Infant Birth Outcomes Among Substance Using Women: Why Quitting Smoking During Pregnancy is Just as Important as Quitting Illicit Drug Use

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Abstract Poor birth outcomes are associated with illicit drug use during pregnancy. While prenatal cigarette exposure has similar effects, cessation of illicit drug use during pregnancy is often prioritized over cessation of smoking. The study goal was to examine the impact of pregnancy tobacco use, relative to use of illicit drugs, on birth outcomes. Women were recruited at entry to prenatal care, with background and substance use information collected during pregnancy. Urine drug screens were performed during pregnancy, and the final sample ($n = 265$) was restricted to infants who also had biologic drug testing at delivery. Participants were classified by pregnancy drug use: no drugs/no cigarettes, no drugs/ cigarette use, illicit drugs/no cigarettes, and illicit drugs/ cigarette use. Groups differed significantly on infant birthweight, but not gestational age at delivery after control for confounders including background and medical factors. Among women who smoked, the adjusted mean birthweight gain was 163 g for those not using hard illicit drugs, while marijuana use had no effect on birth weight beyond the effect of smoking cigarettes. Women who used hard illicit drugs and did not smoke had an adjusted mean birthweight gain of 317 g over smokers. Finally, women who refrained from hard illicit drugs and smoking had a birthweight gain of 352 g. Among substance using pregnant women, smoking cessation may have a greater impact on birthweight than eliminating illicit drug use. Intervention efforts should stress that smoking cessation is at least as important to improving pregnancy outcomes as abstaining from illicit drug use.

Introduction

Significant intervention resources have necessarily and successfully been devoted to helping substance using pregnant women become drug free [1–3]. Unfortunately, however, the vast majority of women who successfully quit using illicit drugs continue to smoke, [4] and health professionals who work with these women often prioritize cessation of illicit drug use over the elimination of smoking during pregnancy [5, 6]. Indeed, several studies of prenatal care provider practices and attitudes reveal that a primary reason for not adequately addressing smoking as part of prenatal care is the need to save the limited time available to focus on other negative health behaviors, including the use of illicit drugs [7, 8]. Even within inpatient substance use treatment programs for pregnant women, smoking cessation treatment practices have not been broadly adopted [6]. This approach may be due in part to the potential risk for neonatal abstinence syndrome as a result of exposure to some illicit drugs, [9] effects much more widely studied and understood than the effects of nicotine withdrawal on newborns [10]. Other studies have demonstrated that public and prenatal care provider perception of the adverse effects of illicit drug use in pregnancy goes far beyond the actual potential for fetal damage, [11] and that tobacco use during pregnancy is regarded as separate from, and less serious than, other drug use [5, 6]. Prioritizing cessation of harder drug use over cessation of smoking may

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also be a result of legal and moral issues and judgments, as well as the desire to eliminate the temporary cognitive and behavioral impairments, or "highs," that can result from the use of many illicit drugs [12, 13].

The relative emphasis on the cessation of illicit drug use over cessation of smoking in pregnancy is unfortunate for many reasons. First, a recent report indicated that drug specific medical problems, dependence, and economic costs related to tobacco use are all higher than those for any illicit substance, while drug-related mortality associated with tobacco use is second only to that from heroin [14]. Related specifically to pregnancy, smoking has been shown to add over $700 in neonatal costs per exposed child, representing an annual US. expenditure of $367 million [15]. In addition, and specific to women who both smoke and use other substances during pregnancy, smoking predicts significantly greater length and severity of neonatal abstinence syndrome in infants born to opioid using women [16, 17]. Further, while the immediate effects of neonatal withdrawal from stimulants or opiates can be significant and should not be discounted, the available research shows that neonatal abstinence syndrome is not significantly associated with any long term health or developmental problems beyond those associated with the gestational substance exposure itself [18]. Finally, a recent population-based study found that elimination of smoking would have a much greater impact on decreasing poor birth outcomes than elimination of any other substance, due to both the magnitude of the effects of prenatal cigarette exposure, as detailed below, and the relative prevalence of cigarette smoking [19].

A substantial body of research has examined the potential link between pregnancy substance use and birth outcomes. Several studies have found both significantly decreased birth weight and gestational age at delivery among infants born to substance using women [20, 21] Marijuana is the most widely used illicit drug during pregnancy, and has been extensively studied in relation to adverse birth outcomes. A handful of studies have reported significant relationships between prenatal marijuana exposure and decreased birth weight [22, 23] and gestational age [24]. However, the majority of investigations revealed no significant risk of either decreased birth weight or gestational age for pregnant marijuana users after controlling for use of other substances and background factors [25–28]. The association between pregnancy cocaine use and birth outcomes has also been examined. As reviewed, [29] findings have been conflicting, with some studies reporting a significant risk of decreased birth weight but not gestational duration in pregnancies exposed to cocaine, [30–33] while one study demonstrated a link with decreased gestational age [34]. Others found no significantly elevated risk of reduced birth weight after control

for the use of other substances and background factors [35, 36]. Similarly, the association of pregnancy heroin exposure with birth weight and gestational age at delivery is uncertain, as the few studies reporting a link did not adequately control for use of other substances [21, 37]. More recently, methamphetamine has become a common drug of choice for many pregnant substance users. Several studies have found an increased risk of low birth weight, and especially fetal growth restriction associated with prenatal methamphetamine exposure, regardless of gestational age at delivery [38–40].

The link between smoking cigarettes during pregnancy and poor birth outcomes has also been well studied, and the evidence is unequivocal [41]. Over 30 years ago, Abel reviewed the research data and concluded that newborns prenatally exposed to cigarette smoke weigh an average of 150–250 g less than those born to non-smokers [42]. Dozens of recent studies have also suggested a significant association between pregnancy smoking and decreased birth weight, with decrements attributable exclusively to smoking ranging from around 190 gm, [43, 44] to approximately 250 gm, [45] and to 350 gm or more for heavy smokers [46–48]. Indeed, a recent study demonstrated that each additional cigarette smoked per day in the third trimester led to an 11.6 gm decrease in birthweight [49]. Some estimate that pregnancy smoking accounts for 5–7% of the variance in infant birth weight after control for other potential predictors [50, 51]. Several studies also noted an increased risk for preterm delivery as a result of pregnancy smoking [38, 43, 46, 50]. However, as noted and quantified by multiple investigative teams, the impact of smoke exposure on gestational age does not appear to be as strong as the effect on birth weight [43, 48, 50]. Thus, it appears that the impact of smoking on birth weight is primarily a result of an influence on fetal growth rather than simply an abbreviated gestation.

That substance use during pregnancy significantly increases the risk of adverse birth outcomes is important, as an infant's gestational age and weight at delivery are the strongest biological predictors of immediate and long term developmental outcomes [52]. Even when an infant is born at term, birth weight at or below the third percentile predicts a significantly increased risk of morbidity and mortality [53]. Permanent growth restriction [54] and brain alterations [55, 56] are significant risks for children born too early or too small, as are SIDS [57] and an increased risk for and severity of infections such as RSV [58]. Cognitive and academic deficits are also associated with preterm and low birth weight delivery, [59, 60] including attention, behavior, and mental health problems [54, 61]. Even seemingly small decreases in birth weight can have a large impact on outcomes and associated costs. For example, one study reported that an increase in birth

weight of only 250 gm saves an average of more than $12 000 (1,987 dollars) per infant in medical costs in the 1 year of life alone [5]. And being born even a week early has been shown to increase the cost of state early intervention services by nearly $1,000 per child [62].

Clearly, cigarette smoking during pregnancy impacts infant birth outcomes at least as much as illicit drug use, with important implications for health and development. Indeed, many researchers have even suggested that pregnancy smoking is associated with more, and more severe, health and developmental problems than exposure to any of the illicit drugs commonly abused in the United States [63, 64]. In fact, prenatal exposure to illicit drugs may actually have a smaller impact on birth outcomes than some studies have reported, and may have at most a minimal direct effect. In a recently published systematic review of influences on birth outcomes, only pregnancy smoking could be considered an established cause; evidence to support an adverse effect of pregnancy cocaine use was fairly weak, and no consistent evidence supported an effect for marijuana, opiates, or poly-drug use [65]. Others have drawn similar conclusions [66]. The co-occurrence of substance use with other social, psychosocial, behavioral, and biomedical risk factors, including smoking, has led to the finding that these factors explain most of the birth weight decrements typically attributed to illicit drug use. For example, a recent study revealed that without adjustment for confounders, marijuana, cocaine, and opiate use during pregnancy were related to birth weight decrements. However, none was significantly associated with low birth weight after control for confounding factors. More than two-thirds of the effect of cocaine was explained by psychosocial factors, most significantly by smoking, and almost all of the effect of opiate use was explained by smoking [67]. Other studies have also pointed to the role of smoking and inadequate prenatal care utilization in explaining the link between pregnancy substance use and poor birth outcomes [68]. Given that the vast majority of women who use illicit drugs during pregnancy also smoke, [28, 69–72] and a significant number are poly-drug users with multiple psychosocial and other medical risk factors, [69, 70, 73] attribution of adverse birth outcomes to specific substance exposure, and illicit drug use versus cigarette smoking specifically, is clearly a challenge [74].

Perhaps because of these challenges, few studies have examined the relative impact of exposure to different substances on child outcomes, including immediate birth outcomes. Most studies examine either the impact of illicit drug exposure or the impact of cigarettes and simply control for exposure to other substances, either statistically or through sample selection. One exception is a study by Bada and her colleagues examining the etiologic fraction of low birth weight and preterm births attributable to different types of prenatal drug exposure [75]. Of the substances examined (cigarettes, marijuana, opiates, cocaine, and alcohol), only tobacco and cocaine accounted for a significant amount of variance in preterm delivery. Cocaine use increased the risk by 25%, while tobacco use increased the risk by 26%. Also examined was intrauterine growth restriction (less than tenth percentile in weight for gestational age), with a two-fold increase in risk related to smoking (OR = 2.0), a more than two-fold increase in risk related to cocaine use (OR = 2.2), and no increased risk for marijuana or opiate use noted after control for confounding factors. Based on the relative frequency of use for each substance, the authors calculated that while less than 1% of small for gestational age births could be prevented by the elimination of opiate use, and about 4% could be prevented if cocaine use were eliminated, nearly 14% of small for gestational age births would be eliminated by the prevention of tobacco use during pregnancy [75].

A study by Schempf and Strobino [67] went one step further and quantified, in birth weight decrements, the effect of pregnancy smoking, and marijuana, cocaine, opiate and alcohol use after adjusting for the use of the other substances and background and medical factors. The adjusted effect on birth weight of prenatal exposure to marijuana was less than 1 g, with the impact of alcohol use similarly non-significant. However, cocaine, opiate, and cigarette use were all significantly associated with birth weight. Specifically, use of opiates during pregnancy was associated with an adjusted birth weight decrement of 165 gm, use of cocaine was associated with a 220 gm decrease, while smoking led to the largest decrement—308 gm [67].

Thus, available evidence suggests that smoking during pregnancy is a significant risk factor for adverse birth outcomes, including low birth weight and possibly reduced gestation. In addition, the impact of smoking may be more profound than the impact of illicit drug use, and may produce much greater risk and greater decrements in birth weight than the use of other substances. Additional research is needed to validate the findings described above, and in the frequent case of limited intervention resources and limited personal resources to give up more than one addictive substance at a time, to identify which substances are the most important to target for cessation during pregnancy.

The goal of the current study was to examine the impact of pregnancy tobacco use, relative to the use of illicit drugs, on birth outcomes in a rural sample with a high rate of smoking. Specifically, we were interested in the link between pregnancy smoking and illicit drug use, and birth weight and gestational age at delivery, and the comparative associated decrement in these birth outcomes. We hypothesized that the impact of pregnancy smoking on birth weight and gestational age would be just as large, if

not larger, than the impact of illicit substance use during pregnancy, even after control for potentially confounding background and health factors.

Methods

Participants

Study participants were pregnant patients at one of six medical practices providing prenatal care in Northeast Tennessee. Previous research in the region revealed pregnancy smoking rates up to 42%, with 20% of pregnant women positive for illicit drug use [76, 77]. A total of 652 women entered prenatal care at the study sites during the enrollment period. After the elimination of women who subsequently did not have a live birth, gave birth to multiples, or gave birth out of the region, a total of 629 women were eligible. Of these women, 405 (65%) consented to participate in the study. All women had at least one urine drug screen (UDS) as part of routine care. Additionally, and in order to further validate maternal self-report, the sample was restricted to women whose infants also had a biochemical test for substance exposure (meconium analysis). Newborn substance testing was not universally performed on all infants, instead testing was conducted only if medical history or behavior led hospital staff to suspect pregnancy substance use. Thus, the final sample included in this report was further reduced to 265 women, a group that consequently oversampled pregnancy substance users.

Procedure and Measures

Study procedures were approved by the authors' university Institutional Review Board and the Research Review Boards of the two area hospital systems. Participants were recruited at entry to prenatal care and were paid $20 for each of two separate pregnancy research interviews. As part of these interviews, women were asked detailed, and previously validated questions regarding background characteristics, health history, and smoking and substance use. In addition to the information available via self-report, drug use was evaluated via UDS at entry to prenatal care. The majority of women (79%) also received at least one additional UDS later in pregnancy. Substances examined as part of the urine screen were amphetamines, barbiturates, benzodiazapines, cannabinoids, cocaine, and opioids.[1]

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[1] Cut-off values for substances of interest for both urinalysis and meconium analysis. Values equal to or greater than the value listed were considered a positive drug screen for that substance. amphetamines, 500 ng/ml; barbiturates, 200 ng/ml; benzodiazepines, 100 ng/ml; cannabinoids; 50 ng/ml; cocaine, 300 ng/ml; opiates, 100 ng/ml.

Smoking status was also biochemically verified during the first and third trimester research interviews through assessment of expired air carbon monoxide (ECO), obtained with a portable expired air monitor[2] [78]. Finally, a biochemical analysis for substance exposure was performed for each infant. For 95% of infants this involved analysis of meconium for the substances mentioned above (plus nicotine), providing a marker of exposure during the third trimester.(See footnote 1)For 5% of infants, however, meconium analysis was not available, and for these infants, a urine drug screen identical to the one administered to the mother, was performed on the first urine.

Prenatal medical charts were reviewed for additional background and health information, including pregnancy prescriptions, and additional self-report of pregnancy substance use or smoking. Hospital delivery charts were reviewed for additional self-report of substance use or smoking, and for delivery outcomes, including birth weight in grams, and gestational age at delivery based on ultrasound dating.

Women were considered to be substance users during pregnancy if any of the following were positive: self-report at any point during pregnancy or at delivery, any positive pregnancy UDS, or positive infant meconium/UDS at delivery. Opiates were the most commonly abused substance (52% of drug users), followed by cannabis (49%) and benzodiazapines (27%). Many women (39%) used only marijuana. Of the women testing positive for a harder illicit substance, 25% used more than one substance. For any of the screened substances with medically approved uses, prenatal charts were cross-referenced for current prescriptions. This review revealed that none of the women with positive drugs screens for medications that could be legally prescribed had pregnancy prescriptions for those substances. Finally, women were considered to be pregnancy smokers if self-report at any point during pregnancy or at delivery, an ECO, or meconium analysis/UDS for nicotine was positive.

Data Analysis

Based on pregnancy drug use status, participants were grouped as follows: non-smokers/no drug use ($n = 46$), smokers/no drug use ($n = 75$), non-smokers/drug use ($n = 21$), and smokers/drug use (n = 123). Group differences on background characteristics were tested with ANOVA F-tests for continuous variables, or through chi-square analysis for categorical variables. Variables significantly related ($P < .10$) to either substance use status or birth outcome were used as control variables in ANCOVAs examining the association between substance use status

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[2] A value greater than 6 ppm was used to indicate cigarette use [78].

and birth outcomes. Follow-up ANCOVAs that included control variables were performed, comparing different substance use groups of interest to produce adjusted group means on birth outcomes.

Results

The final sample was comprised of 265 women, recruited at entry to prenatal care and followed through to delivery. Background characteristics by substance use group are presented in Table 1. The vast majority of participants were Caucasian, unmarried, and had just a high school education. Alcohol use during pregnancy was uncommon. Substance use groups were quite similar on the variables examined, with significant differences evident only for level of education and diagnosis of preeclampsia.

Significant substance use group differences were observed for infant birth weight, but not gestational age at delivery (Table 1). Before control for confounding, infants born to women who smoked but did not use drugs, and those who both smoked and used drugs, had significantly lower birth weights than infants born to women who did not smoke or use drugs. However, infants born to women who only smoked did not differ in birth weight from those infants born to women who used drugs but did not smoke.

Because uncontrolled analyses revealed no significant association between prenatal substance use and gestational age at delivery, no additional analyses were performed for this outcome. Controlled analyses for infant birth weight are presented in Table 2. Control variables were those significantly related to substance use group (education and

preeclampsia) and an additional variable related to infant birth weight (infant race). As can be seen, pregnancy substance use status remained a significant predictor of reduced birth weight, accounting for over 5% of the unique variance.

To examine the relative impact of smoking and substance use on infant birth weight, follow-up analyses compared specific substance use groups of interest after adjusting birth weight for significant confounders (Table 3). First examined was the impact of substance use among women who smoke. Compared with infants born to women who both smoked cigarettes and used marijuana, those born to women who only smoked cigarettes had virtually identical birth weights ($P = .945$). In contrast, comparing infants born to women who both smoked cigarettes and used harder illicit drugs, those born to women who only smoked cigarettes had significantly higher birth weights (i.e. 163 gm higher). Thus, for women who smoke, not using marijuana was not associated with a gain in infant birthweight. However, not using harder illicit drugs was associated with a 5.6% improvement in adjusted birthweight (i.e. 163 gm) among smokers.

Next examined was the impact of smoking among women who use hard illicit drugs. Compared with infants born to women who both smoked cigarettes and used drugs, those born to women who continued to use drugs but did not smoke had birth weights more than 300 gm higher. Thus, for women who use drugs, not smoking was associated with an 11.0% improvement in adjusted birthweight (i.e. 317 gm) among drug using pregnant women.

Finally, we evaluated the impact of both smoking and hard illicit drug use on birth weight. Compared with infants born to women who both smoked cigarettes and used

Table 1 Participant characteristics by substance use group

	No cigarette/no drug use ($n = 46$)	Cigarette use only ($n = 75$)	Illicit drug use only ($n = 21$)	Illicit drug and cigarette use ($n = 123$)	F/χ^2	P
Background characteristics						
Age (years)	25.1	24.4	25.5	25.9	1.24	.296
Race (% white)	89.1%	97.3%	85.7%	93.8%	5.21	.157
Education (years)	12.6	11.8	12.9	11.9	4.61	.004
Marital status (% married)	34.8%	29.3%	33.3%	21.4%	3.79	.285
Parity (% 1st pregnancy)	30.4%	29.3%	33.3%	21.4%	.98	.807
Pregnancy alcohol use (%)	0.0%	4.0%	0.0%	0.9%	4.25	.235
Preeclampsia (%)	15.2%	4.0%	19.0%	3.6%	12.37	.006
Prenatal care utilization (% adequate/adequate +)[a]	45.7%	56.0%	47.6%	39.3%	5.08	.166
Birth outcomes						
Birth weight (gm)	3,232	3,068	3,054	2,954	3.70	.012
Gestational age (wks)	38.9	38.7	38.1	38.5	.89	.447

[a] Based on adequacy of prenatal care utilization (APNCU) index [81]

Table 2 Controlled analysis (ANCOVA) of association between pregnancy substance use and birth weight

Variable entered	Partial eta^2	F	P
Covariates[a]			
Education	.012	2.93	.088
Preeclampsia	.036	9.32	.003
Race	.014	3.40	.067
Pregnancy substance use (4 grps)	.052	4.55	.004

Outcome variable was birth weight in grams

[a] All background variables significantly related ($P < .10$) to either pregnancy substance use or birth weight were included as potential covariates in the analysis

drugs, those born to women who used neither substance were more than 350 gm heavier at delivery. Thus, abstaining from both smoking and illicit drug use was associated with a 12.2% improvement in adjusted birthweight (i.e. 352 gm) compared with the continuation of smoking and substance use through pregnancy.

Discussion

The current study demonstrated that pregnancy smoking had twice the impact on birth weight as illicit drug use. Consistent with many previous studies, pregnancy marijuana use did not adversely impact birth weight beyond the effects of cigarette smoking. Also in line with previous findings, pregnancy substance use was not associated with a decrease in gestational age at delivery, suggesting that the

link with birth weight is due to intrauterine growth restriction rather than shortened gestation.

The current study has several limitations. First, as in similar studies, there is likely some degree of error in the final substance use classification groupings. Self-report of substance use can be unreliable due to social desirability influences, and UDS and ECOs only reveal very recent use. While meconium analysis likely increased reliability of substance use identification, use early in pregnancy would not have been detected with this method. While we believe the use of multiple self-report and biochemical variables in determining substance use status is a strength of this study, it is still possible that women who used drugs or smoked during pregnancy were classified as if they had not. The effect of this would make the groups more similar on birth outcomes, possibly masking existing associations between substance use and outcome measures. In part, this may explain no apparent association between substance use and gestational age in the current sample. Related to this, because participants were considered positive for substance use if any of the markers were positive, someone who smoked or used illicit substances early in pregnancy then stopped would still be coded as a substance user. Since research suggests early pregnancy cessation of illicit substance use can mitigate much of the adverse effect on birth outcomes, [44] this again would have the effect of making the substance use groups more similar, masking potential associations. Still another limitation of this study was due to sample size and significant poly-drug use. With the exception of marijuana we were unable to separately examine the impact of different illicit substances on birth

Table 3 The adjusted effect on birth weight of using/not using cigarettes and illicit drugs during pregnancy

Substance use group	Adjusted birth weight (gm)	Birth weight difference (gm)	F	P
Effect of illicit drug use ($n = 198$ smokers)			3.39	.036
Smoked only ($n = 75$)	3,065	163[a]		
Smoked and used marijuana ($n = 39$)	3,068			
Smoked and hard illicit drug use ($n = 84$)	2,902			
Effect of smoking ($n = 105$ hard illicit drug users)			6.28	.014
Hard drug use only ($n = 21$)	3,207	317[b]		
Hard drug use and smoked ($n = 84$)	2,890			
Effect of both smoking and hard illicit drug use			17.42	<.001
No smoking/No drug use ($n = 46$)	3,248	352[c]		
Smoked and hard illicit drug use ($n = 84$)	2,896			

Birth weight adjusted for education, preeclampsia, and race

[a] Compared with those who both smoked and used hard illicit drugs, those who smoked but did not use hard illicit drugs had a 163 gm gain in birth weight

[b] Compared with those who both smoked and used hard illicit drugs, those who used hard illicit drugs but did not smoke had a 317 gm gain in birth weight

[c] Compared with those who both smoked and used hard illicit drugs, those who used neither substance had a 352 gm gain in birth weight

outcomes. Future work should seek larger sample sizes with significant numbers of women using only one illicit substance. In addition, we did not have data reliable enough to quantify timing, duration or amount of exposure, thus could not draw conclusions regarding these factors. Future work should therefore include measurement of when during pregnancy substances were used, and in what quantity. Finally, there are issues with the representativeness of the current sample. Potential regional effects aside, restriction of the sample to women whose infants had biological substance testing eliminated many participants. While we believe this was necessary to insure more accurate substance use classification, the result was a sample not reflective of pregnant women in general.

Future studies should address the limitations noted above. In addition, while rates of pregnancy alcohol use were exceptionally low in this sample and thus the effects of alcohol were not examined, prenatal alcohol exposure is well known to impact birth outcomes [79, 80] and should be considered in studies in other samples. Finally, investigation of the relative impact of different substances beyond birth outcomes, and on long term child health and development, is needed.

Implications of the current findings are clear, and validate assertions of those who concluded that pregnancy smoking may be even more detrimental to the developing fetus than use of any illicit drug [7, 74]. Findings also support those who advocate that significantly more attention be directed toward deceasing pregnancy smoking and increasing smoking cessation efforts [5, 6, 19]. Prenatal patients and their health care providers must be aware of the significant fetal harm and consequent adverse birth outcomes that result from smoking, especially in conjunction with use of other substances. Pregnant women should be strongly advised regarding risks of continued substance use, and should be assisted in their efforts to eliminate the use of all substances, including tobacco.

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