American Journal of Life Science Researches
2019; 7(1): 9-17
Published online January, 2019 (http://www.diili.org/ojs-2.4.6/index.php/ajlsr/index)
ISSN: 2375-7485 (Print); ISSN: 2332-0206 (Online)

Original Paper

Investigation of Serum Levels of Maternal Heavy Metals and Adverse Birth Outcomes

Rashidat Abidemi Oladiti; Oyewale Thomas Oyediran; Gregory Uchechukwu Joseph; Ayobola Abolape Iyanda*
Department of Chemical Pathology, College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Nigeria.
***Corresponding Author**: E-mail lapeiyanda@yahoo.com, Phone No: +2347039407465

ARTICLE INFO
Article history:
Received 20 September. 2018
Revised 20 October. 2018
Accepted 14 December. 2018

ABSTRACT
Women within reproductive stage are known to be exposed to heavy metals from various sources e.g. occupation, life-style, counterfeit drugs, etc. Contact with toxic metals has been linked with altered physiologic processes. The aim of this study is to assess the serum concentrations of heavy metals in third trimester pregnant women and relate them with birth weight. Forty pregnant women (in third trimester) were recruited at maternity centers within Osogbo metropolis, 40 healthy women, age-matched, non-pregnant served as control. Serum was obtained from 5 mL of blood taken from each participant. Inductively Coupled Plasma-Optical Emission Spectrometry was employed to estimate the concentrations of cadmium, chromium, aluminum, lead, arsenic, mercury, nickel, and cobalt. Pregnancy outcomes- birth weight and ratio of live and stillbirths- were also determined. Student's t-test and Pearson's correlation coefficient were used to analyze the data. $P<0.05$ was considered statistical significant. Results of the study revealed significant increase in the levels of heavy metals at third trimester compared with control. Mean birth weight was 2.39 ± 0.42 kg (normal: 2.5- 4.0) and the ratio of live birth to stillbirth was 9: 1. Cd ($r= -0.443$; $p= 0.008$) and nickel ($r= -0.416$; 0.013) were negatively correlated with birth weight. Data derived from the study indicate that elevated serum levels of maternal heavy metals may be a contributing factor to adverse birth outcomes as both were found to co-exist.

Keywords: Maternal Heavy Metals, Serum Levels, Birth Outcomes

INTRODUCTION

Post-partum outcomes for the mother and child are related to a number of factors such as maternal consumption habits during pregnancy as well as vocational and lifestyle choices [1]. Some of these factors may predispose an individual to toxic (heavy) metal exposure [1]. In the developing nations, it has been reported that many foods, beverages, medications and cosmetics which both pregnant and non-pregnant individuals ingest or are exposed to, are counterfeits. Many counterfeit products are known to contain contaminants e.g. heavy metals [2]; even those with therapeutic usefulness are not exempted from such contamination [3]. Moreover, the increasing pollution originating from industrialization exposes the entire population to several toxic agents such as heavy metals [4]. Therefore, the overall population may undergo a daily contact with pollutants from several sources [5].

Several studies have demonstrated that prenatal exposure to environmental toxins profoundly affects the developmental biology of the fetus. Heavy metals such as As, Pb, Hg, and Cd have been reported to alter various vital physiologic processes in the body, processes which are of great importance during the intra-uterine life. Exposure to such agents *in-utero* may have serious health side effects as some of these substances readily move across the placental barrier. The study was therefore designed to assess the levels of heavy metals in serum of third trimester pregnant women as well as determine pregnancy outcomes (e.g. live/still birth; birth weight). In addition, the correlation between maternal serum level of heavy metals and birth weight was determined.

MATERIALS AND METHODS

Ethical consideration

The ethical clearance for the study was obtained from Health Research Ethics Committee of Hospital Management Board Asubiaro, Osogbo, Nigeria. Informed consents were obtained from the study participants. The data obtained from the study were kept in strict confidentiality.

Sampling technique/ Data collection

Simple random sampling technique was employed for the selection of subjects for both pregnant and control groups. Eighty participants were recruited for the study consisting of 40 pregnant women in the third trimester who were attending the antenatal clinics at maternity centres in Osogbo metropolis and 40 age-matched, non-pregnant apparently healthy women. Patients in first and second trimester were excluded from the study. The weight of the babies was taken. Questionnaire was administered to each participant and data collected on the life-styles e.g. smoking (passive/active); alcohol consumption; use of skin-bleaching cosmetics.

Collection and preparation of blood samples

5 mL of venous blood from the antecubital fosa was collected using pyrogen free needle and syringe with minimum stasis. This was carefully dispensed into dry, anti-coagulant free bottles. Each blood sample was allowed to clot, retracted and centrifuged at 2000 g for 10 minutes after which the serum was separated and stored at – 20^{o}C prior to analyses. Serum levels of Cd, Hg, Ni, As, Cr, Co, Al, and Pb were determined using Inductively Coupled Plasma-Optical Emission Spectrometry (Beckam ICP-OES 4000 series, UK).

Statistical analysis

Data obtained were analysed using SPSS (Statistical Package for Social Sciences) version 20. Student’s t-test and Pearson’s correlation coefficient were employed for this purpose. The results were expressed as mean ± standard deviation (SD). The level of significance was $p \leq 0.05$.

RESULTS

Data were summarized graphically using boxplots as shown in **Figures 1a -1f** below**.** When the mean±standard deviation of Pb, Al, Ni, Cd, Co, Hg Cr, and As of pregnant women were compared with control, there were significant differences ($p<0.01$). In third trimester pregnant women there were significant increases in levels of Pb (0.34 ± 0.14 µg/L); Cr (8.04 ± 2.27 µg/L); As (3.26 ±0.85 µg/L) and Hg (0.88 ± 0.23 µg/L) compared with control values of Pb (0.10 ± 0.04 µg/L); Cr (3.83 ± 2.16 µg/L); As (0.31 ± 0.18 µg/L); and Hg (0.07 ± 0.03 µg/L). Significant increases were also recorded for mean ± SD of Ni (1.72 ± 0.86 µg/L); Co (0.59 ± 0.23 mg/dL);

Al (0.11 ± 0.43 µg/L) and Cd (0.55 ± 0.14 µg/L) at third trimester when compared with non-pregnant values of Ni (0.25 ± 0.19 µg/L); Co (0.14 ± 0.95 mg/dL); Al (0.06 ± 0.02 µg/L); and Cd (0.25 ± 0.07 µg/L). The mean ± SD of birth weight was 2.39 ± 0.42 kg.

Results showed that birth weight was negatively correlated with maternal Cd (r = -0.443; p = 0.008) and nickel (r = -0.416; 0.013) levels. A few inter-element significant correlations were observed. There was a relationship between Cr and Co (r = - 0.396; p = 0.011), as well as with mercury at (r = 0.441; p = 0.004). Nickel shows a significant correlation with Cd at (r = 0.351; p = 0.026) and an inverse correlation with arsenic at (r = -0.335; p = 0.035), while lead shows a significant correlation with cobalt at (r = 0.329; p = 0.038).

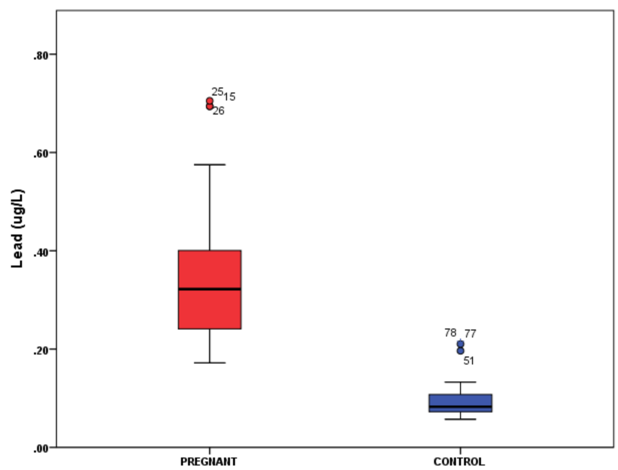

Figure 1a: Serum lead concentrations of pregnant and control subjects.

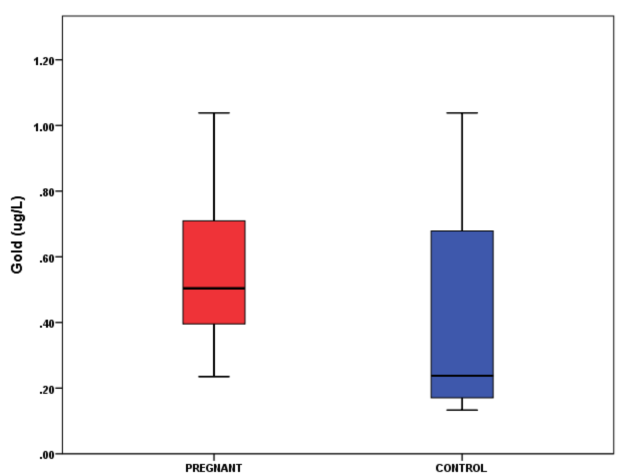

Figure 1b: Serum gold levels of pregnant and control subjects

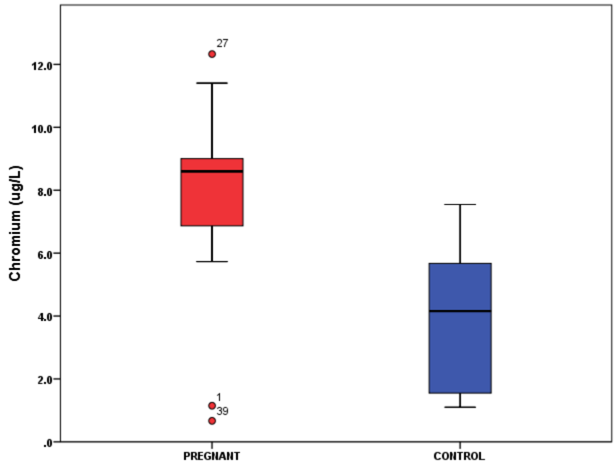

Figure 1c:Serum levels of chromium of third trimester pregnantt and control subjects.

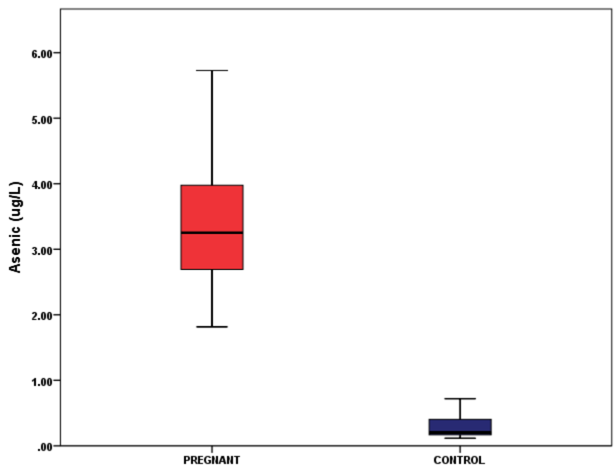

Figure 1d: Serum levels of arsenic of third trimester ppregnant women and ccontrol subjects.

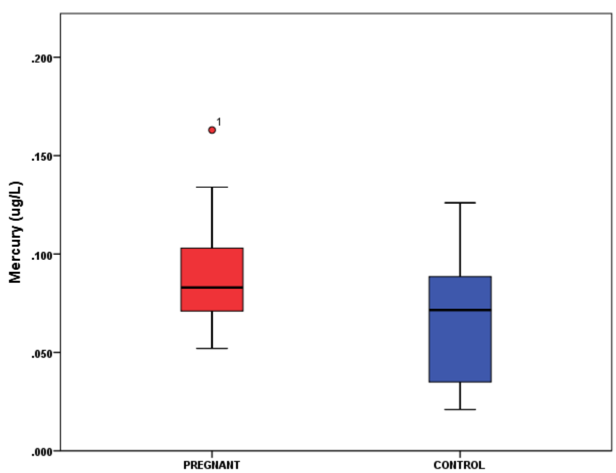

Figure 1e: Serum levels of mercury of pregnant women and control subjects.

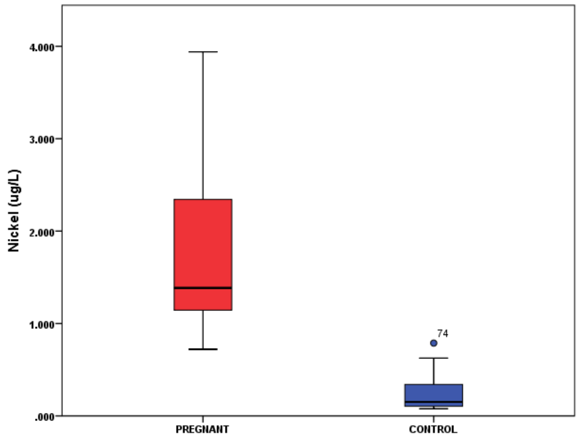

Figure 1f: Serum levels of nickel of pregnant women and control subjects.

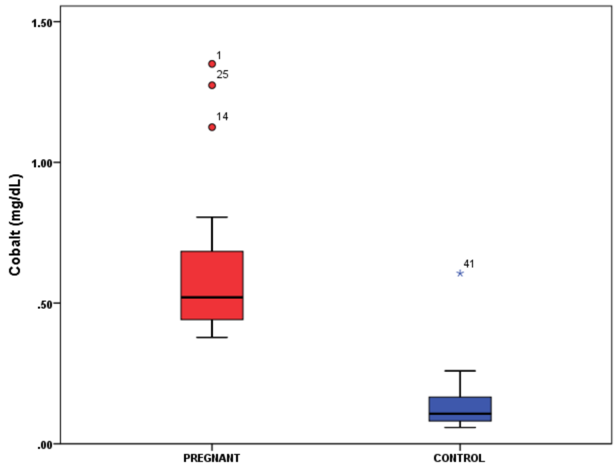

Figure 1g: Serum concentrations of cobalt of pregnant women and control subjects.

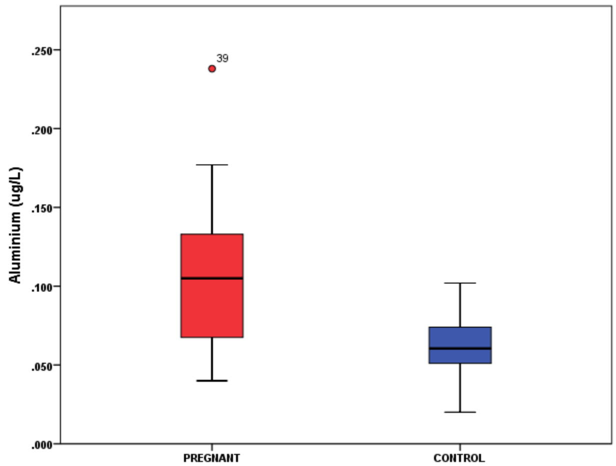

Figure 1h:Serum aluminium of levels of pregnant and control subjects.

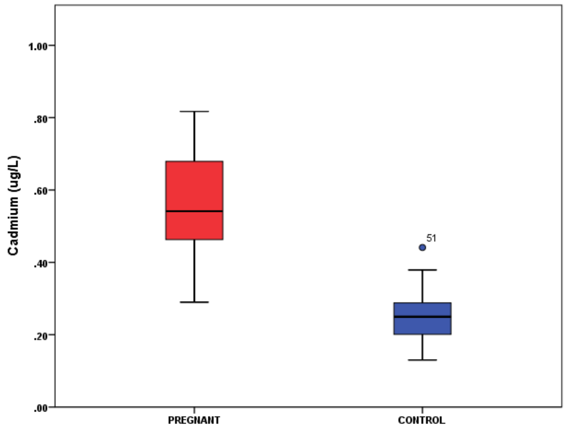

Figure 1i: Serum concentrations of cadmium of pregnant womenand control subjects.

Discussion

Detectable serum concentrations of non-physiologically useful heavy metals have been observed in many categories of human subjects. This may be ascribed to the fact that toxic metals are ubiquitous in the environment [6; 7], and sources of contact are diverse. The significantly higher heavy metal levels in pregnant women compared with non-pregnant ones may be due to physiologic differences between the two groups, especially with respect to hormone levels. Changes in types or levels of reproductive hormones have been reported to alter many metabolic processes. Moreover, it has been established that numerous physiologic adaptations including changes in nutrient metabolism are orchestrated by placental hormones [8]. And since there is a relationship between heavy metals and nutrients, an indirect relationship between placental hormones and heavy metals can be inferred.

Moreover, many toxic metals lack robust pathways for elimination and therefore remain in the body for a long time. During pregnancy, mobilization of stored lead from the mother's bones can leach into the bloodstream [9] leading to an elevated blood concentration even without increase in amount ingested during this period. The significant difference in the serum level of Cd and Pb at third trimester compared with non-pregnant control is in agreement with the report of Ajayi *et al.* [10]. They observed significant increases in maternal serum levels of Cd and Pb in women with history of recurrent spontaneous abortion.

Attention has to be drawn to possible devastating effects of results of this nature on the foetus. While the placental may prevent passage of some potentially toxic substances, still some environmental contaminants can cross the placental barrier [11]. That health risk to the fetus can occur from placental transfer of As, Cd, Pb has been suggested by Zheng *et al.* [12] Caserta et al [13]; Chen *et al.* [14] and Al Saleh *et al.* [15]. The influence of environment on the infant, starting at prenatal to postnatal period has been well described. Birth defects, infant mortality, neurobehavioural dysfunction especially mental retardation and numerous physical dys-morphologies (including retarded growth) are known consequences of toxin exposure during pregnancy. Although the present study did not extend beyond birth period and neurobehavioural dysfunction was not determined; both intra-uterine growth retardation and 5% stillbirth that were recorded further suggest the harmful effects of high maternal heavy metal concentrations. Especially as correlation between birth weight and some of the heavy metals were recorded.

Toxic metals generally exert their harmful effects through production of reactive oxygen species. These entities are known to alter very many physiologic processes through impairment of components of chemical reactions. Prenatal cadmium exposure impairs steroidogenesis which may result in suboptimal fetal growth and development [16]. Lead exposure also interferes with calcium deposition in bone with devastating effect on fetal bone growth [17]. Arsenic has been linked with placental insufficiencies, oxidative stress and therefore intra-uterine growth retardation [18]. According to World Health Organization (WHO), annually approximately 15% of all babies are born with a birth weight lower than 2500 g, with many of them coming from the developing countries [19]. The birth weight of 2.39 ± 0.42 kg indicates intra-uterine growth retardation but while correlation between birth weight and arsenic was not observed, nickel was found to be negatively correlated with birth weight.

In countries like Finland and Singapore, rate of stillbirths was 2 per 1000 pregnancies as against 10 percent recorded in this study. The result of the study though is in agreement with other reports from different regions of the country. Data obtained from such studies revealed that issue of stillbirth was becoming a menace for Nigeria. The study of Dahiru and Aliyu [20] showed that in Nigeria, rate of stillbirth was 12.5 per 1000 pregnancies. Age, household wealth, higher birth order, facility delivery, caesarian delivery, rural residence, and ever use of contraceptive were found to be determinant of stillbirths in that region. According to Njoku *et al.* [21], determinant factors which were identified as possible causes included low education, unbooked pregnancy, anemia in pregnancy, obstructed labor, ruptured uterus. On the other hand, Okeudo *et al.* [22] revealed that within 5-year period (2005-2010) a stillbirth rate 18% (180 out of 1000 pregnancies) was recorded in a health institution, which was much higher than rate of 44 stillbirths per 1000 pregnancies reported by WHO. In none of these studies were attempts made to investigate the possible co-occurrence of stillbirth/low birth weight and altered heavy metal levels, with the view of ascertaining if maternal heavy metal concentration is a determinant factor in aetiology of stillbirth in Nigeria. Yet there are indications that elevated concentrations of heavy metals affect fetal biology. With this study, it can be assumed that high levels of maternal heavy metals can co-exist with adverse birth outcomes.

Conclusion

Data obtained from the study demonstrate that elevated levels of maternal serum heavy metal co-occurred with adverse birth outcomes. The correlation between low birth weight and maternal Ni and Cd suggests that these elements probably play a role in intra-uterine growth retardation. It becomes important therefore, that every effort should be made to investigate if elevated maternal heavy metal levels are determinant of other adverse birth outcomes such as preterm delivery, neonatal death, congenital anomaly, and macrosomia using larger sample size.

Conflicts of interest: none

REFERENCES

1. Wai KM, Mar O, Kosaka S, Umemura M, Watanabe C. Prenatal Heavy Metal Exposure and Adverse Birth Outcomes in Myanmar: A Birth-Cohort Study. Int J Environ Res Public Health. 2017;14(11). pil:E1339 doi:10.3390/ijerph14111339 https://doi.org/10.3390/ijerph14111339

2. Kim Y, Kim BN, Hong YC, Shin MS, Yoo HJ, Kim JW. (2009). Co-exposure to environmental lead and manganese affects the intelligence of school-aged children. Neurotoxicology. 2009;30(4):564-571. https://doi.org/10.1016/j.neuro.2009.03.012 PMid:19635390

3. Iyanda AA Serum levels of toxic metals in wistar rats treated with counterfeit sildenafil citrate. Annals Experi Biol. 2014; 2 (3):8-11

4. Gascon M, Morales E, Sunyer J, Vrijheid M. Effects of persistent organic pollutants on the developing respiratory and immune systems: a systematic review. Environ Int. 2013;52:51-65. doi: 10.1016/j.envint.2012.11.005. https://doi.org/10.1016/j.envint.2012.11.005

5. Jones RE, Lopez KH. (2006). Human reproductive biology (3rd Edition) academic press: Burlington, USA.

6. Pohl HR, Roney N, Abadin HG. Metal ions affecting the neurological system. Met Ions Life Sci. 2011;8:247-262. PMid:21473383

7. Singh R, Gautam N, Mishra A, Gupta R. Heavy metals and living systems: An overview. Indian J Pharmacol. 2011;43(3):246-53. https://doi.org/10.4103/0253-7613.81505 PMid:21713085 PMCid:PMC3113373

8. Handwerger S, Freemark M. The role of placental growth hormone and placental lactogen in the regulation of human fetal growth and development. J Pediatr Endocrinol Metab. 2000; 13(4):343-56. https://doi.org/10.1515/JPEM.2000.13.4.343 PMid:10776988

9. Manton WI, Angle CR, Stanek KL, Kuntzelman D, Reese YR, Kuehnemann TJ. Release of lead from bone in pregnancy and lactation. Environ Res. 2003;92(2):139-151. PMID: 12854694

10. Ajayi OO, Charles-Davies MA, Arinola OG. Progesterone, selected heavy metals and micronutrients in pregnant Nigerian women with a history of recurrent spontaneous abortion. African Health Sciences 2012;12(2): 153 – 159. https://doi.org/10.4314/ahs.v12i2.12 PMid:23056021 PMCid:PMC3462535

11. Needham LL, Grandjean P, Heinzow B, Jørgensen PJ, Nielsen F, Patterson DG, et al. Partition of environmental chemicals between maternal and fetal blood and tissues. Environ Sci Technol. 2011;45:1121–1126. https://doi.org/10.1021/es1019614 PMid:21166449 PMCid:PMC3031182

12. Zheng G, Zhong H, Guo Z, Wu Z, Zhang H, Wang C, et al. Levels of heavy metals and trace elements in umbilical cord blood and the risk of adverse pregnancy outcomes: A population-based study. Biol Trace Elem Res. 2014;160:437–444. https://doi.org/10.1007/s12011-014-0057-x
PMid:25008990

13. Caserta D, Graziano A, Lo Monte G, Bordi G, Moscarini M. Heavy metals and placental fetal-maternal barrier: A mini-review on the major concerns. Eur Rev Med Pharmacol Sci. 2013;17: 2198–2206. PMid:23893187

14. Chen Z, Myers R, Wei T, Bind E, Kassim P, Wang G,et al. Placental transfer and concentrations of cadmium, mercury, lead, and selenium in mothers, newborns, and young children. J Expo Sci Environ Epidemiol. 2014;24:537–544. https://doi.org/10.1038/jes.2014.26 PMid:24756102 PMCid:PMC4329243

15. Al-Saleh I,Shinwari N, Mashhour A, Rabah A. Birth outcome measures and maternal exposure to heavy metals, (lead, cadmium and mercury) in Saudi Arabian population. Int J Hyg Environ Health. 2014;217:205–218. https://doi.org/10.1016/j.ijheh.2013.04.009 PMid:23735463

16. Stasenko S, Bradford EM, Piasek M, Henson MC, Varnai VM, Jurasovi´c J, et al. Metals in human placenta: Focus on the effects of cadmium on steroid hormones and leptin. J Appl Toxicol. 2010;30:242–253. https://doi.org/10.1002/jat.1490 PMid:19847775

17. Potula V, Kaye W. Report from the CDC. Is lead exposure a risk factor for bone loss? J Womens Health 2005;14:461–464. https://doi.org/10.1089/jwh.2005.14.461 PMid:16114996

18. Vahter ME. Interactions between arsenic-induced toxicity and nutrition in early life. J Nutr 2007;137:2798–2804. https://doi.org/10.1093/jn/137.12.2798 PMid:18029502

19. Dahlui M, Azahar N, Oche OM, Abdul Aziz. Risk factors for low birth weight in Nigeria: evidence from the 2013 Nigeria Demographic and health survey. Glo Health Action. 2016;9:10.3402/gha.v9.28822. https://doi.org/10.3402/gha.v9.28822

20. Dahir T, Aliyu AA. Stillbirths in Nigeria: rates and risk factors based on 2013 Nigeria DHS Scientific Research 2016; 3(8): Article ID: 69762, 12 pages PMCid:PMC5124543

21. Njoku CO, Emechebe CI, Eyong EM, Ukaga JT, Anachuna KC. Prevalence and risk factors for stillbirths in a tertiary hospital in Niger-Delta area of Nigeria a ten year review. International journal of Medicine and Biomedical research. 2016;5(3):106-113. https://doi.org/10.14194/ijmbr.5.3.1

22. Okeudo C, Ezem BU, Ojiyi EE. Stillbirth rate in a teaching hospital in South-Eastern Nigeria- a silent killer. Ann Med Health Sci Res. 2012;2(2):172-179. https://doi.org/10.4103/2141-9248.105667, PMid:23439739 PMCid:PMC3573514