Sys Rev Pharm 2023; 14(7): 498-502
A multifaceted review journal in the field of pharmacy
E-ISSN 0976-2779 P-ISSN 0975-8453 / DOI: 10.31858/0975-8453.14.7.498-502

Research Article

Accuracy of Whole Blood for Bedside Pregnancy Test

Khadija Shukaili*
Emergency Department, Ibri Hospital, Ibri, Oman

Article History: *Submitted: 26.06.2023* *Accepted: 21.07.2023* *Published: 28.07.2023*

ABSTRACT

Objective: Point-of-care pregnancy testing is widely used in emergency departments. Three prior studies demonstrated the accuracy of whole blood compared with urine in bedside pregnancy tests. Our study demonstrates the accuracy of the available point-of-care kit, which differs from previous studies. The primary aim of this study was to assess the sensitivity, specificity, Negative Predictive Value (NPV), and Positive Predictive Value (PPV) of whole blood in bedside pregnancy tests at three levels of serum beta hCG (5, 10, and 25 mIU/mL). The secondary aim was to get the reading time difference using whole blood versus laboratory serum human Chorionic Gonadotropin (hCG).

Materials and methods: Healthy females of 12-50 years old who required a pregnancy test for diagnostic studies or treatment were included in the study. A triage nurse or phlebotomist drew 5 ml of blood from the patients who met the inclusion criteria. A few drops were applied to an SD bioline bedside hCG test. The results were read after five minutes, and the laboratory technician processed the remaining blood. The nurse who read the SD bioline hCG whole blood tests and the laboratory technician who processed the quantitative serum hCG tests were blinded to each other, and the reading time was recorded for both methods. The SD bioline hCG whole blood test results were compared according to three quantitative serum hCG levels (5, 10, and 25 mIU/mL).

Results: Of the 278 patients in the study, 130 patients (47%) had a serum hCG level of ≥ 5 mIU/mL, 125(44%) had a serum hCG level ≥ 10 mIU/mL, and 123(44%) had a serum hCG level ≥ 25 mIU/mL. The sensitivity and negative predictive values were 90% and 91.93%, respectively, at serum hCG levels ≥ 5 mIU/mL. At serum hCG levels ≥ 25 mIU/mL, the sensitivity and negative predictive values were 95.12% and 96.27%, respectively. The specificity and positive predictive value were 100% at serum hCG levels of 5, 10, and 25 mIU/mL. Our study showed a time savings of 70 minutes with the use of whole blood compared with laboratory serum hCG, with a p-value <0.05.

Conclusion: The SD bioline hCG whole blood test can rapidly detect early pregnancy with high sensitivity, specificity, NPV, and a PPV with threshold of 10 mIU/mL.

Keywords: Whole blood, Human Chorionic Gonadotropin (hCG), Point-of-care test, Early pregnancy

***Correspondence:** Khadija Shukaili, Emergency Department, Ibri Hospital, Ibri, Oman, E-mail: khadijashukaili@gmail.com

INTRODUCTION

Rapid detection of pregnancy in women of reproductive age is essential in the Emergency Department (ED) to rule out ectopic pregnancy and avoid exposing pregnant women to potential teratogens. In one study done in an urban ED with annual visits numbering 40,000, the rate of unrecognized pregnancy was 6.3% (Stengel CL, *et al.*, 1994). Among those pregnant, 33% were exposed to radiation, and 75% received medications (Stengel CL, *et al.*, 1994; Fromm C, *et al.*, 2012). The serum beta Human Chorionic Gonadotropin (bHCG) has long been the gold standard in diagnosing pregnancy due to its high sensitivity, specificity, and 100% negative predictive values for ruling out pregnancy. However, its disadvantage is that it must be processed in a biochemistry lab, potentially taking a long time to be released and negatively affecting patient management in the ED. Additionally, it carries a higher cost than the bedside pregnancy test. Point-of-Care Testing (POCT) is diagnostic testing performed at or near the site of clinical care. With increasing pressure on physicians to see more patients and spend less time with each patient, POCT has become a popular means of meeting the demands for faster laboratory testing, especially in the emergency department. POCT devices use a small amount of unprocessed specimen, requiring less blood, thereby allowing for finger sticks and avoiding phlebotomy risks. A broad menu of analyses is available, including blood gas, electrolytes, pregnancy, and cardiac testing (Nichols JH, 2007). Multiple studies have shown that the impact on the length of stay is probably the most critical advantage of POCT use in the ED (Loten C, *et al.*, 2010; Murray RP, *et al.*, 1999; Hsiao AL, *et al.*, 2017). The literature has given conflicting results for the accuracy of Human Chorionic Gonadotropin (hCG) point-of-care devices, especially at low serum beta hCG concentrations. Commonly used beta hCG point-of-care devices may give false-negative results at low urine beta hCG levels (20-50 U/L) (Kamer SM, *et al.*, 2015; Habboushe JP and Walker G, 2010; Grenache DG, 2015; Teixeira JL, *et al.*, 2015; Greene DN, *et al.*, 2013). Additionally, urine collection can take time for various reasons and lead to a critical delay in patient management, for example, in the case of a patient in hypovolemic shock due to a ruptured ectopic pregnancy (Habboushe JP and Walker G, 2010). Using whole blood as an alternative to urine can be a solution. There are few published studies in the literature demonstrating the use of whole blood instead of urine in bedside pregnancy tests. One study was conducted in an emergency department in Maimonides Medical Center in Brooklyn, NY, using the Beckman Coulter ICON 25 rapid hCG immunoassay kit (Fromm C, *et al.*, 2012). The study showed a sensitivity of 95.8%, specificity of 100%, and an NPV of 97.9% (Stengel CL, *et al.*, 1994). The study was limited by the use of a single pregnancy test kit, the Beckman Coulter ICON 25 rapid hCG immunoassay kit (Fromm C, *et al.*, 2012). Another study was conducted on a total of 265 patients at an urban tertiary care hospital to determine the difference in result times between urine and whole blood testing, also using the Beckman Coulter ICON 25 rapid hCG immunoassay kit (Gottlieb M, *et al.*, 2016). The study showed a savings of 21 minutes without significant accuracy changes when using whole blood rather than urine (Gottlieb M, *et al.*, 2016). A third study also demonstrated high sensitivity (96.3%), specificity (100%), NPV (99.3%), and PPV (100%) when using 10 mIU/mL as a positive threshold level (Legoupil C, *et al.*, 2019).

Most of the studies demonstrate using either urine or serum in point-of-care testing for rapid pregnancy detection, and the majority of commercially available rapid immunochemical assay kits

are validated for urine and serum but not whole blood (Fromm C, *et al.*, 2012). The disadvantage for those tests is that it may take longer to perform due to difficulty obtaining urine in some patient and serum test takes a long time. Using whole blood for bedside pregnancy test instead of urine and serum would detect pregnancy status more rapidly by obtaining whole blood.

MATERIALS AND METHODS

Inclusion criteria

Healthy women of childbearing age from 12-50 years old, who require a pregnancy test for diagnostic studies or treatment.

Exclusion criteria

- Hemodynamically unstable
- Severely ill patients
- Unable to obtain consent
- Patient appears obviously pregnant

Sample size

Based on the literature, the sensitivity of whole blood for the bedside pregnancy test was considered 95%, and the gold standard serum hCG was 98%. With a calculated sample size power of 80% and an alpha of 5%, we need to study a minimum of 200 samples.

Subjects who met the eligibility criteria and agreed to participate in this study were enrolled as participants *via* the triage nurse. Written consent was obtained. A triage nurse completed standardized data collection sheets, which were then reviewed by the study investigator. After that, the subjects were sent to the phlebotomist, who drew 5 ml of whole blood from each participant. Each blood sample was labeled with the patient hospital ID number. One or two drops from each blood sample was used immediately by the nurse to perform the SD bioline hCG immunoassay test. The kit is provided by Sultan Qaboos University Hospital. The result was read after 5 minutes. The remainder of the whole blood specimen will be sent to the biochemistry laboratory at Sultan Qaboos University Hospital for a quantitative serum total hCG test using a cobas analyzer as a gold standard test. A positive pregnancy test will have a quantitative serum hCG ≥ 5 mIU/mL. Nurses who performed the whole blood pregnancy test and laboratory technicians who performed serum hCG tests were blinded to each other. According to our laboratory technician, quantitative serum hCG 5-10 mIU/mL was considered weakly positive and usually repeated after 48 hours. The SD bioline hCG immunoassay has a detection limit of 25 mIU/mL. Therefore, our study compared the SD bioline whole blood test with three levels of serum hCG (5,10, and 25 mIU/mL).

Data analysis

Data was analyzed using the EpiData system. Sensitivity, specificity, Negative Predictive Values (NPVs), Positive Predictive Values (PPVs), and accuracy were calculated. A paired t-test was used to compare the mean time to obtain the bedside whole blood test and the mean time to obtain the laboratory serum hCG (*Table 1*). P-value less than 0.05 was considered as significant.

Statistical analysis

The results of the quantitative variables are expressed with means and standard deviations. For the comparison of means, the student's t-test was used. The correlations between MDA levels and quality of life were estimated with Pearson's correlation coefficient. The relationship between MDA levels and quality of life, controlling degree of bronchial obstruction i.e, Forced Expiratory Volume (FEV1) was modeled using linear regression. P-value less than 0.05 was considered as significant. Data was analyzed with the SPSS/PC statistical package, version 8.0 (Chicago, IL).

RESULTS

Between January 2018 and July 2018, 290 patients were enrolled in the study. Twelve were excluded due to missing data. The mean age (± SD) of the patients was 30 (± 7.4) years, and the mean gestational age (± SD) was 8 (± 3.3) weeks. Positive and negative results were taken according to three levels of serum beta hCG (i.e., 5, 10, and 25 mIU/mL). At cutoff serum, hCG ≥ 5 mIU/mL, 130 (47%) had positive values, and 148 (53%) had negatives values. At ≥ 10 mIU/mL, 125 (45%) had positive values, and 153 (55%) had negative values. At ≥ 25 mIU/mL, 123 (44%) had positive values, and 155 (56%) had negative values (*Table 2*). Sensitivity, specificity, NPV, and PPV were calculated to three different cutoff values for serum beta hCG level (5, 10, and 25 mIU/mL) (*Table 3*). Since the detection limit for the SD bioline hCG test is 25 mIU/L, the whole blood's overall accuracy beside the test was 97.8%. The sensitivity of 95% and NPV of 96% for the same cutoff level. If we consider a beta hCG level of 10 mIU/mL as cutoff, the sensitivity and NPV will be 93.6% and 95%, respectively. These were reduced to sensitivity of 90.0% and 91.93% at serum beta hCG level of ≥ 5 IU/mL as cutoff value. The specificity and PPV were both 100% for the SD bioline whole blood test at three cutoff values (*Table 3*).

Our study's secondary outcome was to compare the time needed to receive the result of the pregnancy test using whole blood and serum beta hCG. The mean time to obtain the whole blood result was 4.6 minutes versus 76 minutes using serum beta hCG.

In our study, 13 samples had false-negative results when the whole blood test laboratory hCG quantitative values were ≥ 5 mIU/mL (*Table 4*).

Table 1: Paired sample test

Pair 1	Paired differences					t	Degrees of freedom (df)
	Mean	Standard deviation	Standard error mean	95% Confidence interval of the difference			
				Lower	Upper		
Time required to obtain whole blood result-time required to obtain serum hCG level	-71.741	30.553	1.859	-75.402	-68.08	-38.583	269

Table 2: Patients characteristics (n=278)

Characteristics	Outcomes
Mean age (SD)	30 (7.4) years
Mean gestational age (SD)	8 (3.3) weeks
hCG value, n (%)	>5 mIU/mL, 130 (47%)
	<5 mIU/mL, 148 (53%)
	>10 mIU/mL, 125 (45%)
	<10 mIU/mL, 153 (55%)
	>25 mIU/mL, 123 (44%)
	<25 mIUm/L, 155 (56%)

Table 3: Sensitivity, specificity, negative predictive value, and positive predictive value for whole blood test

HCG >25 mIU/L (n=123)	Value
True positive	117
False positive	0
False negative	6
True negative	155
Sensitivity	117/123 (95.12%)
Specificity	155/155 (100.0%)
Negative predictive value	155/161 (96.27%)
Positive predictive value	116/116 (100.0%)
Overall accuracy	97.84%
HCG >10 mIU/L (n=125)	
True positive	117
False positive	0
False Negative	8
True negative	153
Sensitivity	117/125 (93.6%)
Specificity	153/153 (100.0%)
Negative predictive value	153/161 (95.0%)
Positive predictive value	116/116 (100.0%)
Overall accuracy	97.12%
HCG >5 mIU/L (n=130)	
True positive	117
False positive	0
False negative	13
True negative	148
Sensitivity	117/130 (90.0%)
Specificity	148/148 (100.0%)
Negative predictive value	148/161 (91.93%)
Positive predictive value	116/116 (100.0%)
Overall accuracy	95.32%

Table 4: False negative results with cutoff hCG value >5 mIU/mL

Time (in minutes) required to get whole blood test	Serum beta hcg level (mIU/mL)	Patient gestational age (weeks)	Patient age (years)	Whole blood result
7	6.5	Unknown	30	Negative
5	7.5	Unknown	30	Negative
6	8.5	Unknown	29	Negative
5	8.9	Unknown	24	Negative
5	9	Unknown	29	Negative
6	15.4	5	31	Negative
3	16.8	4	23	Negative
5	136	5	31	Negative
3	140	4	21	Negative
8	191	8	40	Negative
8	265	8	36	Negative
2	309	5	36	Negative
2	425	5	31	Negative

DISCUSSION

Rapid detection of pregnancy status is crucial in crowded EDs to detect early pregnancy complications and avoid teratogenic medication. The time needed for a urine pregnancy test depends on the patient's ability to provide a urine sample, which can potentially prolong the stay in the ED. Receiving the serum beta hCG results also takes time. It is easier and more practical to get whole blood that can be applied to a pregnancy kit for a faster result. Our study first assessed the sensitivity and specificity of bedside pregnancy tests using whole blood and compared it to the gold standard serum beta hCG. As per our second aim, we compared the time needed to receive the result using each method. The SD bioline hCG test in our study showed a sensitivity of 93.6% using whole blood with a ≥ 10 mIU/mL hCG detection limit and 96% with a 25 mIU/mL detection limit. If we consider the lowest detection limit of ≥ 5 IU/mL, the sensitivity is 90%.

In our study, 13 samples showed false negative values with ≥ 5 mIU/mL as a cutoff limit. Eight samples that had negative bedside SD bioline hCG tests had serum beta hCG levels lower than 5 mIU/mL, which could be explained by the detection limit of ≥ 25 mIU/mL for the SD bioline hCG kit. Another 3 negative bedside whole blood tests and serum beta hCG levels ≥ 25 mIU/mL had reading time of 2 minutes, which requires less than 5 minutes when compared with that of SD bioline HCG kit. The remaining 2 patients with serum beta hCG ≥ 25 mIU/mL and negative bedside whole blood tests with reading time of 5 minutes could not be explained. Our study included only patient age and gestational age, missing other confounding factors like smoking, comorbidity, medication history, etc., that can affect final results. This is one limitation of our study.

Using SD bioline hCG tests for bedside pregnancy testing using whole blood reduced the time to obtain a result from 75 minutes to 5 minutes, saving 70 minutes of time with significant p-value (0.000). This result is similar to a previous study that showed saving of 85 minutes (Legoupil C, *et al.*, 2019). Although the total length of stay in the ED was not recorded in our study, in general, point-of-care testing reduced length of stay in the ED (Loten C, *et al.*, 2010; Murray RP, *et al.*, 1999; Hsiao AL, *et al.*, 2017), with a primary benefit of avoiding missing early pregnancy complications.

Our study's strengths were first; it was done in a prospective setting using an available bedside HCG kit. In addition to that, there was a high rate of positive tests (42%) in our study population. Furthermore, the sensitivity was calculated to different levels of serum beta hCG (5, 10, and 25 mIU/L).

Limitations of our study include the potential for a false-negative result in early pregnancy due to using the SD bioline hCG test with a ≥ 25 mIU/mL detection limit. The SD bioline hCG kit, like other POC pregnancy tests, is still not approved by the FDA for whole blood use (Gottlieb M, *et al.*, 2016). A study parallel to this one used a 5-10 IU/L detection level, which is critical to prevent missing early pregnancy status (Legoupil C, *et al.*, 2019). Additionally, only one POC pregnancy test was assessed in this study, but previous studies used two different kits and showed similar accuracy. Furthermore, five minutes is probably not enough time to read the result for the whole blood POC pregnancy test (Fromm C, *et al.*, 2012). Because whole blood is thicker than urine, it requires more time to receive a result. Finally, our study was limited by missing patient characteristics variables from *Table 1*, which can affect the false-negative results.

CONCLUSION

Our study showed that the SD bioline hCG immunoassay kit for bedside pregnancy testing is accurate and effectively similar to the results of previous studies. SD bioline hCG whole blood can be used to detect pregnancy with ≥ 10 mIU/mL as a positive threshold with an average time saving of 70 minutes. However, the accuracy is low at the 5 mIU/mL positive threshold. This study assessed the sensitivity and specificity of whole blood for bedside pregnancy tests and compared the time required to obtain the result for whole blood compared to serum beta hCG.

REFERENCES

1. Stengel CL, Seaberg DC, MacLeod BA. Pregnancy in the emergency department: Risk factors and prevalence among all women. Ann Emerg Med. 1994; 24(4): 697-700.
2. Fromm C, Likourezos A, Haines L, Khan AN, Williams J, Berezow J. Substituting whole blood for urine in a bedside pregnancy test. J Emerg Med. 2012; 43(3): 478-482.

3. Nichols JH. Point of care testing. Clin Lab Med. 2007; 27(4): 893-908.
4. Loten C, Attia J, Hullick C, Marley J, McElduff P. Point of care troponin decreases time in the emergency department for patients with possible acute coronary syndrome: A randomised controlled trial. Emerg Med J. 2010; 27(3): 194-198.
5. Murray RP, Leroux M, Sabga E, Palatnick W, Ludwig L. Effect of point of care testing on length of stay in an adult emergency department. J Emerg Med. 1999; 17(5): 811-814.
6. Hsiao AL, Santucci KA, Dziura J, Baker MD. A randomized trial to assess the efficacy of point-of-care testing in decreasing length of stay in a pediatric emergency department. Pediatr Emerg Care. 2017; 23(7): 457-462.
7. Kamer SM, Foley KF, Schmidt RL, Greene DN. Analytical sensitivity of four commonly used hCG point of care devices. Clin Biochem. 2015; 48(6): 448-452.
8. Habboushe JP, Walker G. Novel use of a urine pregnancy test using whole blood. Am J Emerg Med. 2010; 29(7): 840-e3.
9. Grenache DG. Variable accuracy of home pregnancy tests: truth in advertising? Clin Chem Lab Med. 2015; 53(3): 339-341.
10. Teixeira JL, Rabaioli P, Savaris RF. Sensitivity and specificity of a urinary screening test used in an emergency setting to detect abnormal first trimester pregnancies. Am J Obstet Gynecol. 2015; 212(1): e1-e5.
11. Greene DN, Schmidt RL, Kamer SM, Grenache DG, Hoke C, Lorey TS. Limitations in qualitative point of care hCG tests for detecting early pregnancy. Clinica Chimica Acta. 2013; 415: 317-321.
12. Gottlieb M, Wnek K, Moskoff J, Christian E, Bailitz J. Comparison of result times between urine and whole blood point-of-care pregnancy testing. West J Emerg Med. 2016; 17(4): 449.
13. Legoupil C, Enderle I, Le Baccon FA, Bendavid C, Peltier L, Bauville E, *et al.* Performance of a quick pregnancy test on whole blood in early pregnancy units: A prospective cohort study. Eur J Emerg Med. 2019; 26(2): 105-111.