Brief Report

Abnormal Urine Drug Screens in Pregnancy- Opportunity for Laboratory Stewardship

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Background: Clinical testing for drugs of abuse typically involves initial screening followed by confirmatory testing. Due to limited evidence-based guidelines, the healthcare provider makes the decision to confirm abnormal screens based on the clinical context. This two-step approach proved to be inadequate in scenarios like maternal substance abuse and subsequent fetal/ newborn exposure. The goal of this study is to assess and improve the confirmatory testing rate of abnormal screens among pregnant patients at our women's center.

Methods: A retrospective chart review was conducted to assess the confirmation rates among positively screened pregnant patients, and a lab stewardship initiative was implemented to remind ordering physicians about the importance of confirmatory drug tests. Abnormal screens were classified as expected positives based on the medication-related interference, social history and self-reported substance use from the provider notes.

Results: Only 28% of pregnant patients with unexpected positive drug screens underwent confirmatory testing during the pre- intervention period, which rose significantly to 67% during the post-intervention period. Furthermore, outcome analysis revealed that 50% of patients with concordant confirmatory test results were referred to social work and psychiatry in the post-intervention period.

Conclusions: This study highlights the value of laboratory stewardship in optimizing drug testing practices for pregnant patients.

Introduction

Drug testing is indicated in various contexts, such as pain management, medication adherence, monitoring controlled substance abuse, work-up for sudden unexplained symptoms, forensics, workplace safety and athlete compliance [1]. In clinical settings, drug testing typically involves a two-step sequential approach, with an initial screen followed by a confirmatory test [2]. Urine is the preferred matrix for drug testing due to its relatively long analyte detection window and high analyte concentrations compared to blood. Urine drug screens are primarily immunoassay-based qualitative tests and are prone to both false positive and false negative results [3]. Moreover, immunoassay-based screens are unable to identify synthetic analogs [4]. Hence, screening results are considered presumptive until confirmed with a definitive test using liquid chromatography-tandem mass spectrometry (LC-MS/MS) or gas chromatography-mass spectrometry (GC-MS). Given limited evidence-based guidelines, healthcare providers often make the decision to confirm a presumptive positive screen depending on the clinical context as well as the institutional policy [2].

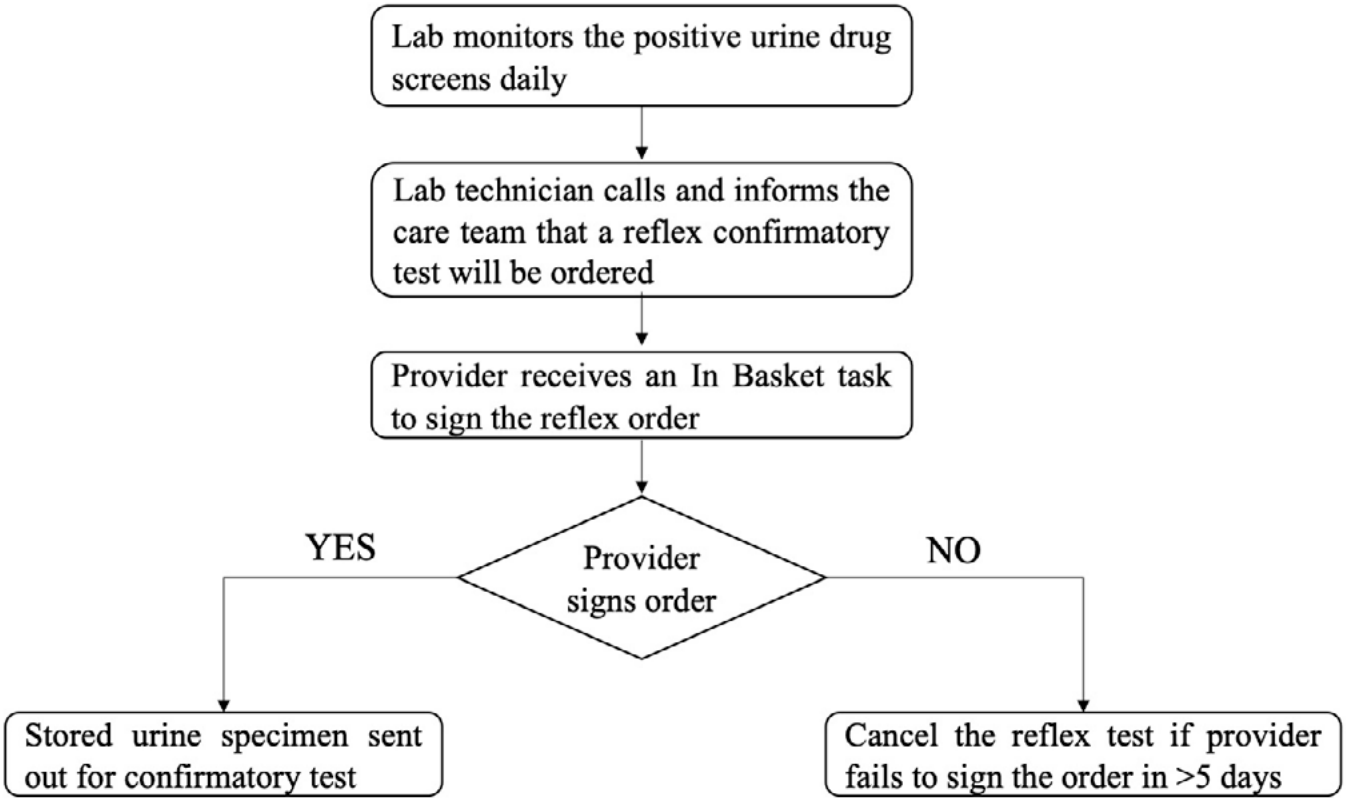
Several studies have underscored the inconsistent and inadequate drug testing practices in children and pregnant women [5-7]. Importantly, timely and accurate interpretation of urine drug tests is critical for clinical decision-making in these populations as it might also have social and legal ramifications. As per the United States National Poison Data Center, ~40% of substance exposure cases correspond to the pediatric population [8]. Additionally, maternal substance use causes debilitating effects on newborns, including cognitive impairment, neonatal abstinence syndrome, respiratory insufficiency and behavioral problems [9]. In 2017, the American College of Obstetrics and Gynecology (ACOG) and the American Society of Addiction Medicine jointly recommended all pregnant women be universally screened for substance use at the first prenatal visit [10]. Pregnant patients are first assessed using verbal questionnaires such as National Institutes of Drug Abuse Quick Screen and high-risk individuals undergo urine drug screening [10]. Confirmatory testing of discordant screens often involves sending specimens to the reference laboratories for LC-MS/MS or GC-MS analysis, further delaying the medical and social interventions in these patient populations. In this study, we launched a laboratory stewardship initiative to improve the drug confirmation rates among abnormally screened pregnant patients at our women's center and highlighted the need for optimal drug testing panels.

Methods

This study was conducted in accordance with the protocol approved by the Baylor College of Medicine Institutional Review Board. We performed a retrospective cohort study involving pregnant patients who have undergone urine drug screens at our women's hospital from May 2022 to May 2023 (pre-intervention period) and November 2023 to May 2024 (post-intervention period). The urine drug screens were performed on the PROFILE-V MEDTOXScan Drugs of Abuse Test System, which employs a one-step, competitive later-flow immunoassay. The panel included the following drug classes with indicated cutoffs: tetrahydrocannabinol (50 ng/mL), phencyclidine (25 ng/mL), cocaine (150 ng/mL), methamphetamine (500 ng/mL), opiates (100 ng/mL), amphetamines (500 ng/mL), benzodiazepines (150 ng/mL), tricyclic antidepressants (300 ng/mL), methadone (200 ng/mL), barbiturates (200 ng/mL), oxycodone (100 ng/mL), propoxyphene (300 ng/mL) and buphenorphine (10 ng/mL). Of note, Fentanyl (1 ng/mL; ARK Diagnostics, Inc.) was added to the panel during the post-intervention period.

In collaboration with Obstetrics and Gynecology physicians and nurses, laboratory implemented a pilot scale stewardship initiative (Figure 1). Our major intervention was having the bench technician call the ordering provider to suggest confirmatory testing for positive urine drug screens. Additionally, a standardized risk assessment strategy devoid of racial and ethnic disparities was implemented during the post-intervention phase. As per our hospital policy, all the presumptive positive urine specimens were stored in the freezer at -20°C for 30 days. Upon the physician's request, presumptive positive urine specimens were sent for confirmatory testing to ARUP reference laboratory (test code: 0092186). In certain cases, alternate specimens, such as maternal serum or meconium from the newborn, were sent for confirmatory testing (test codes: 0092420 and 3004583). A blinded reviewer performed chart reviews for patients with positive screening results to retrieve the status of confirmatory testing, medication history and provider's progress notes. Abnormal screens were classified as expected positives if the patient self-reported the substance use or was on a medication that could potentially interfere with the assay. A 2-tailed Fisher's exact test was used to compare the confirmatory testing rates in the pre- and post-intervention periods. Results with $p<0.05$ were considered statistically significant.

Figure 1: Confirmatory urine drug test stewardship.



Results

During the pre-intervention period, a total of 370 urine drug screens were ordered for pregnant patients at our women's hospital, of which 83 were positive (Table 1). A majority of positive screens were noted for tetrahydrocannabinol, followed by methamphetamine and benzodiazepines (Table 2). Among the 83 positive screens, 25 cases were expected positives due to self-reported substance use or medication-related interference (Table 1). Out of 58 unexpected positive screens, confirmatory testing was pursued in 16 cases, of which 8 showed positive results and 8 showed negative results (Table 1). Hence, the confirmation rate during the pre-intervention period was 19% for all positive screens and 28% for unexpected positive screens.

Table 1: Confirmatory testing status in patients with positive urine drug screen.

Drug Tests	Pre-intervention	Post-intervention
Total Unique Patients	370	143
Positive screens	83	106
Expected positive screens	25	64
Unexpected positive screens	58	42
Total confirmations	16	68
Positive on confirmation	8	30
Negative on confirmation	8	38

Table 2: Distribution of abnormal urine drug screens.

Drug Class	Pre-intervention	Post-intervention
Tetrahydrocannabinol	30	23
Phencyclidine	0	0
Cocaine	7	10
Methamphetamine	12	15
Opiates	9	9
Amphetamines	6	5
Benzodiazepines	12	11
Tricyclics	2	3
Methadone	0	0
Barbiturates	3	1
Oxycodone	2	0
Propoxyphene	0	0
Buprenorphine	0	1
Fentanyl	na	28

During the post-intervention period, a total of 143 urine drug screens were ordered, of which 106 were positive (Table 1). Fentanyl showed the highest proportion of positive screens, followed by tetrahydrocannabinol and methamphetamine (Table 2). However, patients with positive Fentanyl screen were expected cases due to epidural administration for labor pain relief. Among the 106 positive screens, 64 cases were expected positives due to social history or medication-related interference (Table 1). Confirmatory testing was pursued in 68 cases, which included 28 unexpected and 40 expected positive screens (Table 1). Confirmatory testing showed concordant results in 30 cases and discordant results in 38 cases. Hence, the confirmation rate in the post-intervention period was significantly high at 64% ($p<0.00001$) for all the positive screens and 67% ($p=0.002$) for the unexpected positive screens compared to pre-intervention period. Notably, half of the patients with concordant confirmatory testing results were subjected to social work or psychiatry as deemed necessary by the ordering physician. Altogether, this data highlights the role of laboratory stewardship in promoting better patient care for pregnant patients with substance use disorders.

Discussion

Due to a lack of standard guidelines, clinical drug testing practices are highly variable [11]. Factors such as clinical context, medical urgency, individual physician's practice and availability of orderable drug panels influence the drug testing approaches. Our retrospective analysis revealed overall suboptimal drug confirmatory testing rates among the positively screened pregnant population during the pre-intervention phase. Only 28% of pregnant patients with unexpected positive urine drug screens underwent confirmatory testing. This inadequacy led us to launch a pilot-scale lab stewardship initiative, which involved reminding the ordering physician of the importance of confirmatory testing among positively screened pregnant patients. Moreover, we ensured ACOG's universal screening recommendation by integrating a standardized risk assessment questionnaire devoid of racial and ethnic disparities. Our strategy proved to be effective as the confirmation rates increased significantly from 28% in the pre-intervention phase to 67% in the post-intervention phase. Our ultimate goal is to develop a clinical decision support tool to exclude the expected positive screens and perform reflex testing on the rest. This study underscores the importance of developing optimal drug testing panels and standardizing the screening practices in an institute-wide manner.

In contrast to the conventional staged approach, various alternate strategies depending on the clinical need may be implemented, such as 1) reflexive testing panels (positive immunoassay triggers LC-MS/MS testing), 2) direct-to-definitive testing panels (skips immunoassay) and 3) hybrid testing panels (combination of 1 and 2) [6,12]. For instance, a recent study implemented a reflexive testing approach for opioid monitoring, which involved universal drug screening of all pregnant women admitted to the labor and delivery ward with immunoassay followed by rapid confirmation with LC-MS/MS (turnaround time-1 day) [6]. Interestingly, this approach not only improved the early identification of newborns at risk for neonatal opioid withdrawal syndrome, but it also substantially reduced the burden of the neonatal intensive care unit by allowing the discharge of newborns with false positive screens [6]. Moreover, the utility of comprehensive direct-to-definitive testing by liquid chromatography-high-resolution mass spectrometry in pediatric patients presenting to the emergency room with suspected drug exposure was recently demonstrated [5]. A major limitation of direct-to-definitive testing is the need for frequent updates and validation of the panels due to the

constant evolution of designer drugs.

During the pre-intervention phase, 8 positive screens showed negative results upon confirmatory testing. Whereas during the post-intervention phase, 38 positive screens showed negative results upon confirmatory testing. Although mass spectrometry based confirmations are more reliable than immunoassay-based screens, it is important to consider various factors such as the clinical presentation, medication history, drug cross-reactivity, detection window and specimen quality/validity while interpreting these results. The integration of drug screening and confirmatory test results within the electronic medical records, along with a clinical chemist's interpretation, was found to aid clinicians in efficiently initiating medical and social interventions [11]. Furthermore, this approach may also prevent test misinterpretation owing to the provider's limited analytical knowledge related to drug cross-reactivity, drug metabolism, assay cutoffs, and medication interference [13]. However, there are several challenges that need to be addressed in an institute-wide manner before implementing reflexive testing panels like: 1) excluding expected positive screens for confirmatory testing, 2) specimen storage and integrity monitoring and 3) medicare coverage for reflexive panels, 4) obtaining the patient's consent. Therefore, the development of institutional drug testing guidelines requires the active participation of stakeholders from various subspecialties, such as chemistry, toxicology, pain management, legal/risk management, healthcare finance management, social services and laboratory information systems. Local drug surveillance and positivity rates should be factored in while designing orderable reflexive drug panels. Overall, this study highlights the need to standardize drug testing practices in pregnant patients by designing clinical context-specific orderable panels.

Disclosures

None.

CRediT author statement

Anil K. Chokkalla: Conceptualization, Methodology, Investigation, Formal Analysis, Writing -Original Draft. Sahil Malik: Methodology, Investigation. Ridwan Ibrahim: Methodology, Investigation. Sridevi Devaraj: Conceptualization, Investigation, Formal analysis, Writing -Original Draft, Supervision.

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Abbrieviations

LC-MS/MS, liquid chromatography-tandem mass spectrometry; GC-MS, gas chromatography-mass spectrometry, ACOG, American College of Obstetrics and Gynecology.

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