	0.982[b]	1.000	–
MPM (fl/nl)	− 0.076	0.889[b]	0.998[b]	− 0.107[a]	− 0.116[a]	− 0.133[b]	1.000

[a]Correlation coefficient significant at $P<0.05$.
[b]Correlation coefficient significant at $P<0.01$.

Table 4. Linear multiple regression analysis of variables that affect platelet indices among lead-exposed workers.

Independent variables	*PLT ($\times 10^3/\mu$l)*	*PCT (%)*	*PDW (fL)*	*MPV (fL)*	*P-LCR (%)*	*MPM (fl/nl)*
Age (years)	− 0.024	0.120	0.094	0.063	0.082	0.012
BMI (kg/m^2)	0.080	0.105[a]	− 0.027	0.007	− 0.001	0.101[a]
BLLs (μg/dl)	− 0.143[b]	− 0.115[a]	0.086	0.084	0.122[a]	− 0.110[a]
Duration of exposure (years)	− 0.079	− 0.102	− 0.013	− 0.010	− 0.014	− 0.105
Alcohol consumption	− 0.038	− 0.039	0.022	0.027	0.014	− 0.039
Smoking	0.000	− 0.002	0.035	0.026	0.019	− 0.003

Linear multiple regression model included age, BMI, BLLs, duration of exposure (years), alcohol consumption and smoking.
[a]Standard regression coefficient β is significant at $P<0.05$.
[b]Standard regression coefficient β is significant at $P<0.01$.

decreased platelet count, PCT and MPM and increased PDW, MPV and P-LCR in alcoholics as compared with nonalcoholics. Akkani et al.[33] reported significantly decreased platelet count in heavy alcohol consumers as compared with nonalcoholics. In this study, both univariate and linear multiple regression analysis showed no significant association between alcohol consumption and platelet indices. This was because subjects were using minimal to moderate amount of alcohol. Gitte[34] reported significantly increased platelet count in male smokers, who smoke 20 or more cigarettes per day in 20 years of duration. In the current study, the univariate and linear multiple regression analysis showed no significant association between smokers and platelet indices. The findings of this study were similar to the study of Suwanskasri et al.[35]

The effect of Pb intoxication of animal has reported higher levels of PLT, MPV and PDW as compared with controls.[21–23] Shaik and Jamil[24,25] reported no significant differences in PLT of lead battery workers as compared with controls. These studies assessed only platelet counts among lead battery workers. In the current study, we assessed the effect of Pb exposure on platelet indices among lead-exposed workers. The reduced platelet count was reported in acute lead intoxicated in female battery workers,[36] lead exposed to workers in traditional tile factories[37] and fish exposed to lead.[38] The univariate analysis indicated that the levels of PLT, PCT and MPM were significantly decreased with an increase of BLL and PDW, and the MPV and P-LCR were increased with an increase of BLL. The levels of PLT, PCT and MPM were significantly reduced in operators, who were occupied in assembly, casting, pasting, charging, plate cutting and acid filling, as compared with executives. The results of linear multiple regression analysis showed that the platelet count, PCT and MPM were inversely associated and P-LCR was positively associated with BLLs.

Adeyemo et al.[39] and Kianoush et al.[40] reported a negative association between BLL and PLT in fish exposed to Pb and car battery industry workers exposed to Pb. In the current study, we found a negative association between BLL and PLT, and PCT and MPM, and a positive association between BLL and PDW, and MPV and P-LCR. The significant association was noted between BLL and PLT and P-LCR.

The alteration of platelet indices in lead-exposed workers may be the effect of intracellular Ca_2^+ homeostasis, either by mimicking Ca^{2+} action or antagonizing Ca^{2+}-dependent cellular functions and activation of protein kinase C[41] and also its actions on endothelial tissue injury, decreased levels of nitric oxide, tissue plasminogen activator and an increased level of plasminogen activator inhibitor-1.[20]

The levels of PLT, PCT and MPM were significantly decreased and PDW, P-LCR and MPV were increased with an increase of BLL. The levels of PLT, PCT and MPM were negatively associated with BLL, and the levels of PDW, MPV and P-LCR were positively associated with BLL. The results of the study may indicate that lead exposure may impair coagulation function through endothelial tissue injury and reduction of nitric oxide.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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