Is serum level of trace elements and heavy metals associated with threatened abortion?

Yi-Le Lee[a,b], Huann-Cheng Horng[a,b], Peng-Hui Wang[a,b,c,d,*]

[a]Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]Department of Obstetrics and Gynecology, National Yang-Ming University, Taipei, Taiwan, ROC; [c]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, ROC; [d]Department of Medical Research, China Medical University Hospital, Taichung, Taiwan, ROC

We read the publication entitled "Change of the levels of trace elements and heavy metals in threatened abortion" in the recent issue of the *Journal of the Chinese Medical Association* with interest.[1] The authors used nonpregnant women as the controls to evaluate the role of trace elements and heavy metals of serum on threatened abortion and found that at least four trace elements (zinc [Zn], ferrum [Fe], magnesium [Mg], and manganese [Mn]) were significantly deficient in women with threatened abortion (lower than controls) and, in addition, some heavy metals, such as copper (Cu), cadmium (Cd) and lead (Pb), were statistically and significantly increased in these studied subjects compared to normal controls.[1] The authors concluded that imbalance of some essential trace elements (especially decreases in Fe and Zn) and elevated concentrations of some toxic heavy metals (especially increases in Cd and Pb) might be important diagnostic and prognostic parameters for threatened abortion.[1] We congratulate the authors' success for publication; however, there are some questions and we hope to receive the authors' response. We should emphasize that our comments do not argue against the value of their study.

First, although the authors said their blood samples from all participants were taken at the same time, the audience might be interested to know when the blood samples were obtained (gestational weeks, seasons, and time of day). In addition, why the authors did not use the similar gestational age of "normal" pregnant women without threatened abortion as the control group for comparison? It is well-known that blood volume was significantly different between nonpregnant and pregnant women, which might influence the serum levels of studies targets. Did the authors kindly provide the "normal value" of their studied parameters, either from the similar studies from their country or their hospital?

Second, it is difficult to evaluate the essential trace elements in sera because sometimes, it is hard to reproduce the data, partly because the concentration distributions of elements varied vastly.[2] For example, the serum levels of lead obtained from "normal controls" varied greatly, ranging from 0.16 to 10.12 μg/dL and mean data ranged from 2 to 7 μg/dL.[3] If the data of the normal controls varies so greatly, it is hard to define the normal range, and subsequently, it might be also difficult to make the definition of "potential toxic level". All contribute to unpractical use in clinical practice. In addition, samples obtained from the different time of day might also influence the final results of concentration. For example, serum Zn concentrations in samples collected in the afternoon or evening were significantly lower than the fasting or nonfasting morning sample values.[4] Furthermore, one study showed that a single measurement of elements in sera seems not enough to describe exposure levels throughout pregnancy, because many factors could affect the levels of trace elements.[2] Dr. Liang and colleagues found that season affects exposure levels of trace elements with moderate interclass correlation coefficients and comments that the studies which would like to test the serum levels of these trace elements or heavy metals should take sampling seasons into consideration carefully.[2]

Although the authors mentioned there are some limitations of their study, including small population, the major concern of the current study is the study population containing the different outcomes of patients, which is also raised by editorial comment.[5] This heterogeneity is so great and it might impede the data presentation. The authors need to compare the serum levels of these trace elements and heavy metals among the women with threatened abortion, based on the different pregnancy outcome (such as preterm births and term births) to clarify the prognostic value. Could the authors kindly provide this data?

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**Address correspondence: Dr. Peng-Hui Wang, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC. E-mail addresses: phwang@vghtpe.gov.tw; pongpongwang@gmail.com; or phwang@ym.edu.tw (P.-H. Wang).*

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