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The Influence of Sustained Mercury Exposure on Prothrombin Time and Partial Thromboplastin Time among Sudanese Gold Mining Workers

Rimonda Emil Tadros[1], Elharam Ibrahim Abdallah[1], Alaa Eltayeb Omer[2], Abdel Rahim Mahmoud Muddathir[3], Lienda Bashier Eltayeb[2*]

[1]*Department of Hematology and Blood Transfusion, Faculty of Medical Laboratory Sciences Alzaeim Alazhari University, Khartoum, Sudan*
[2]*Department of Medical Laboratory Sciences, College of Applied Medical Sciences Prince Sattam Bin Abdulaziz University, Al-Kharj, Saudi Arabia*
[3]*Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences Taibah University, Medina, Kingdom of Saudi Arabia*

Abstract

Background: Gold mining is the world's leading source of anthropogenic mercury pollution, negatively impacting not only miners but also the surrounding inhabitants; it has many effects on human health, especially cardiovascular problems, which lead to coagulation disorders and an increase in morbidity and mortality rate. The present study aimed to determine the prothrombin time (PT) and partial thromboplastin time (PTT) among Sudanese gold mining workers exposed to mercury.

Methods and Results: This cross-sectional study was carried out among mining workers in the Red Sea state. A total of 50 mining workers were enrolled in the case group, and 50 non-mining apparently healthy subjects were the control group. About 5 ml of whole blood samples were collected in 3.2% sodium citrate blood collection tubes. Platelet poor plasma (PPP) for prothrombin time (PT) and partial thromboplastin time (PTT) measurements was obtained by using high-speed centrifugation. PT and PTT tests were performed using a standard method (Practical-Haemostasis.com.) with a Helena C2 coagulometer (Germany) and reagents manufactured by the Bio-med trademark (China). The mean age of miners was 33.5±11.5 years and occupation time - 1.94±2.1 years. The mean value of PTT was greater in the case group than in the control group (42.43±6.18 sec vs. 37.76±5.33 sec, *P*=0.000). In the age subgroup <40 years, the PT level was longer than in the age subgroup >40 years: 14.04±1.38 sec vs. 13.15±1.35 sec (*P*=0.045), respectively. The correlation analysis revealed a significant, direct correlation between PTT and occupation time (r=0.357, *P*=0.011).

Conclusion: Prolonged coagulation time, notably PTT, has been revealed among mining workers, implying that these workers may have a clinically silent state of coagulation abnormalities.(**International Journal of Biomedicine. 2022;12(2):251-255.**)

Key Words: Mercury • mining workers • prothrombin time • partial thromboplastin time • platelet poor plasma

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Abbreviations

INR, international normalized ratio; **MV,** microvesicle; **PT,** prothrombin time; **PTT**, partial thromboplastin time; **PPP**, platelet poor plasma; **PS**, phosphatidylserine.

Introduction

Mercury is a heavy metal of known toxicity, noted for inducing public health disasters,[1,2] and human exposure to mercury is still a major public health concern; exposure to it is the second most common cause of toxic metal poisoning. The clinical impact of smaller mercury exposures remains controversial.[3,4]

Sudan's gold mining activities are largely conducted in the so-called "informal" economy, during which participants operate unapproved or without legal authorization.[5] Thus, ensuring efficient regulation of mercury emissions is incredibly challenging. These miners significantly contribute to the regional and global sectors of the economy, producing 15% to 25% of the world's gold,[6] so even though each individual mining activity may be limited, the procedure is widespread. The burden on human health is incredible as a result of the remarkable quantities of mercury handled directly by miners and discharged into the atmosphere.[7]

Human toxicity varies with the form of mercury, the dose, and the rate of exposure. The target organ affected by inhaled mercury vapor is the brain, while mercurous and mercuric salts chiefly damage the gut lining and kidneys, and methyl mercury is widely distributed throughout the body. Toxicity varies with dosage: large acute exposures to elemental mercury vapor induce severe pneumonitis, which in extreme cases can be fatal.[8,9] Mercury vapor (an extremely toxic form to humans) inhaled by miners results in impaired cognitive function, neurological damage, kidney damage, and several other health problems. In some cases, amalgams are processed near the home or in gold shops in villages or cities, so the mercury vapor generated in the process affects non-miners living in these areas.[10]

Numerous toxic effects of mercury have been demonstrated in vitro and in animal and human studies. Mercury has a high affinity for sulfhydryl groups, various enzymes and amino acids, N-acetyl cysteine, alpha lipoic acid, and glutathione, which provide about 10% to 50% of the plasma protein antioxidant capacity[11,12] and protect against oxidative stress and inflammation. Mercury increases free-radical production and inactivates antioxidant defenses,[13-15] increases lipid peroxidation[16,17], endothelial dysfunction,[18] and platelet aggregation, production of Factor VIII, platelet factor 4,[19,20] and thrombin.[17,21] All of these abnormalities have the potential to increase the risk for CVD.[15,20,22-26]

Mercury's well-documented hemolytic and anemia-inducing effects suggest that the erythrocyte may be an appropriate priority of mercury. Minimal Hg2+ exposure has been shown to induce phosphatidylserine (PS) translocation to the erythrocyte cell membrane via modulation of a clotrimazole-sensitive potassium ion (K+) channel.[27] Nevertheless, no mention was made of the role of PS-externalized erythrocytes in procoagulant stimulation and subsequent cardiovascular diseases. Another study found that changes to the erythrocyte membrane, such as PS exposure and PS-bearing microvesicle (MV) formation, could make erythrocytes procoagulant, allowing erythrocytes to actively participate in thrombosis MVs derived from deformed erythrocytes via vehiculation, and could also contribute to acceleration of the coagulation cascade and via strong procoagulant activity by representing as a rich source of PS.[28,29] The present study aimed to determine the PT and PTT among Sudanese gold mining workers exposed to mercury.

Materials and Methods

This cross-sectional study was carried out among mining workers in the Red Sea state (Mooch and Arbaate). All adult male mining workers were involved in the study. Exclusion criteria: diseases that affect blood coagulation, and alcohol intake.

A total of 50 mining workers were enrolled in the case group, and 50 non-mining apparently healthy subjects were the control group. About 5 ml of whole blood samples were collected in 3.2% sodium citrate blood collection tubes. Platelet poor plasma (PPP) for prothrombin time (PT) and partial thromboplastin time (PTT) measurements was obtained by using high-speed centrifugation. PT and PTT tests were performed using a standard method **(**Practical-Haemostasis.com.) with a Helena C2 coagulometer (Germany) and reagents manufactured by the Bio-med trademark (China). Laboratory work was conducted at Al Shifa Medical Center (Sudan).

Statistical analysis was performed using the IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Baseline characteristics were summarized as frequencies and percentages for categorical variables. For descriptive analysis, results are presented as mean ± standard deviation (SD). For data with normal distribution, inter-group comparisons were performed using Student's t-test. Pearson's correlation coefficient (r) was used to determine the strength of the relationship between the two continuous variables. A probability value of $P<0.05$ was considered statistically significant.

The study was approved by the Ethics Committee of the department of the Faculty of Medical Laboratory Sciences, Alzaeim Alazhari University (Khartoum, Sudan). Written informed consent was obtained from each research participant.

Results

All 50 mining workers (Case group) were divided into 2 age subgroups: >40 years - 14(28%) participants and ≤40 years - 36(72%) participants. Regarding the duration of mining work, the majority of miners (86%) have less than 5 years of work experience. The mean age of miners was 33.5±11.5 years and occupation time - 1.94±2.1 years (Tables 1 and 2).

Table 1.

Demographic data of study participants

	Case group n (%)	Control group n (%)
Age subgroup		
≤ 40 years old	36 (72.0)	29 (58.0)
>40 years old	14 (28.0)	21 (42.0)
Work experience		
≤ 5 years	43 (86.0)	-
> 5 years	7 (14.0)	-

Parameters of PT, PTT, and INR of subjects in both groups are presented in Table 3. The mean value of PTT was greater in the case group than in the control group (42.43±6.18 sec vs. 37.76±5.33 sec, $P=0.000$). The mean level of PT in the 2 groups

did not differ significantly (P=0.078). In the age subgroup <40 years, the PT level was longer than in the age subgroup >40 years: 14.04±1.38sec vs. 13.15±1.35sec (P=0.045), respectively. The levels of INR and PTT did not differ between the age subgroups (Table 4).

Table 2.

Age and work experience of mining workers

Variable	Minimum	Maximum	Mean ±SD
Age, yrs	16.0	61.0	33.5±11.5
Work experience, yrs	0.05	7.52	1.94±2.09

Table 3.

Mean levels of the study parameters in the case and control groups

Parameters	Case group	Control group	*P*-value
PT, sec	13.79±1.41	13.38±0.82	0.078
PTT, sec	42.43±6.18	37.76±5.33	0.000
INR	1.13±0.24	1.07±0.06	0.090

Table 4.

Mean levels of the study parameters in the age subgroups of mining workers

Parameter	≤40 years n=36	>40 years n=14	*P*-value
PT, sec	14.04±1.38	13.15±1.35	0.045
PTT, sec	42.80±5.98	41.48±6.81	0.503
INR	1.12±0.21	1.14±0.31	0.794

The correlation analysis (Figure 1-3) revealed a significant, direct correlation between PTT and occupation time (r=0.357, P=0.011).

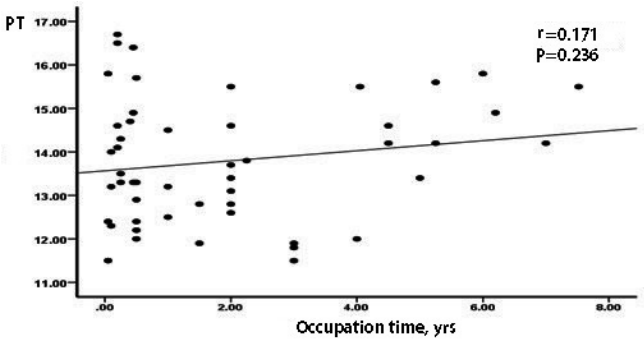

Fig. 1. *Correlation between PT and occupation time*

Discussion

Coagulation studies are one of the most important tools in investigating and monitoring the toxicity of chemicals and their effects on human health. The impact of mercury on human health ranges from moderate to severe, depending on many factors. Exposure to dust from mining can lead to many pathological effects, depending on mineralogical composition, size, shape and levels, and duration of exposure.

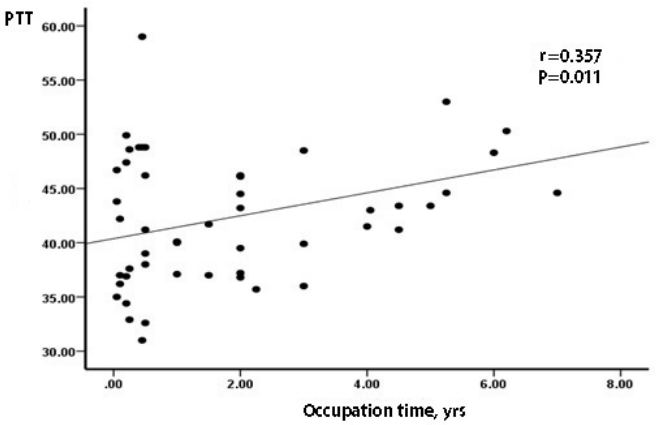

Fig. 2. *Correlation between PTT and occupation time.*

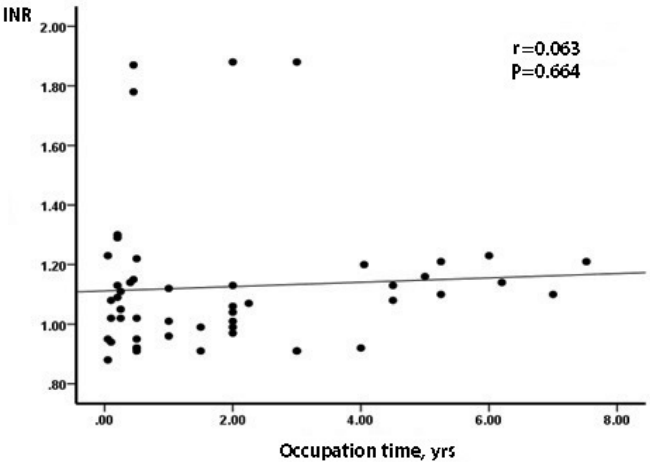

Fig. 3. *Correlation between INR and occupation time.*

Little is known about the current health status of miners, in part because no health surveillance systems exist for this population, but some studies have been developed with the concern about heavy metal exposure and related complications. Hence, the current study aimed to determine PT and PTT among Sudanese mine workers exposed to mercury. Our study showed that, there was a significant increase in PTT (42.43±6.18, P<0.000) when compared with healthy individuals (37.76±5.33 sec). Dhanapriya et al.[30] described a case of a patient with unknown substance poisoning who developed acute kidney injury and disseminated intravascular coagulation. The patient's coagulation profile showed PT of 18 sec, INR of 1.6, and APTT of 60 sec. Renal biopsy showed acute tubular necrosis. Later, the consumed substance was proven to be mercuric chloride. Bai et al.[31] described a case of acute severe mercuric chloride in a 38-year-old woman who orally took about 50g of $HgCl_2$ powder. The coagulation tests displayed that PT was 26.7 sec, APTT - 45.7 sec, INR - 2.36, and fibrinogen - 0.63 g/L. The patient was diagnosed with acute oral $HgCl_2$ poisoning, multiple organ dysfunction syndrome (MODS), and digestive tract hemorrhage. At the

same time, Lim et al.[32] demonstrated that mercury could provoke procoagulant activity in erythrocytes through protein-thiol depletion-mediated PS exposure and MV generation, ultimately leading to enhanced thrombosis.

The interaction of mercury ions with hemoglobin or plasma proteins might result in mercury diffusion, which could be distributed in various tissues and organs, such as the liver, large intestine, and small intestine, particularly the kidney, via blood circulation. As a consequence, patients with acute mercury poisoning commonly have multiple organ function failures. Furthermore, the combination of mercury ion and sulfhydryl enzyme in the body may cause degeneration and necrosis of the renal proximal convoluted tubule, tubule blockage, and renal parenchymal lesion, likely to result in oliguric acute renal failure. Routine follow-up using a coagulation profile, especially PTT, must be applied. Furthermore, mercury ions may inhibit the activity of cytochrome oxidase and pyruvate kinase, as well as affect functional groups, negatively impacting cell biological activities and standard metabolism and ultimately leading to cell degeneration and necrosis.

Limitation of the Study and Prospective

A deep investigation of the intrinsic pathway of coagulation factors must be done (VIII, IX, XI, XII). Routine medical assessments for mining workers in order to minimize the risks they potentially face through their duties should be applied.

Conclusion

Prolonged coagulation time, notably PTT, has been revealed among mining workers, implying that these workers may have a clinically silent state of coagulation abnormalities.

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Competing Interests

The authors declare that they have no competing interests.

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***Corresponding author**: Dr. Lienda Bashier Eltayeb. Department of Medical Laboratory Science, College of Applied Medical Science, Prince Sattam bin Abdulaziz University, Al-Kharj, Saudi Arabia. E-mail: lindarose009@hotmail.com*

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