Inappropriate Off-label Use of a Qualitative, Point-of-care hCG Device

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Dear Editor,

We read with interest the recent study by Gottlieb et al[1] describing the reduction in turnaround time achieved by substituting whole blood for urine on a qualitative point-of-care (POC) hCG device. The device used in this study is FDA-approved and CLIA-waived only when the manufacturer's instructions are followed: three drops of urine or serum are applied to the device and results are recorded within three minutes (urine) or five minutes (serum) after application of sample.[2] However, the practice described by the authors differs considerably from the manufacturer's instructions, as whole blood was used rather than urine or serum and results were interpreted after 10 minutes. Modification of an approved device constitutes off-label use, is considered a laboratory-developed test and requires extensive validation to establish the modified device's performance characteristics before it is used in a clinical setting.

We commend the authors for noting that qualitative POC hCG devices are not FDA-approved for use with whole blood and we acknowledge their concurrent testing of urine on the same POC hCG device as a reference method. However, in addition to a method comparison study, CMS requires that laboratory-developed tests undergo an evaluation of precision, analytical sensitivity, analytical specificity, reportable range, reference interval and any other pertinent performance characteristics prior to being released for clinical use.[3] Although a method comparison was performed, many additional device performance characteristics have not been defined. Furthermore, validation study results are limited to the specific clinical setting in which the study was performed and are not transferable to another institution, meaning that each institution that intends to offer a laboratory-developed test for clinical use must perform its own validation study. Use of an uncharacterized device to make clinical decisions puts patients at risk for adverse outcomes, particularly if inappropriate treatment is administered to a pregnant patient, an ectopic pregnancy goes undiagnosed due to a false negative result, or if necessary surgical intervention is delayed because of a false positive result. Use of modified devices without the required validation studies also jeopardizes the hospital laboratory's accreditation and may result in forced discontinuation of laboratory testing, which negatively impacts patient care throughout the hospital.

We support the authors' assertion that an FDA-approved device capable of rapid hCG detection in a whole blood specimen at the point of care would be valuable in healthcare delivery settings. We would like to point out that two FDA-approved test platforms are already available for exactly that: the Abbott i-STAT βhCG cartridge and the NowDiagnostics ADEXUSDx hCG test. In addition to receiving FDA approval, the performance characteristics of both of these devices have been independently evaluated in academic medical centers.[4,5] We strongly recommend that the authors engage with laboratory professionals at their institution to discuss available testing options and select appropriate test methods that meet the clinical need without jeopardizing patient care.

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In reply to: "Inappropriate Off-label Use of a Qualitative, Point-of-care hCG Device"

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Dear Dr. Robert D. Nerenz, Dr. Ann M. Gronowski, and Dr David G. Grenache,

Thank you for your comments regarding our recently published article describing a reduction in turnaround time achieved by the substitution of whole blood for urine on a qualitative point-of-care hCG device.[1] We appreciate the insights and comments noted by Robert D. Nerenz, Ann M. Gronowski and David G. Grenache. The authors of this letter highlight the importance of multiple validation studies prior to routine implementation of non-FDA approved devices. We also agree with this and would like to highlight that the primary purpose of our study was to determine whether the substitution of whole blood for urine would decrease turnaround time, with the potential to reduce risks associated with delayed diagnoses of ectopic pregnancies, as well as expediting necessary imaging and treatment options that would be contingent upon pregnancy status.

While our study does support prior literature demonstrating similar accuracy between whole blood and urine for point-of-care hCG testing,[2] our study clearly emphasizes that further study is necessary prior to routine acceptance. One of the primary goals of our article was to justify and encourage further study into this application in order to appropriately validate it for routine clinical use.

At the time of our study, there were no FDA-approved point-of-care hCG devices that could utilize whole blood. We were excited to hear of the FDA approval of two alternate point-of-care hCG devices for use with whole blood. While our study was the first to provide evidence of an advantage in turnaround times when using whole blood in place of urine, we look forward to further studies to determine whether similar results will be seen with these newer devices.

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