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The Prevalence of Maternal Drug Use During Pregnancy

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Prenatal substance abuse is an ongoing concern across socioeconomic lines due to the characteristic physical and mental developmental problems that result from drug abuse during pregnancy. Females constitute approximately 30% of the substance addicted population in the United States and most are of childbearing age[4]. Among pregnant women aged 15 to 44 years who participated in the 2006 National Survey on Drug Use and Health, 4.0% reported having used illicit drugs within one month of the survey[2]. National findings from the 2006 survey indicate that the rate of illicit drug use among pregnant women aged 15 to 44 years has remained steady since 2003[2]. Estimating the prevalence of drug use among pregnant women based on maternal history or broad scale surveys often proves unreliable due to guilt, embarrassment, fear of reprisal, or of loss of custody[5]. As a result, identification of the drug exposed neonate is a difficult task and even in the case of maternal admission, information regarding the type and extent of drug use is often inaccurate[6]. A recent study conducted on the prevalence of cocaine use during pregnancy in the early 1990s reported that 37 out of 600 (6.25%) infants born across three metropolitan hospital nurseries in the Toronto area tested positive for cocaine[10]. These findings were consistent with estimations made by Birchfield *et al* who concluded that rates of infants exposed prenatally to cocaine range between 2.6% and 11% of all live births[11]. A nationwide survey carried out in the early 1990s at urban teaching hospitals indicated that 10-45% of the women cared for at those hospitals use cocaine during pregnancy[12]. A separate survey of 36 hospitals reported that 11% of the women studied had used illicit drugs during pregnancy[7]. A follow-up report by the same authors in 1992 estimated that between 500,000 and 750,000 newborns are exposed to illicit drugs each year[13].

Various neonatal health and developmental problems are thought to be directly related to fetal exposure to drugs, alcohol, chemical agents, or other xenobiotics [6, 14-16]. Despite extensive research and continued evidence of fetal and neonatal health risks, a large number of pregnant women are involved in illicit drug use[5]. Drug use during gestation is associated with higher risks for poor obstetrical outcomes, including placental abruption, premature labor, low birth weight, microcephaly, congenital anomalies, necrotizing enterocolitis, neonatal withdrawal, neurobehavioral effects, subarachnoid and intracerebral hemorrhage, and fetal death[17-25]. Due to the detrimental effects resulting from prenatal exposure to illicit substances, correct diagnosis of drug use during pregnancy is essential. Correct diagnosis and early intervention will allow the child to receive the specialized treatment and the care required to ensure that their development is not further compromised. Successful diagnosis of drug abuse during pregnancy will also assist in preventing the same mother from giving birth to subsequent drug-exposed children[26].

However, it is extremely important to ensure that the early diagnosis of drug abuse during pregnancy not only brings about beneficial changes in the environment of the infant but also aids in the successful rehabilitation of substance addicted mothers[27]. Although the early identification of prenatal substance

abuse will aid in the long-term wellbeing of the infant, without the implementation of a well defined intervention road map, such diagnosis also have the potential to cause harm to mothers, children, and families alike[28]. Careful consideration of the circumstances surrounding each and every positive result will ensure that a mother who has used drugs or alcohol at some time during pregnancy is not mislabeled as a substance abuser in the absence of true abuse. Review of positive results with mothers suspected of substance abuse will help to ensure that infants are not separated from their mothers and placed in living situations that offer no benefit[28].

Traditional identification of neonatal drug exposure is accomplished using a combination of maternal history, newborn clinical symptoms, and laboratory toxicology testing of the mother and the infant[27]. Generally, toxicological testing of the mother and infant will only occur if the consulting physician has reason to believe that prenatal substance abuse may be an issue based on maternal history or if the infant's physical features meet certain criteria that are commonly associated with prenatal exposure to drugs. Many states mandate toxicology testing of all mothers and infants regardless of maternal history or certain physical features of the infant. Indiana's Maternal & Children's Special Health Care (MCSHC) Department mandates laboratory testing of meconium specimens to detect the presence of controlled substances for those infants born in Indiana who meet selected criteria at birth. Toxicology testing is performed on high-risk newborns (1) whose weight is less than 2500 grams and whose head circumference is smaller than the 10th percentile for the infant's gestational age when there is no other medical explanation for these conditions; (2) when there is maternal history of current or past drug use; (3) mother had no or inconsistent prenatal care (frequently missed appointments, hospital hopping); (4) infant shows signs/symptoms suggestive of drug effects or withdrawal; or (5) unexpected abruption placentae[29]. Approximately 1,600 newborn infants meet one or more of these criteria in Indiana alone, and many additional meconium specimens are submitted for analysis based on recommendations from the consulting physician[29].

Traditional toxicological analyses aimed at identifying prenatal exposure to illicit substances have utilized various maternal and neonatal specimens over the years. Maternal blood is routinely analyzed for the presence of illicit substances in the mother. However, due to the short window of detection and the invasiveness of sample collection, blood analysis is somewhat limited. Toxicological analysis of neonatal blood is rarely performed as serum drug levels in the infant largely depend on the time interval between the mother's last drug intake and the subsequent testing of the neonatal blood. This time interval can be substantial, and as a result, drug levels in the neonatal blood will likely fall below detection limits for common screening techniques[39]. Neonatal urine is the most widely analyzed biological fluid for the determination of in utero drug exposure and offers several distinct advantages over blood. Drug concentrations in neonatal urine will be higher than those in corresponding blood (serum) specimens due to the concentrating ability of the kidneys[40]. Neonatal urine also offers a slightly longer window of detection than blood and should indicate the presence of any substances that the neonate was exposed to in the last 3-7 days prior to delivery[41]. Urine also offers a larger volume for collection than blood, and from a toxicological standpoint, it is easier to analyze than blood because it is devoid of protein and cellular constituents that can complicate extraction and/or analysis techniques[40].

Although neonate urine has been the most widely analyzed biological fluid for the identification of in utero exposure to drugs, it does have several disadvantages, which can complicate collection and subsequent analyses. Neonatal urine collection is difficult, invasive, and must be performed as close to

birth as possible as appreciable levels of drugs and/or metabolites are expected to be present in the first specimen only[39, 41]. Drugs present in the infant's urine represent recent drug use by the mother and depending on the physiochemical properties of the drug, the urine may test negative if the mother is an infrequent user or abstained from use in the days leading up to delivery[39, 41]. Another common drawback to neonatal urine analysis is the fact that most laboratories adopt pre-existing urine-based methodologies to screen the infant's urine for drugs of abuse. Unfortunately, neonatal urine is far from an ideal specimen for such analyses. Pre-existing urine-based methodologies have most likely been developed and validated for use in workplace or forensic drug analysis[42]. Such screening techniques adopt cutoff levels deemed suitable for their intended purpose and will most likely be too high for the drug concentrations in clinical samples such as neonatal urine.

Recently, meconium has become the specimen of choice for the detection of prenatal exposure to several drugs of abuse[26, 46]. Meconium is the first blackish tarlike material passed from the rectum by the newborn and is not fully evacuated until 125 hours post natal [47-49]. Meconium is a dark-green mass of water, epithelial cells, mucopolysaccharides, bile pigments, and other lipids that begins to form between the twelfth and sixteenth week of gestation and accumulate until birth. Formation of meconium occurs in the fetal gut and results from swallowed amniotic fluid and sloughed gastrointestinal epithelial cells[50]. Accumulation of drugs and other xenobiotics occurs in the meconium as a result of fetal swallowing. This phenomenon occurs when the fetus releases urine containing drugs and metabolites into the amniotic fluid, where it is subsequently swallowed and deposited into the meconium. Subsequent exposure, excretion, and reabsorption through fetal swallowing, combined with maternal metabolism and elimination and placental transfer results in the concentration of drugs and their metabolites in meconium[51, 52]. At approximately the sixteenth week of gestation, the fetus possesses fully functional liver enzymes capable of metabolizing drugs, allowing for excretion into the bile and urine. The urine is then excreted into amniotic fluid, which is subsequently ingested by the fetus causing drugs to accumulate in the meconium[53].

Meconium is one of the most sensitive matrices for the detection of prenatal drug exposure due to the accumulation of substances over several months of gestation. The usefulness of meconium as an alternative toxicological specimen was first demonstrated by Ostrea et al[54] in the late 1980's, and its popularity as a tool for the identification of prenatal exposure has continued to increase over the past two decades for several reasons. The first reason is the relatively simple and non-invasive procedure used to collect meconium samples, making it more successful than urine collection[55]. Meconium analysis also extends the window of drug detection to approximately the last 20 weeks of gestation as well as extending the window for specimen collection.

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