



Maternal, Fetal, and Neonatal Outcomes of Opioid-Dependent Mothers in Iran: A case Study of Iran

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Abstract

Background: The present research aimed to identify the maternal, fetal, and neonatal complications experienced by opioid-dependent mothers (ODMs) within the geographical context of Kerman, Iran.

Methods: This study meticulously compared the outcomes of 326 ODMs and an equal number of non-ODMs in Iran, using the data obtained from the Iranian Maternal And Neonatal (IMAN) network, a national health information system in Iran. The selection process involved a census approach, and the participants were carefully matched based on age, gestational age, and nationality. To determine the statistical relationship between opioid dependence during pregnancy and the occurrence of pregnancy and neonatal complications, the chi-square test was employed for analysis.

Findings: Women with ODMs exhibited significantly higher rates of placental abruption ($P=0.01$) and chorioamnionitis ($P=0.04$) compared to non-ODMs. Neonates born to ODMs had increased risks of adverse outcomes, including neonatal death ($P=0.05$), respiratory distress syndrome (RDS) related mortality ($P=0.01$), intrauterine growth restriction (IUGR) ($P=0.001$), neonatal intensive care unit admission ($P<0.001$), hypoglycemia ($P=0.006$), neurological complications ($P=0.004$), low birth weight (LBW) ($P<0.001$), and meconium-stained amniotic fluid ($P=0.001$). No significant differences were found in congenital anomalies, Apgar scores, or intrauterine fetal death.

Conclusion: Pregnant women with opioid dependence exhibit a heightened susceptibility to antepartum and postpartum complications compared to their non-opioid-dependent counterparts. The sequelae of these complications may be modulated by the caliber of antenatal care received. This research emphasizes the critical importance of consistent clinical management and robust support systems for this population throughout the gestational period and the puerperium.

Keywords: Pregnant mothers, Drug addiction, Neonatal complications, Maternal complications

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Introduction

The growing opioid crisis poses substantial health risks, with pregnant individuals exhibiting heightened susceptibility.¹ Opioid use disorders (OUDs) during gestation are correlated with elevated engagement in hazardous behaviors and severe health sequelae, adversely impacting both maternal and neonatal health outcomes.^{2,3} The critical need to address OUDs within this demographic is emphasized by the profound ramifications for both mothers and their newborns.²

OUDs are associated with a higher incidence of adverse pregnancy outcomes, such as spontaneous abortion, pre-eclampsia, premature rupture of membranes, fetal mortality, and placental abruption. These complications represent significant threats to maternal health and negatively impact the course of pregnancy¹. Moreover,

neonates exposed to OUDs in utero face substantial risks, including preterm birth, low birth weight (LBW), microcephaly, being small for gestational age, and an elevated susceptibility to sudden infant death syndrome (SIDS).⁴⁻⁶

Iran's geographic adjacency to Afghanistan, a primary source of opiate production, coupled with its function as a significant transit route for illicit drug trafficking, contributes to a substantial rate of narcotic consumption, notably opiates. In 2018, substance use disorders (SUDs) affected 2.8 million individuals within Iran, with women constituting 9.6% of this population.⁷ The trajectory of substance use and addiction among Iranian women demonstrates an upward trend. This is further complicated by impediments, such as societal stigmatization, limited availability of resources, and insufficient services,



which collectively impede both access to and successful completion of addiction treatment.⁸ Furthermore, the challenge of relapse within addiction treatment, influenced by a multiplicity of variables, has the potential to exacerbate the risk of human immunodeficiency virus (HIV) transmission.⁸

Recognizing the profound implications of opioid consumption during gestation is crucial. The application of validated diagnostic instruments for the identification of SUDs, coupled with focused interventions and integrated referrals to specialized healthcare, forms the bedrock of effective patient management.^{9,10} Furthermore, it is paramount to augment the accessibility of treatment modalities and advocate for policies that shield pregnant individuals with OUDs from obstacles that might impede their engagement with prenatal care.¹⁰

This research endeavors to address a current gap in the existing body of knowledge by furnishing thorough data concerning the maternal, fetal, and neonatal complications linked to opioid dependence within Kerman, Iran. By focusing on a geographical area characterized by a high prevalence of substance abuse, this study seeks to elucidate the intricate effects of OUDs on pregnant individuals and their newborns, consequently contributing significant insights to the fields of addiction studies and maternal-fetal medicine.

Materials and Methods

Study design

The current cross-sectional study aimed to evaluate and contrast the maternal and neonatal outcomes between pregnant individuals with OUDs and those without OUDs, within the geographical context of Kerman, Iran.

Subjects

The research cohort comprised 326 opioid-dependent mothers (ODMs) and 326 non-ODMs, all aged between 20 and 40 years and with a minimum gestational age of 22 weeks. Participant recruitment employed a census sampling technique, encompassing all eligible pregnant women presenting at Afzalipur hospital in Kerman throughout the period of 2017 to 2018. The control group, comprising non-ODMs, was selected from the identical source population as the ODMs. This ensured that the control group satisfied the same inclusion criteria, with the singular exception of opioid dependence. The total number of eligible non-ODMs was ascertained through an examination of hospital records spanning the duration of the study, thereby yielding a matched sample size comparable to the case group. Data pertaining to both cohorts were methodically retrieved from the Iranian Maternal And Neonatal (IMAN) network, a robust health information infrastructure established for the purpose of comprehensive data acquisition and surveillance concerning maternal and child health throughout Iran.

Within the scope of this study, IMAN functioned as a critical asset, providing access to granular information encompassing demographic profiles, prior medical conditions, and the spectrum of outcomes associated with pregnancy and neonatal well-being.

In order to mitigate potential confounding variables, individuals with pre-existing endocrine disorders, such as hypothyroidism, and autoimmune conditions, as well as those with pre-pregnancy diabetes, were excluded from the study. Furthermore, to ensure homogeneity in cultural and demographic factors, the study population was restricted to individuals holding Iranian nationality.

Statistical analysis

Statistical analyses were performed using SPSS software. For categorical variables, the association between opioid dependence and pregnancy outcomes was assessed via the Chi-square test. Statistical significance was defined as a *P* value below 0.05.

Results

This research involved the examination of 652 pregnant individuals, categorized into a case group (mean age = 30.85 years) and a control group (mean age = 29.55 years). Statistical analysis revealed no significant inter-group disparities in fundamental demographic variables, encompassing maternal age, gestational age, number of births, number of pregnancies, prior cesarean sections, and socioeconomic status.

Maternal complications in opioid-dependent mothers and non-opioid-dependent mothers groups

Concerning maternal complications, the incidence of placental abruption ($P=0.01$) and chorioamnionitis ($P=0.04$) was statistically significantly elevated in the ODMs group than in the non-ODMs group. Additionally, the case group demonstrated a higher prevalence of preterm birth, hepatitis B, cesarean sections, and pregnancy-related disorders; however, these differences did not reach statistical significance between the two

Table 1. Comparison of frequency distribution and significance level of maternal complications in opioid-dependent mothers and non-opioid-dependent mothers groups

Variable	ODMs (n=326) No. (%)	Non-ODMs (n=326) No. (%)	χ^2	<i>P</i>
Placental abruption	9 (2.8)	1 (0.3)	6.5	0.01
Preterm delivery	80 (24.5)	74 (22.7)	0.21	0.6
Hepatitis B	1 (0.3)	0 (0)	1.002	0.3
Cesarean section	194 (59.5)	181 (55.5)	1.06	0.3
Pregnancy-induced diseases	37 (11.3)	33 (10.1)	0.142	0.7
Chorioamnionitis	4 (1.2)	0 (0)	4.02	0.04

ODMs: Opioid-dependent mothers; Non-ODMs: Non-opioid-dependent mothers.

groups (Table 1).

Fetal/neonatal complications in opioid-dependent mothers and non-opioid-dependent mothers groups

Concerning fetal and neonatal morbidities, the ODMs group exhibited significantly elevated incidences of neonatal mortality ($P=0.05$), intrauterine fetal death ($P=0.9$), mortality associated with respiratory distress syndrome (RDS) ($P=0.01$), intrauterine growth restriction (IUGR) ($P=0.001$), hospitalization for respiratory complications ($P=0$), the necessity for neonatal intensive care unit (NICU) admission ($P=0.001$), hospitalization for hypoglycemia ($P=0.006$), hospitalization for neurological issues or suspected asphyxia ($P=0.004$), LBW ($P=0.001$), infant mortality within the initial 72 hours postnatal ($P=0.03$), deprivation syndrome ($P=0.001$), and meconium-stained amniotic fluid ($P=0.001$). The prevalence of apparent congenital anomalies identified at birth was higher in the offspring of the ODMs group (4.9% in the case group compared to 3.4% in the control group). Similarly, hospitalizations suspected to be related to infection were more frequent in the ODMs group (6.7% in the case group compared to 4.3% in the control group). However, these observed differences between the two groups did not reach statistical significance (Table 2).

Congenital abnormalities of newborns in opioid-dependent mothers and non-opioid-dependent mothers groups

Table 3 indicates that the incidence rates of general, neurological, cardiovascular, urinary, skeletal, and ear, nose, and throat abnormalities were elevated in neonates with ODMs compared to those with non-ODMs. However, statistical analysis revealed that the observed differences between the two groups were not statistically significant.

Five-minute Apgar scores in opioid-dependent mothers and non-opioid-dependent mothers groups

According to the data presented in Table 4, the five-minute Apgar scores were greater than 6 in a high proportion of both neonates with ODMs (96%) and those with non-ODMs (97%). However, statistical analysis indicated that the observed difference in these scores between the two groups was not statistically significant.

Discussion

This research meticulously compared maternal and neonatal outcomes between 326 ODMs and 326 non-ODMs. The findings rigorously demonstrated a significantly higher prevalence of maternal complications within the ODMs group relative to the non-ODMs group. Similarly, neonates born to ODMs exhibited a greater incidence of neonatal and fetal complications compared to the offspring of non-ODMs. Conversely, statistical analysis revealed no significant association between maternal opioid dependence and the occurrence of congenital malformations, low Apgar scores, preterm delivery, hepatitis B infection, the necessity for cesarean sections, or pregnancy-related diseases.

Prenatal exposure to opioids constitutes a salient public health issue,¹¹ given its correlation with elevated rates of neonatal mortality and morbidity, especially within the population of infants diagnosed with neonatal abstinence syndrome (NAS).^{12,13} The findings of our study reveal that neonates born to ODMs exhibit less favorable outcomes in comparison to infants born to non-ODMs. These adverse outcomes encompass a higher incidence of neonatal and intrauterine deaths, respiratory and neurological complications, IUGR, NAS, and the presence of meconium-stained amniotic fluid. These observations are consistent with existing literature that has documented comparable associations between prenatal

Table 2. Frequency distribution of fetal/neonatal complications in opioid-dependent mothers and non-opioid-dependent groups

Variable	ODMs (n=326) No. (%)	Non-ODMs (n=326) No. (%)	χ^2	P
Neonatal death	28 (8.6)	15 (4.6)	4.2	0.02
Intrauterine fetal death	7 (2.1)	2 (0.6)	2.8	0.09
Hospitalization for respiratory problems	132 (40.5)	35 (10.7)	74.3	0
RSD-associated mortality	25 (7.7)	9 (2.8)	5.7	0.01
IUGR	30 (9.2)	9 (2.8)	12	0.001
Need for NICU	172 (52.8)	93 (28.5)	52	0
Hospitalization for hypoglycemia	10 (3.1)	1 (0.3)	7.4	0.006
Hospitalization for neurological problems/suspected asphyxia	17 (5.2)	3 (0.9)	8.3	0.004
LBW	114 (35.0)	67 (20.6)	20	0
Infant mortality during the first three days of birth	11 (3.4)	7 (2.1)	4.6	0.03
Deprivation syndrome	145 (44.5)	0 (0)	184	0
Meconial amniotic fluid	14 (4.3)	2 (0.6)	10.2	0.001

ODMs: Opioid-dependent mothers; Non-ODMs: Non-opioid-dependent mothers; RSD: Respiratory distress syndrome; IUGR: Intrauterine growth restriction; NICU: Neonatal intensive care unit; LBW: Low birth weight

Table 3. Frequency distribution of abnormalities in opioid-dependent mothers and non-opioid-dependent groups

	Addicted		Non-Addicted	
	No.	%	No.	%
Congenital disorder	16	4.9	11	3.4
Central nervous system disorders	3	0.9	0	0.0
Cardiovascular disorders	9	2.8	5	1.5
Abnormal respirations	0	0/0	0	0.0
Gastrointestinal disorder	1	0.3	5	1.5
Skeletal and muscular disorders	3	0.9	1	0.3
Congenital urogenital anomalies	3	0.9	1	0.3

opioid exposure and adverse neonatal sequelae.^{11,13,14}

This research reinforces the outcomes of earlier scholarly work¹⁵⁻¹⁷ that explored the relationship between LBW and ODMs. Aligning with preceding research,^{18,19} our findings demonstrated a greater incidence of IUGR within the ODMs group compared to the non-ODMs group. Notably, one study¹⁴ reported that ODMs exhibited significantly lower body mass indices (BMIs) than non-smoking mothers and non-ODMs, suggesting that maternal BMI, rather than opioid use, nicotine use, or the infant’s sex, constituted a key factor influencing IUGR in pregnancies involving ODMs. Considering the heightened susceptibility of infants born to ODMs to both LBW and IUGR, it is recommended that ODMs undergo consistent prenatal screening and healthcare management.

Contrary to extant literature that has established a statistically significant association between maternal opioid use and an elevated risk of preterm birth, our study revealed no significant disparity in the incidence of preterm delivery when comparing ODMs and non-ODMs (24.5% versus 22.7%, respectively; $P > 0.05$).^{15,20,21} A study conducted in California indicated a statistically elevated risk of very preterm birth (gestational age < 32 weeks) among opioid users (2.9%) in comparison to non-users (0.8%). Conversely, the same study revealed a decreased likelihood of term birth (gestational age 39-42 weeks) in opioid users (49.6%) relative to non-users (66.1%).²¹ In contrast, a separate study, which primarily focused on the use of opioid analgesics, such as acetaminophen in combination with oxycodone, codeine, or hydrocodone, did not identify a statistically significant correlation between opioid use and the incidence of preterm birth.²¹ One potential explanation for the lack of significant findings in our study pertains to disparities in healthcare access and quality between neonates with ODMs and non-ODMs. These differences may have mitigated the detrimental impact of opioid exposure on preterm birth.

Reports regarding the teratogenic potential of opioids in newborns born to ODMs have yielded inconsistent findings. While some studies have suggested an elevated risk of congenital anomalies in these infants,²² others

Table 4. Frequency distribution of five-minute Apgar scores in opioid-dependent mothers and non-opioid-dependent groups

Apgar score	Addicted		Non-Addicted	
	No.	%	No.	%
< 4	7	2.1	6	1.8
4-6	7	2.1	4	1.2
6 <	312	96	316	97

have not corroborated this association. For instance, a systematic review encompassing 30 studies indicated that 17 of them identified a statistically significant correlation between prenatal opioid exposure and the occurrence of at least one congenital malformation.¹ In 10 case studies, the most frequently observed congenital anomalies were orofacial clefts and ventricular septal defects. Conversely, clubfoot was a common finding in seven cohort studies. The present investigation revealed a higher incidence of congenital abnormalities affecting the birth process, neurological, cardiovascular, urinary, and skeletal systems, as well as the ear, nose, and throat, in the case group compared to the control group. However, these observed differences did not reach statistical significance.

A significant impediment to effectively managing the health concerns of ODMs and their newborns is the limited accessibility of sufficient prenatal and postnatal healthcare services. Research findings suggest that, in comparison to non-ODMs, ODMs exhibit a lower propensity for receiving standard medical attention throughout pregnancy, thereby elevating the potential for both maternal and neonatal adverse outcomes.¹⁹ Furthermore, ODMs face significant barriers in accessing medication-assisted treatment (MAT), such as methadone or buprenorphine. This pharmacological intervention is crucial as it can effectively reduce the severity of NAS, a condition that affects newborns exposed to opioids in utero.¹⁹ Beyond the administration of MAT, ODMs necessitate comprehensive postpartum care. Such care should include dedicated substance use treatment programs, strategies for relapse prevention, and resources aimed at enhancing parenting skills. Evidence-based interventions with the potential to improve outcomes for ODMs and their neonates encompass strategies such as screening protocols, referral mechanisms, psychoeducation, supportive guidance, the promotion of breastfeeding, and the utilization of the ‘eat, sleep, console’ assessment tool. Nevertheless, the effective implementation of these interventions is frequently compromised by the societal and healthcare-related stigma and discrimination experienced by ODMs.

Limitations

This study presents several limitations that necessitate careful interpretation of its findings from an academic standpoint. Firstly, the participant selection, based

on a census approach, potentially compromises the external validity or generalizability of the results to broader populations or diverse settings. Employing a random sampling methodology could have yielded a more representative sample, thereby reducing potential selection bias. Secondly, the reliance on IMAN, a national health information system, as the primary data source introduces a potential for inaccuracies or incomplete documentation concerning opioid use and its associated outcomes. Acquiring data through direct interviews or assessments conducted with mothers and their infants might have yielded more dependable results. Thirdly, the study omitted information regarding the specific type, dosage, duration, and frequency of opioid use among ODMs, factors that could exert differential impacts on maternal, fetal, and neonatal outcomes. A more granular characterization of opioid exposure could have facilitated a better understanding of the dose-response relationship and potential confounding variables. Furthermore, the study's limitations include the absence of data regarding the co-consumption of other narcotics with opioids, smoking habits, maternal BMI, the frequency of prenatal care visits, and the results of mothers' prenatal tests, all of which represent potential confounders.

Conclusion

The findings reveal that ODMs exhibit elevated incidences of maternal, neonatal, and fetal complications in contrast to non-ODMs. Nevertheless, statistical significance was not observed across all associations, potentially attributable to variations in access to and quality of healthcare services between the two groups. This study emphasizes the necessity of consistent prenatal screening and care for ODMs, alongside thorough postpartum support encompassing substance use treatment and parenting guidance. Furthermore, it advocates for continued investigation into methods for mitigating stigma and elucidating the potential teratogenic consequences of opioids, as well as other variables impacting ODMs.

Authors' Contribution

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Competing Interests

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