

Hormonal Disorders among Stone Miners in Igarra, Akoko Edo Local Government Area, Edo State, Nigeria

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Abstract

Mining releases several reproductive toxicants during mining processes and occupationally exposed miners could be directly affected. The awareness of reproductive health hazards may help modify the lifestyle of individuals at risk. This study seeks to determine the hormonal status of occupationally exposed male stone miners in Edo North, Edo, Nigeria. Serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), and testosterone were determined in 146 stone miners age range 18-40 years and 50 age-matched non-occupationally male subjects using enzyme-linked Immunosorbent assay method. Data were compared using chi square or Students t-test as appropriate. Serum LH and testosterone were significantly lower ($p<0.001$) while serum FSH and prolactin were significantly higher ($p<0.001$) among stone miners than non-stone miners. The hormonal imbalance was observed among 30.8% of stone miners and hormonal disorders observed were 6.2% with hyperprolactinaemia, 24.7% with hypogonadism while 69.2% had normal hormone levels. Hormonal abnormalities are common among stone miners. Further study involving a large population is required to know the magnitude of the potential danger to reproductive health in humans.

Keywords: Miners, Humans, Local government, Nigeria

Introduction

Male reproductive health indices have been reported to be on the decline since the 20th century across the world as a result of industrialization. In Africa, the male infertility prevalence rate is higher and ranges from 20-45% (1-5). The so-called infertility belt lies around the equatorial region of Africa stretching from West Africa through Central to East Africa (4). In Nigeria, male factor infertility accounts for 40-50% of infertility (6, 7) and affects approximately 7% of all men (8). Causes of male infertility are multifactorial but environmental pollutants have been reported to be major contributing factors (9). The earth's crust contains several reproductive toxicants which are released during mining processes and miners who are directly exposed to these toxicants could be worse affected.

Despite the health hazards associated with this job, most of the miners do not use protective devices, and somewhat worrisome is the under-regulation and occupational health and safety negligence bewildering the mining sector, especially in developing countries such as Nigeria. Evidence suggests that some toxicants inhibit spermatogenesis, cause induction of oxidative stress and consequently cause perturbation of the reproductive hormones (10). Stone Crushing/mining is an important industrial sector in Nigeria and the miners are involved in the production of various sizes of stone depending upon the requirement which acts as raw material for several construction activities including building roads, bridges, houses, and canals. Stone mining is a source of earning for several educated and uneducated people especially in developing countries like Nigeria where employment is not readily available. Even though stone mining is an important socio-economically sector, it is a major source of environmental pollution which does not only creates health hazards to the workers but also to individuals residing close to

the mining site (11). The mammalian male reproductive function may be affected via a direct effect on the testis, leading to declining or altered sperm production, through inhibition of the accessory sex gland secretions, or indirectly via the endocrine system, resulting in hormonal abnormalities (12). The functionalities of the male reproductive system are largely dependent on hormones that are produced by endocrine glands. Imbalance in hormone production and transportation challenges to the sites of action has been reported as one of the causes of male infertility (13). The contribution of endocrine abnormalities to male infertility is continuously identified and some authors have attributed it to differences in environmental pollutions as a result of crude oil exploration and exploitation (14, 15). Although infertility is not a life-threatening disorder, it may lead to other medical challenges and psychosocial problems including marital disharmony, stigmatization, depression, and psychiatric challenges (16). The awareness of reproductive health hazards may help modify the lifestyle of individuals at risk. This study, therefore, seeks to assess the hormonal status of occupationally exposed male stone miners in Edo North, Edo, Nigeria.

Materials and methods

Study participants were occupationally exposed male stone miners who were randomly recruited from stone mining sites/factories in selected communities (Sassaro, Egbigere, Ikpeshi) in Igarra, Akoko Edo Local Government Area, Edo North Senatorial district Edo State, Nigeria. Control subjects were selected from age-matched healthy occupationally unexposed males in the same area. Study participants were within the age range of 18-40 yrs.

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Ethical Consideration

Ethical approval for this study was obtained from the Ethics and Research Committee of the Ministry of Health, Edo State (ref HA560.Vol.2/185; dated 10th September 2019). Informed consent of study participants was obtained verbally after a thorough explanation of the rationale of the study.

Inclusion criteria

Only the participants who met the inclusion criteria were recruited in the study. They consist of males aged 18-40 years who were occupationally exposed to stone dust and miners, gave consent, without physical abnormalities or chronic illnesses were included in the study. Subjects who are occupationally unexposed without chronic clinical illnesses were included and used as controls.

Exclusion criteria

After physical and clinical examinations, individuals with known pathological or congenital conditions such as severe hypertension, diabetes mellitus, sexually transmitted diseases, testicular varicocele, and genital warts were excluded from the study. Also, subjects currently on antioxidant food supplements, smoke cigarettes, and abuse alcohol were excluded.

Sample size

The sample size was determined using the sample size determination formula for health studies (Lwanga and Lemeshow, 1991). $N=Z^2P(1-P)/d^2$ using a health risk related to different types of minerals prevalence of 6.7% (Stephen and Ahern, 2001). The calculated sample size was 96 which was increased to 146 for this study. Therefore, 146 stone miners and 50 controls were recruited for this study.

Sample collection and storage

A blood sample (5 mL) was collected by vacuum venipuncture from the median cubital vein into properly labeled plain clean bottles following standard safety guidelines. Samples were allowed to clot, retracted, and spun at 3000 rpm for 5 minutes to obtain the serum. Serum aliquots were then separated into properly labeled tubes and stored (at -20 °C) before analysis.

Sample analysis

Samples were thawed, all reagents were brought to ambient temperature and analytic equipment was allowed for equilibration before analysis. Serum hormone levels (Luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), total testosterone (tT)), were quantitated by the Microplate Immunoenzymometric Assay (IEMA/ELISA) using AccuBind ELISA Microwells.

Principle

This is based on the principle of immunoenzymometric assay (Type 3). In this procedure, the immobilization takes place during the assay at the surface of a microplate well through the interaction of streptavidin-coated on the well and exogenously added biotinylated monoclonal anti-hormone antibody. Upon mixing monoclonal biotinylated antibody, the enzyme-labeled antibody, and a serum containing the native antigen, the reaction results between the native antigen and the antibodies without competition or steric hindrance to form a soluble sandwich complex. Simultaneously the complex is deposited to the well through the high-affinity reaction of

streptavidin and biotinylated antibody. After equilibrium is attained, the antibody-bound- fraction is separated from unbound antigen by decantation or aspiration. The enzyme activity in the antibody-bound fraction is directly proportional to the native antigen concentration. The concentration of an unknown antigen was then determined by utilizing a dose-response curve generated from different serum references of known antigen values.

Data Analysis

Data analysis was done using the statistical software SPSS version 21 (SPSS Inc, Chicago, IL, USA). The Student t-test and Chi-square were used to compare variables where appropriate and a $p<0.05$ was considered statistically significant.

Results

A total of 196 subjects comprising of 146 male stone miners and fifty 50 non- stone miners (controls) living in the same environment were recruited for the study. The mean age of the male stone miners was 30.03 ± 0.48 years and that of the controls was 28.62 ± 0.88 years. The difference in the educational status of the participants was statistically significant ($p<0.04$) when compared with the controls. The duration on the job indicates that 52.7% of the subjects had spent 0-5 on the job, while 32.9%, 10.3%, and 4.1% had spent 6-10 years, 11-15 years, and >15 years on the job respectively (table 1). Table 2 shows the comparison of measured sex hormone levels between stone miners and non-stone miners. Serum LH and testosterone were significantly lower ($p<0.001$) while serum FSH and prolactin were significantly higher ($p<0.001$) among stone miners than non-stone miners. The hormonal disorders observed among stone miners are shown in table 3. It indicates that 45/146 (30.8%) had hormonal imbalance consisting of 9/146(6.2%) had hyperprolactinaemia, 36/146(24.7%) had hypogonadism while 101/146(69.2%) had normal hormone levels.

Discussion

Reproductive toxicants are agents or materials that adversely impact human reproductive function, fertility, or fetal development and growth (17, 18). They include chemical, physical, environmental, physical, and emotional stress (19). Studies have shown that stone dust contains such toxicants and small-scale mines are more hazardous than large-scale mines regarding risks of accidents or injuries. Also, small-scale mines tend to be surface mines that employ young inexperienced workers (20). Scientific understanding of the impacts of mining on reproduction has grown. Workers in large-scale factories have been able to use scientific evidence for improved hazard awareness, health, and safety legislation. But, most of the small-scale mining operations do not fall within formal legislative protection or scientific analysis. Also, evidence of the reproductive health risk of stone mining on workers is scarce in our setting. Any study that creates awareness of reproductive health risks among small-scale stone miners may help the practitioners to modify their lifestyle to avoid the inherent dangers associated with their occupation. In this study hormonal imbalance was observed among 30.8% of stone miners consisting of hyperprolactinaemia and hypogonadism. Also, the mean serum LH and testosterone were significantly lower while FSH and prolactin were higher among stone miners than controls.

Table 1. Social demographics characteristics of male stone miners and non-stone miners (Mean± SD)

Social-demographic	Male stone miners n(%) n=146	Controls (Non-stone miners) n(%) n=50	X ² (p-value)
Mean Age	30.03±0.48	28.62±0.88	1.43 (0.17)
Age Range			
≤20 years	12(8.2)	6(12.0)	
21-25 years	29(19.9)	10(20.0)	
26-30 years	45(30.8)	19(38.0)	0.14(0.74)
31-35 years	32(21.9)	8(14.0)	
>35 years	28(19.2)	7(14.0)	
Educational status			
Primary	33(22.6)	10(20.0)	
Secondary	55(37.7)	8(16.0)	4.27(0.04)
Tertiary	58(39.7)	32(64.0)	
Duration on Job			
0-5 Years	77(52.7)	NA	
6-10 Years	48(32.9)	NA	
11-15 Years	15(10.3)	NA	

Table 2. Comparison of measured sex hormones in the male stone miners and male non-stone miners (Mean±SD)

Measured Hormones (Reference range)	Male stone miners (n=146)	Controls (n=50)	Student-t- Test	P-value
LH (0.7-7.4IU/L)	2.29±0.05	6.81±0.14	30.15	0.001
FSH(1.0-14IU/L)	10.75±0.19	7.31±0.23	-11.46	0.001
PRL(1.8-17ng/mL)	3.95±1.06	2.93±0.10	1.48	0.143
Testosterone (2.8-10ng/mL)	3.23±0.70	4.87±0.33	9.19	0.001

LH=luteinizing hormone; FSH=follicle stimulating hormone; PRL=Prolactin

Table 3. Pattern of hormonal distribution among stone miners

Parameters	Hormonal	Pattern	Normogonadotropic-normogonadism
	Hyperprolactinaemia	Normogonadotropic-Hypogonadotropin-	
No of Subjects	09	36	101
LH (0.7-7.4U/L)	1.82±0.51	5.41±1.81	5.32±2.11
FSH (1.0-14U/L)	3.11±0.80	4.92±0.41	5.12±0.51
Prolactin (1.8-17ng/mL)	25.1±0.5	3.18±0.21	3.92±0.41
Testosterone (2.8-10ng/mL)	11.8±0.28	2.02±0.11	4.91±0.32

This finding aligns with the recent observation that environmental pollutants are major contributors to the development of reproductive health challenges including hypogonadism and erectile dysfunction. Environmental factors and other endocrine disruptors present in stone are important contributing factors of hypogonadism and erectile dysfunction (21). These environmental toxicants use several mechanisms, such as stimulation of reactive oxygen species (ROS) generation, depletion of available antioxidants in the system, and creation of a state of oxidative stress in the reproductive tissues. In an earlier report, it was observed that exposure to endocrine disruptors can modulate hormone metabolism by changing the metabolism of testosterone, FSH, LH, or other hormones (22). The hypothalamic-pituitary-gonadal (HPG) endocrine axis is one of the targets of environmental toxicants present in stones. The HPG is one of the three systems needed for normal male reproduction which are the hypothalamic-

pituitary-gonadal (HPG) endocrine axis, the spermatogenesis in the testes, and the transport system of the genitalia (23). The toxicants present in stone appear to adversely impact these sites. Elemental analyses of rock in some parts of Nigeria and the resulting dust particles contained iron, zinc, cadmium, nickel, lead, chromium, barium, beryllium, and aluminum (24). The mechanism by which reproductive toxicants adversely impact reproduction in humans is very complex, but several authors have explained that such damages can occur during absorption, distribution, metabolism, excretion, and repair at different levels in the body. When toxicant enters the body and it disrupts the material transfer, energy transfer, and information transfer between cells, thus inhibiting cells, organs, and systems from performing their physiological functions optimally. Most of the toxicants present in stone dust might go through this process to disrupt the hypothalamus, and testis inhibiting their physiological function and hence decline in

reproductive potentials (18, 23, 25). These could lead to decreased spermatogenesis and apoptosis of germ cells. Hormonal imbalance in males can lead to decreased libido, erectile dysfunction, and poor quality and quantity of spermatozoa (26). It is important therefore to consider reproductive toxicants in men, by probing to know their occupation and possible occupational exposures when evaluating men with infertility.

Hypogonadism is characterized by inadequate serum testosterone production by the Leydig cells of the testis. It occurs as a result of the disruption of the normal functioning of the hypothalamic–pituitary–gonadal (HPG) axis, which ultimately changes the functioning of Leydig cells in the testis. This does not only inhibits the process of spermatogenesis but also alters normal reproductive physiology (21). Previous studies which examined the impact of work conditions and occupation like the exposure to toxic substances on reproduction reported that industrial and construction workers had a higher incidence of infertility rate than other professions. This may be due mainly to greater exposure to stress and toxicants. The authors concluded that workers in these sectors may be exposed to a higher level of stressors than other professions. These workers were observed to have abnormal sperm indices, hormonal imbalance, varicocele, and/or cryptorchidism (27, 28). It was recently reported that occupation and exposure to harmful environmental contaminants are major contributors to infertility (18). The authors suggested that actions must be taken to halt occupational effects on male infertility. These can be done by creating awareness for employees, providing adequate preventive measures when performing hazardous duties, and general routine medical checks for the workers. These might go a long way to preventing male infertility. More than half of the subjects evaluated for infertility in some States in Nigeria were reported to have a form of hormonal abnormality; such as 46.9% reported from Ilorin (29), 40% among azoospermia, 40% among oligozoospermia from Kano, respectively (30, 32).

Some studies which evaluated toxic metal levels in the blood and seminal fluid have consistently been associated with reduced sperm quality and quantity (32, 34). Mean seminal plasma Pb, Cd, and Cd/Zn ratios were reported to be significantly higher ($P<0.001$) in infertile males than controls. Cd/Zn ratio ($r=-0.242$; $P<0.04$) correlated negatively ($P<0.001$) with serum testosterone among infertile men in Nigeria. The authors concluded that evaluation of seminal plasma Cd, Pb, Zn, and Cd/Zn ratio may be considered in a comprehensive investigation of the infertile men while informed risk modeling to preventing exposure to toxic metals may help to mitigate their health consequences (34). Mining is a very hazardous occupation to workers in Nigeria. Others have suggested that a lot needs to be done before the industry, the workers, and the community agree over the real health impacts of the sector and the real responsibility of each of the actors in the sector (20). Stone mining in Nigeria represents an unorganized industrial sector. There is poor awareness of associated hazards in the industry and poor usage of the personal protective device, lack of knowledge, discomfort, and poor perception of its importance were associated with reproductive health risk (35).

Conclusion

A large proportion of stone miners were observed to have a hormonal imbalance. Evidence suggests that occupational exposure to stone dust may be responsible for the hormonal imbalance. Human study on exposure to stone dust and altered

hormone levels among stone miners is quite limited. Further study involving a large population is required to know the magnitude of the potential danger to reproductive health in humans.

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Conflict of interests

The authors declare that there is no conflict of interest.

Authors' contributions

This work was conducted and approved in collaboration between all the authors. MA designed the study; JO sourced for funding; MA, JO wrote the protocol; JO contributed in literature search; JO did the experiments; MA, JO did statistical analysis; JO drafted the manuscript; MA supervised the study; MA Wrote the final manuscript; MA proofread the manuscript.

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