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EDITORIAL

Serum progesterone levels in the emergency department should not change the care of patients with first trimester bleeding

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Early pregnancy loss occurs in an estimated 20% of all pregnancies [1]. Approximately 80% of losses, which include spontaneous and missed miscarriages and ectopic pregnancy, occur in the first 12 weeks of pregnancy [1]. A recent health services study in Ontario demonstrated over 80% of patients with first trimester bleeding or abdominal pain sought treatment in the emergency department (ED), a health care environment where patients are often exposed to long wait times, lack of resources for immediate transvaginal ultrasound, and uncertainty about their condition at the time of discharge [2, 3]. In patients with first trimester bleeding, ectopic pregnancy remains the most life-threatening condition on the differential, and early diagnosis in the ED is key in preventing significant mortality or morbidity [1]. Even in the best scenario, with the availability of transvaginal ultrasound and serum beta human chorionic gonadotropin (BHCG), it is often difficult to exclude ectopic pregnancy in the ED without subsequent follow-up assessment.

In this month's issue of the *Canadian Journal of Emergency Medicine*, Ghaedi and colleagues performed a systematic review and meta-analysis to determine if a single serum progesterone level can predict fetal viability among symptomatic patients in early pregnancy. Fifty-four studies met eligibility criteria, and of these, 33.3% enrolled patients in the ED. A total of 15,878 patients with gestational ages between 3 and 13 weeks were included, and 8014 (50.5%) were confirmed to have a non-viable pregnancy. Of the non-viable pregnancies, 1747 (21.7%) were ectopic pregnancies [4].

Based on the results of the meta-analysis, the authors concluded more than 90% of patients presenting with vaginal bleeding in early pregnancy can be diagnosed with a non-viable pregnancy if the progesterone level is < 6.3 ng/mL (< 20.034 nmol/L) or with a viable pregnancy if the level is above 20–25 ng/mL (63.6–79.5 nmol/L). The authors also suggest that progesterone levels at the index ED visit can allow for expedited referral to definitive management, may improve patient satisfaction and may reduce return visits to the ED.

At first glance, these findings are in keeping with other reviews describing the accuracy of serum progesterone to predict pregnancy outcome. In fact, these results are nearly identical to a meta-analysis published in the *BMJ* in 2012 that showed a progesterone level less than 6 ng/mL (19.1 nmol/L) reliably excluded viable pregnancy in women with first trimester bleeding, with a negative predictive value of 99% [5]. Reviews on the clinical management of first trimester bleeding also suggest serum progesterone may be useful in distinguishing between an early viable or non-viable pregnancy, especially in the setting of inconclusive ultrasonography [6].

However, in 2012, Canadian ED providers did *not* rush to use serum progesterone levels in their evaluation of patients with first trimester bleeding. They are also unlikely to do so in 2022 (a decade later), because the fact remains—a serum progesterone level cannot distinguish an intrauterine pregnancy from an ectopic pregnancy, the ultimate goal of an ED provider.

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With this limitation in mind, the authors' assertions that serum progesterone may alter the timing of follow-up is not likely to feasible or safe when a concern for ectopic pregnancy remains. In patients with first trimester bleeding, it is often the case that an intrauterine or extrauterine pregnancy cannot be visualized (i.e. the fetal pole or yolk sac are not visible), and a pregnancy of unknown location (PUL) is diagnosed. Given nearly 20% of PULs will be ectopic pregnancies, all of these patients need definitive and timely follow-up with an early pregnancy care provider, irrespective of the serum progesterone level [6].

Further, treatment decisions cannot be made in the ED based on the findings of an indeterminate ultrasound in the setting of a low serum progesterone level. It is a slippery slope to treating a miscarriage and missing the ectopic pregnancy. As previous research has shown that EDs often fail to provide the emotional support, patient education materials, and follow-up women require during this distressing time [3], the ED is not equipped to provide the counseling and the follow-up required to make treatment decisions based on a serum progesterone levels in the ED.

A single serum progesterone level may be useful in settings where there is adequate follow-up to exclude ectopic gestation or PUL. A study by Bishry and Ganta concluded that a combination of single serum progesterone measurements and serum BHCG is helpful in managing women with suspected ectopic pregnancies, when the ultrasound is inconclusive [7]. Such a test may be useful in dedicated Early Pregnancy Assessment Clinics (EPAC), where adequate follow-up with access to serial vaginal ultrasound and quantitative serial serum BHCG are available.

As this study by Ghaedi and colleagues underscores, diagnostic clarity is desired by patients presenting to the ED with symptoms of early pregnancy loss. High single progesterone level is reassuring with viable pregnancies; however, a low progesterone cannot distinguish between miscarriage and ectopic pregnancy. Therefore, a single serum progesterone level in the ED cannot safely change the disposition plan for these patients especially where ectopic pregnancy could not be excluded. As Canadian ED providers, we need access to urgent follow-up care for these patients with early pregnancy providers in dedicated EPACs that can further provide a supportive role for the ED. Our goal as healthcare providers treating pregnant individuals undergoing early pregnancy loss is to advocate for EPACs as a standard of care.

Declarations

Conflict of interest The authors state no conflict of interest.

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