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Editorial

Hyperemesis gravidarum

Pregnancy-associated nausea and vomiting is a very common condition with an estimated prevalence rate ranged from 50% to 85%, but for the majority self-management suffices.[1−4] The popular term "morning sickness" is a misnomer and may be minimized by obstetricians or other obstetric providers, and pregnant women, resulting in high possibility of undertreatment. Practice bulletin of the American College of Obstetricians and Gynecologists recommends that early intervention and treatment of nausea and vomiting of pregnancy is needed to prevent progression to hyperemesis gravidarum, which is characterized by persistent vomiting, weight loss of more than 5%, ketonuria, electrolyte abnormalities (hypokalemia), and dehydration (high urine specific gravity), resulting in the diminishment of the woman's quality of life and significant contribution to health care costs and time lost from work.[5,6] However, hyperemesis gravidarum is a clinical diagnosis of exclusion, based on the above-mentioned typical presentation in the absence of other diseases, such as gastrointestinal conditions (e.g., appendicitis, hepatitis, pancreatitis or biliary tract disease), pyelonephritis, and metabolic disorders, such as diabetic ketoacidosis, porphyria, or Addition's disease, that could explain the finding. In addition, the presence of fever, abdominal pain, or headache is atypical in women with hyperemesis gravidarum and suggests another cause.[6]

The etiology of nausea and vomiting of pregnancy is still uncertain, and many hypotheses have been proposed, including a psychologic predisposition (a conversion or somatization disorder and inability of the woman to respond to excessive life stress), evolutionary adaptation (avoidance of toxins during pregnancy), and hormonal stimulus (human chorionic gonadotropin and estrogen)[5]; however, none of them is sufficient alone to come to diagnosis. In addition, there is no single test, which may predict when it comes to the extreme end of the spectrum of nausea and vomiting of pregnancy − hyperemesis gravidarum. Therefore, we welcome the studies investigating the relationship between markers and the presence of hyperemesis gravidarum and its severity during pregnancy. We are glad to learn that Dr. Desdidioglu's study published in this issue of the *Journal of the Chinese Medical Association* attempted to use the serum markers to investigate the association between these markers and pregnant women with hyperemesis gravidarum.[7]

The authors prospectively enrolled 60 singleton pregnant women with less than 14 weeks of gestational age in the Ataturk Training and Research Hospital, to study the serum levels of soluble urokinase-type plasminogen activator receptor (suPAR) and interleukin-6 (IL-6) in these pregnant women with and without hyperemesis gravidarum.[7] The results showed that serum levels of both suPAR and IL-6 were elevated in women with hyperemesis gravidarum compared to those in women without. However, the authors suggested that only suPAR could be considered to be associated with the etiopathogenesis of hyperemesis gravidarum.[7] Although the finding in the current study was interesting, it needs a further discussion.

First, both serum suPAR and IL-6 levels were high in the women with hyperemesis gravidarum. Why the authors only focused on serum levels of suPAR and suggested that suPAR might involve etiopathogenesis of hyperemesis gravidarum? Angiogenesis is an important process during normal and abnormal pregnancy. Many pregnancy-related diseases, for example, preeclampsia, and eclampsia are considered as dysfunction of endothelial system and aberration of angiogenesis during implantation (placenta formation).[8−10] Urokinase plasminogen activator receptor (uPAR) signaling pathway is one of main components of angiogenesis.[11] However, etiology of hyperemesis gravidarum is rarely discussed about endothelial cell dysfunction or aberration of angiogenesis, suggesting that aberration of angiogenesis (for example, expression of suPAR) might be a secondary effect. For example, hyperemesis gravidarum results in malnutrition or so-called unbalanced nutrition of these pregnant women, resulting in aberration of angiogenesis or occurrence of inflammatory process.

Second, since the authors enrolled these patients were diagnosed with hyperemesis gravidarum, the changes of serum levels of suPAR and IL-6 might be a concomitant finding or subsequent sequelae when the patients have an attack of hyperemesis gravidarum. In fact, as shown above, the most commonly cited criteria of hyperemesis gravidarum include persistent vomiting not related to other causes, a measure of acute starvation (usually large ketonuria), and some discrete measure of weight loss, most often at least 5% of prepregnancy weight.[5] All of them result in "stress" and/or "disease" status of these pregnant women. It is reasonably suspected that

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the elevated serum levels of both markers might be an end product but not an initiator of women with hyperemesis gravidarum. Therefore, the authors' observation might be of little value. The better study design should be initiated at the much earlier stage of pregnancy. The authors should enroll all women with nausea and vomiting initially, and finally 0.3−1% of these women might be diagnosed as hyperemesis gravidarum. The comparison between these 1% pregnant women with hyperemesis gravidarum and remaining other 99% of the above-enrolled pregnant women might provide a better understanding of the role of suPAR and IL-6 on the etiopathogenesis of hyperemesis gravidarum.

In conclusion, studies might show some statistical findings or the scientific value, as shown in our past comment.[12] Since the value for clinical practice is low, we do not recommend the need to test serum levels of suPAR and IL-6 in pregnant women with nausea and vomiting.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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