Introduction

The term “ectopic pregnancy” (EP) comes from the word ektopos which means “out of place” (1), indicating the implantation of the blastocysts outside of the uterine cavity endometrium since the majority of them are implanted in the fallopian tube in which the embryo ceases growing (2). In addition, EP is considered as the major cause of maternal mortality and morbidity (3).

Glycodelin (GD) is a glycoprotein that is primarily expressed in the tissues of reproductive organs. During human pregnancy, GD peaks at first trimester of pregnancy. GD has several glycoforms (e.g., A, S, F, & C), some of which are regulated by progesterone, while others act as the inhibitors on sperm motility (i.e., oocyte binding), as well as immunosuppression and immunomodulation actions, indicating the role of GD in fertilization and implantation (4). The current work aimed to assess the use of GD as a potential marker for predicting EP.

Materials and Methods

Study Design

This case-control study was conducted during June 2016 to May 2017 in the Obstetrics and Gynecological Department of Baghdad University at Baghdad teaching hospital/medical city complex. In this study, 100 pregnant women in their first trimester of pregnancy were included after clinical and ultrasonic findings.

Results

Based on the results, GD levels in EP were significantly lower than those with normal intrauterine pregnancy (1.58 ± 1.18 vs. 30.1 ± 11.9). In addition, using receiver operator curve analysis, the cut-off GD level of 9.5 and less had acceptable validity results (100% sensitivity, 100% specificity, 95% positive predictive value, 100% negative predictive value, and accuracy 100%) to predict EP.

Conclusions

In general, serum GD is considered as an excellent predictor of unruptured EP.

Keywords: Abdominal pain, Ectopic pregnancy, Glycodelin, Vaginal bleeding
parity, miscarriage, past medical and surgical history, and previous mode of delivery while GA was significantly lower in an EP (Table 1).

Similarly, GD levels in EP were significantly lower than those with normal IUP (1.58 ± 1.18 vs. 30.1 ± 11.9), and these lower levels were maintained in different GAs (i.e., 6th, 7th, and 8th weeks). The results further revealed that in EP, an increased in GA led to a decrease in GD levels while in normal pregnancy, GD levels increased with an increase in GA (Table 2 and Figure 1).

Moreover, receiver operator characteristic analysis was performed to assess the validity of GD as the predictor of EP. Eventually, GD was found to be an excellent predictor of EP with an optimal cut point of <9.5 ng/mL for predicting EP with 100% sensitivity, 100% specificity, 95% positive predictive value, 100% negative predictive value, and 100% accuracy (Table 3).

**Discussion**

EP is still regarded as one of the important causes of maternal death worldwide although mortality has simultaneously declined from 35 deaths/10,000 EPs in 1970 to 4 deaths/10,000 EPs in 1985 (5). In the United Kingdom, the number of ectopics and deaths has been fixed in the last 12 years with the mortality rate at 4 per 10,000 maternal pregnancies (6).

In the current study, serum GD (previously named...
as placent al protein 14) was significantly lower in EP compared to normal pregnancy (1.58 ± 1.18 vs. 30.1 ± 11.9 ng/mL, respectively) these findings were consistent through sixth, seventh, and eighth of pregnancy. Further analysis using the receiver operator curve demonstrated that test serum GD at the cut-off of ≤9.5 ng/mL had an excellent ability to predict EP with 100% sensitivity and 100% specificity, which is in agreement with the findings of Pedersen and Ruge (7). The results of another study showed that the GD level was low (<5th percentile of the reference range of GD) in 81% of women with EP (8). In addition, several other studies reported similar findings such as Ruge et al (9) and Foth & Römer who studied 169 women in their first trimester and found that GD serum level was significantly lower compared to normal pregnancy and those with incomplete abortion (10). In a more recent study that examined multiple markers for predicting EP in the first trimester, GD was reported as the best individual marker of extra-uterine location (AUC 0.61) and further analysis at the cut-pint of ≤1.39 ng/mL had higher sensitivity to predict EP; this study showed the clear role of GD as a screening marker for EP, especially when incorporated with other biomarkers (11). The findings of all these studies are in line with the results of the current study, indicating that serum GD was significantly lower in EP compared to normal pregnancy.

In the current study, GD levels had an inverse relationship with GA, namely, it decreased with advanced GA (3.03 ± 1.3, 1.21 ± 0.9, and 0.34 ± 0.16 from sixth to eighth weeks of GA) while the relationship was direct between GA and GD levels in a normal pregnancy. Foth and Römer (10) revealed that the level of GD decreases with increasing GA in the first trimester of the ectopic patients, which corroborates with the findings of the present study.

Currently, no single biomarker for EP has yielded sufficient diagnostic accuracy and good reproducible results. Generally speaking, the makers of normal trophoblast and decidual function are usually lower in EP compared to normal IUP (12). In a normal pregnancy, the GD level increases as pregnancy progresses until 8-10 weeks of gestation; this can be attributed to the hormonal effect in this period of pregnancy, a procedure which is done by the corpus luteum (13). In ectopic pregnancies, the low GD levels might be a consequence of abnormalities in the functions of the corpus luteum (14).

Limitation of the Study
Small sample size within a short period of the study, single-center for research, the absence of temporal relationship, and selection bias were among the limitations of the current study.

Conclusions
Overall, the serum level of GD significantly decreased in the first trimester of EP while in normal pregnancy, it steadily increased the validity results of GD (i.e., 100% sensitivity, 100% specificity, 95% positive predictive value, 100% negative predictive value, and accuracy 100%) in the prediction of EP at the cut point of 9.5 ng/mL.

Conflict of Interests
Authors declare that they have no conflict of interests.

Ethical Issues
The study was approved by the local committee in the Iraqi Ministry of Health, the Council of Arab Board of Health Specialization. The purpose and procedures were explained to all women, and they were given the right to participate in the study. Then, written informed consent was taken with the reassurance that obtained interpretation would be kept confidential and not be used for another research object, in accordance with the Declaration of Helsinki (as revised in Edinburgh, 2000).

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References

