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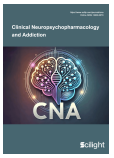

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Substance Use during Pregnancy: A Retrospective Multicenter Clinical Report from Four Italian Centers

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Abstract: Background: Rising substance use during pregnancy is a major global health concern associated with adverse maternal and neonatal outcomes. Despite growing international literature, Italian real-world multicenter data remain limited. Methods: We conducted a retrospective descriptive analysis of 31 women who reported substance use during a current or previous pregnancy across four Italian clinical centers using data collected between January 2024 and October 2025. Each participant contributed one index pregnancy to the maternal and neonatal outcome analysis. The 54 pregnancies recorded for the overall cohort represented cumulative obstetric history and were not treated as independent observations. Collected variables included type of substance, maintenance therapy, psychiatric diagnosis, infectious serology, neonatal outcomes, obstetric history, and partner relationship quality. Results: Opioid use (alone or in combination) was present in 77.4% of participants, cocaine/crack in 54.8%, and cannabis in 22.6%. Polysubstance use was common. Prematurity occurred in 13 of 31 index pregnancies (41.9%), and neonatal abstinence syndrome was documented in 10 of 31 index pregnancies (32.3%), all of which were opioid-exposed. Human immunodeficiency virus (HIV) positivity was

present in 29.0% of participants and Hepatitis C Virus in 16.1%, exclusively among opioid-exposed women. Conflictual or unstable partner relationships were reported in 45.2% of participants. Conclusions: In this small, selected Italian multicenter clinical sample, substance use during pregnancy was heterogeneous and frequently associated with medical, psychiatric, and psychosocial vulnerability. Opioid exposure predominated, and all cases of neonatal abstinence syndrome occurred among opioid-exposed index pregnancies, while cocaine/crack and cannabis use were also frequently documented. Given the descriptive design and small sample size, these findings should not be interpreted as population-level prevalence estimates or as evidence of causal relationships between individual substances and pregnancy outcomes.

Keywords: substance use disorder; pregnancy; opioids; cocaine; neonatal abstinence syndrome; prematurity; multidisciplinary care; Italy

1. Introduction

Substance use during pregnancy represents a major public health concern with significant implications for maternal and neonatal health [1,2]. In Italy, epidemiological data on substance use during pregnancy remain limited, though available studies suggest that approximately 0.4% of pregnant women report illicit drug use, with cannabis being the most used substance [3,4]. More broadly, approximately 73% of Italian pregnant women receive at least one medication prescription during pregnancy, though data specifically addressing opioid and stimulant use disorders are scarce [5].

European data from Ireland demonstrate that substance use in pregnancy affects approximately 1 in 160 women, with recent trends showing a reduction in opioid substitute therapy but increasing cocaine and cannabis use [6]. In Belgium, preconception prevalence of illicit drug use was 4.2%, dropping to 0.6% in the first trimester after pregnancy recognition [7]. In the United States, approximately 8% of pregnant individuals report recent illicit drug use, with the prevalence of opioid use disorder at delivery increasing more than fourfold between 1999 and 2014, from 1.5 to 6.5 cases per 1000 delivery hospitalizations [8,9]. Globally, the opioid epidemic has significantly impacted women of reproductive age, with data suggesting that 20% of women filled at least one prescription for an opioid during pregnancy and that overdose has become a leading cause of death in postpartum women in some countries [10]. These international trends underscore the urgent need for Italian-specific data to inform clinical practice and policy development.

Opioid exposure during pregnancy is associated with substantial maternal and neonatal morbidity and increased healthcare expenditure [11]. Neonatal abstinence syndrome (NAS) occurs in 52–69% of infants exposed to opioids in utero [12], with complications including preterm birth, low birth weight, small for gestational age infants, and placental complications including abruption [12–15]. Maternal risks, particularly among individuals who inject drugs, include increased susceptibility to infectious diseases such as human immunodeficiency virus (HIV) and hepatitis C virus (HCV), and elevated rates of severe maternal morbidity and mortality [8,16].

Cocaine and stimulant use during pregnancy have been linked to adverse obstetric outcomes, with meta-analyses demonstrating significantly elevated odds of preterm birth, low birth weight, and small for gestational age infants [17]. The mechanisms underlying these complications include placental vasoconstriction, impaired nutrient transfer, and increased risk of placental abruption [17–19]. Globally, cocaine use has increased, with an estimated 18.2 million users worldwide, and women of childbearing age represent a particularly vulnerable population [18].

Cannabis use during pregnancy has also risen substantially, partly due to changing legal frameworks and evolving social perceptions [20,21]. While the teratogenic potential of cannabis remains uncertain, emerging evidence suggests associations with neurodevelopmental outcomes in exposed children [22]. Recent meta-analyses indicate a modest but statistically significant increased risk of attention-deficit/hyperactivity disorder (ADHD) in offspring, as well as increased likelihood of offspring cannabis use [23]. Studies have also reported associations with autism spectrum disorder, psychotic-like experiences, and cognitive impairments, though findings remain heterogeneous and effect sizes are generally small [23–26].

Importantly, substance use during pregnancy occurs within a complex psychosocial context. Pregnant individuals with substance use disorders (SUDs) experience significantly higher rates of psychiatric comorbidities, including depression, anxiety, and post-traumatic stress disorder [27–30]. Pregnant individuals with SUDs may also experience adverse childhood experiences, intimate partner violence, socioeconomic instability, food

insecurity, and limited social support [27,28,31]. Polysubstance use is common, with nearly one in five pregnant individuals who use substances reporting use of multiple substances [32,33]. These overlapping vulnerabilities underscore the need for integrated, multidisciplinary care models that address both SUDs and co-occurring psychosocial risk factors [15,34,35].

Despite growing international literature on this topic, real-world multicenter data from Italy remain limited. The present report aims to provide a descriptive overview of clinical and psychosocial characteristics of 31 women who reported substance use during pregnancy and were assessed across four Italian clinical centers. Each participant contributed one index pregnancy to the analysis of maternal and neonatal outcomes, whereas the 54 pregnancies reported for the overall cohort represent cumulative obstetric history and were not treated as independent observations. The study is intended to contribute to the understanding of this complex clinical population within the Italian healthcare context.

2. Methods

2.1. Study Design and Setting

This retrospective descriptive report includes women assessed in SS. Annunziata Hospital (Chieti, Italy), Torrette Hospital (Ancona, Italy), the Addiction Unit (Servizio per le Dipendenze, SerD), ASL Roma1 (Rome, Italy), and Gemelli Hospital (Rome, Italy). The study was conducted using clinical data collected between January 2024 and October 2025.

2.2. Ethics Statement

This study was based on a retrospective analysis of anonymized clinical records collected during routine clinical care. Each participating center extracted and anonymized the relevant data before sharing them with the investigators. According to the institutional regulations of the participating centers, formal ethics committee approval was not required.

2.3. Informed Consent Statement

Individual informed consent was waived because only anonymized data extracted from routine clinical records were used for the purposes of this retrospective study, in accordance with institutional regulations.

2.4. Participants

Eligible participants were women who reported substance use during a current or previous pregnancy during routine clinical evaluation. Substance use was identified from the information documented in the clinical records, including patient-reported substance use recorded during routine care. Consecutive cases meeting inclusion criteria during the study period were included. The primary unit of analysis was the individual participant. Each of the 31 participants contributed data from one index pregnancy for the analysis of maternal and neonatal outcomes. The total of 54 pregnancies represented the cumulative number of pregnancies reported in the obstetric histories of the 31 participants and was not treated as independent observations. No formal exclusion criteria were applied.

2.5. Data Collection

Data were extracted retrospectively from clinical records using a standardized data collection form. Variables collected included:

- Type of substance used (opioids, cocaine/crack, cannabis, alcohol, amphetamines)
- Presence of polysubstance use
- Maintenance therapy (e.g., methadone)
- Other pharmacological therapies
- Psychiatric diagnoses documented in the clinical records following clinical assessment based on DSM-5 criteria
- Education level
- Infectious disease status (HIV, HCV serology)
- Preterm birth status (yes/no; defined as delivery at <37 weeks)
- Neonatal outcomes, including a documented clinical diagnosis of neonatal abstinence syndrome (NAS)
- Breastfeeding
- Total number of pregnancies reported in the participant's obstetric history

- Relational context, including presence of conflictual or unstable partner relationship

Unless otherwise specified, all maternal, obstetric, and neonatal outcomes—including prematurity, fetal growth restriction, major malformations, neonatal abstinence syndrome, and breastfeeding—referred to the participant's index pregnancy.

2.6. Definitions

Prematurity was defined as delivery before 37 completed weeks of gestation. NAS was defined according to the clinical diagnosis recorded in the neonatal clinical record. Polysubstance use was defined as the use of ≥2 substances, including alcohol but excluding tobacco.

A conflictual or unstable partner relationship was identified when the clinical record documented recurrent partner conflict, relational instability, inadequate practical or emotional support during pregnancy, intimate partner violence, and/or involvement of social services because of relationship-related concerns. Because this variable was derived retrospectively from clinical documentation rather than from a standardized, validated instrument, it was treated as a descriptive clinical variable.

The index pregnancy was defined as the pregnancy for which the most complete substance-exposure, maternal, obstetric, and neonatal information was available in the clinical record. Each participant contributed only one index pregnancy to the principal outcome analyses.

2.7. Statistical Analysis

The analysis was descriptive. Continuous variables are presented as means and standard deviations, where appropriate, and categorical variables as frequencies and percentages. Percentages relating to participant characteristics were calculated using the 31 participants as the denominator. All maternal, obstetric, and neonatal outcomes were calculated using the 31 index pregnancies as the denominator. Subgroup percentages were calculated using the corresponding subgroup as the denominator. The cumulative total of 54 pregnancies was used only to describe the participants' overall obstetric history and was not treated as a set of independent observations. No inferential statistical testing was performed due to the small sample size and exploratory nature of the study.

3. Results

3.1. Descriptive Statistics

The sample included 31 women who contributed one index pregnancy each to the maternal, obstetric, and neonatal outcome analyses. A total of 54 pregnancies were reported in the obstetric histories (1 pregnancy: 14 women, 45.2%; 2 pregnancies: 11 women, 35.5%; 3 pregnancies: 6 women, 19.4%). The 54 pregnancies were not treated as independent observations. Detailed clinical and substance-use characteristics are reported in Table 1. A graphical summary of the principal substance exposures and clinical outcomes is presented in Figure 1.

3.2. Substance Use and Maintenance Therapy during Pregnancy

Opioid use (alone or in combination) was present in 24 of 31 participants (77.4%). Among opioid-exposed women, 16 (66.7%) received opioid agonist maintenance therapy, including 12 on methadone (75%) and 4 on levomethadone (25%), with dosing and duration varying across participants. Cocaine/crack use was documented in 17 women (54.8%), while cannabis exposure was observed in 7 women (22.6%). Polysubstance use was common, affecting 22 women (71.0%), including alcohol but excluding tobacco. The most frequent patterns included opioids with cocaine/amphetamines (9 women, 29.0%), opioids with alcohol (4 women, 12.9%), and more complex combinations such as opioids, cocaine, and alcohol or amphetamines (6 women, 19.4%). Cannabis was co-used with other substances in 3 women (9.7%). A smaller proportion of women had opioid dependence in remission (4 women, 12.9%), while 3 women (9.7%) had no active psychiatric diagnosis documented in their clinical records.

3.3. HIV and HCV Seropositivity among Opioid-Exposed Women

HIV positivity was present in 9 of 31 women (29.0%) and HCV positivity in 5 of 31 women (16.1%). All participants with HIV or HCV positivity were among the 24 opioid-exposed women.

3.4. Index Pregnancy Outcomes and Breastfeeding

Premature delivery occurred in 13 of 31 index pregnancies (41.9%). Fetal growth restriction or underdevelopment was documented in 7 of 31 index pregnancies (22.6%), and major malformations were reported in 3 of 31 index pregnancies (9.7%). NAS was observed in 10 of 31 index pregnancies (32.3%). All 10 cases occurred among opioid-exposed index pregnancies. Breastfeeding following the index pregnancy was reported in 13 of 31 women (41.9%).

3.5. Quality of Partner Relationships

Partner relationships varied across the sample. Conflictual or unstable relationships were reported in 14 of 31 women (45.2%), including 12 of the 24 women with opioid use (50.0%). Among the 6 women using alcohol, 5 (83.3%) reported conflictual or unstable relationships. These relationships were characterized by documented partner conflict, relational instability, or lack of support during pregnancy; in some cases, they were associated with intimate partner violence or involvement of social services. Satisfactory relationships were reported in 9 women (29.0%), and good relationships in 8 women (25.8%), mostly among non-opioid and non-alcohol users. Because relationship quality was derived retrospectively from clinical documentation rather than from a standardized instrument, these findings are presented descriptively.

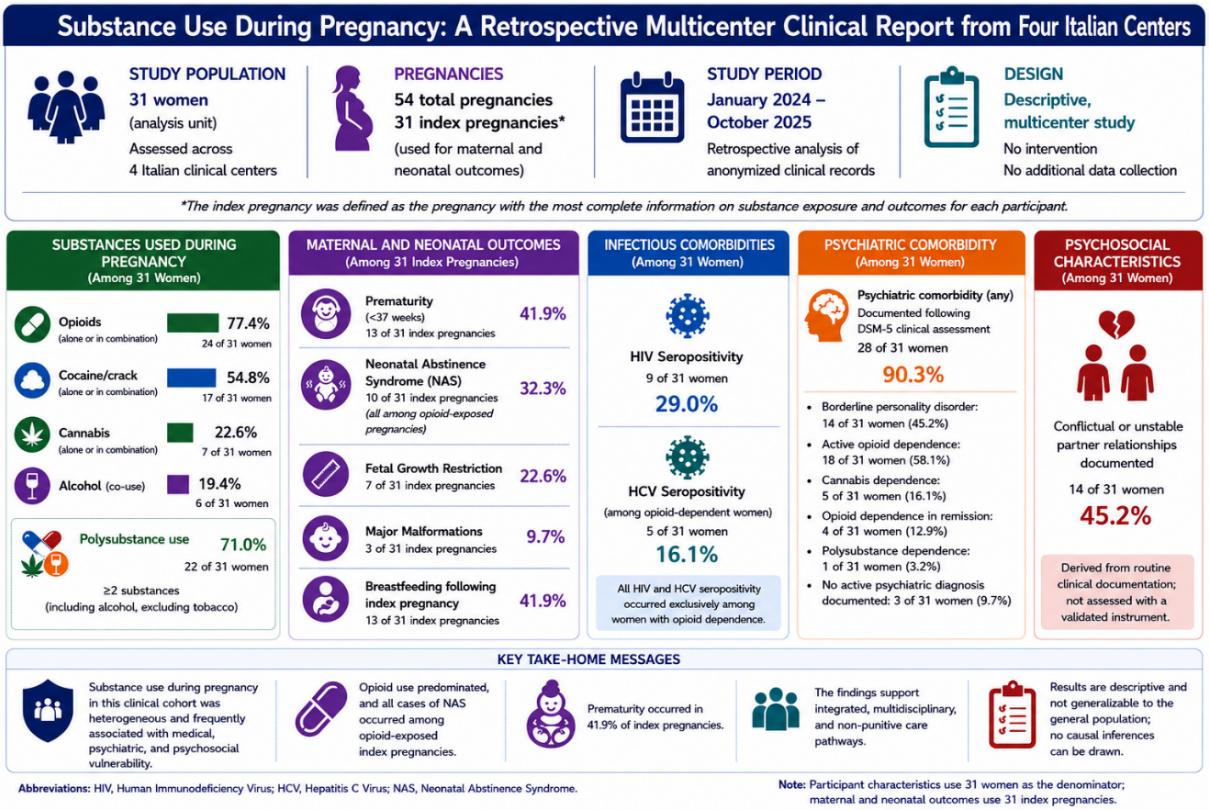

Figure 1. Summary of the principal substance exposures and maternal, neonatal, infectious, psychiatric, and psychosocial characteristics of the study cohort. The figure provides a graphical overview of the principal findings among 31 women with substance use during pregnancy assessed across four Italian clinical centers. It summarizes the most frequently reported substances used during pregnancy together with the principal maternal, neonatal, infectious, psychiatric, and psychosocial characteristics observed in the cohort, including prematurity, neonatal abstinence syndrome (NAS), HIV and hepatitis C virus (HCV) seropositivity, documented psychiatric comorbidity and diagnostic categories, and conflictual or unstable partner relationships. Maternal and neonatal outcomes refer to the 31 index pregnancies (one per participant), whereas participant characteristics refer to the 31 women included in the study. The 54 pregnancies reported in participants' obstetric histories represent cumulative obstetric history and were not analyzed as independent observations. Given the descriptive study design, small sample size, and frequent polysubstance use, the figure is intended to summarize the cohort characteristics and should not be interpreted as indicating causal relationships or population-level prevalence estimates. Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus; NAS, neonatal abstinence syndrome.

Table 1. Clinical, psychiatric, psychosocial, and obstetric characteristics of the study sample. Participant-level variables use 31 women as the denominator. Maternal and neonatal outcomes refer to the 31 index pregnancies, one per participant. The 54 pregnancies represent cumulative obstetric history and were not treated as independent observations. Subgroup-specific denominators are reported where applicable.

Variable	n	%/Mean (SD)	Notes
Participants	31	100%	Each participant contributed one index pregnancy to the outcome analyses
Maternal age (yrs)	–	33.9 ± 6.7	Range: 27–52
Number of pregnancies	54	–	1 pregnancy: 14 women (45.2%) 2 pregnancies: 11 women (35.5%) 3 pregnancies: 6 women (19.4%) These were not treated as independent observations
Substance use			
Opioids (alone or combined)	24	77.4%	16/24 (66.7%) received opioid agonist maintenance therapy (methadone 12, levomethadone 4) 8/24 (33.3%) did not
Cocaine/crack	17	54.8%	–
Cannabis	7	22.6%	–
Alcohol (co-use)	6	19.4%	–
Polysubstance use (≥2 substances)	22	71.0%	9 opioids + cocaine/amphetamines (29.0%); 4 opioids + alcohol (12.9%); 3 opioids + cocaine + alcohol (9.7%); 3 opioids + cocaine + amphetamines (9.7%); 3 cannabis co-used with opioids or other substances (9.7%).
Opioid agonist maintenance therapy	16	66.7% of opioid-exposed (24)	12 methadone (75%) 4 levomethadone (25%)
Psychiatric comorbidity (any)	28	90.3%	Based on diagnoses documented following clinical assessment
Borderline personality disorder	14	45.2%	–
Active opioid dependence	18	58.1%	–
Cannabis dependence	5	16.1%	–
Polysubstance dependence	1	3.2%	–
HIV positive	9	29.0%	Exclusively opioid-exposed women
HCV positive	5	16.1%	Exclusively opioid-exposed women
Premature delivery, index pregnancy	13	41.9%	Delivery before 37 completed weeks
Neonatal abstinence syndrome (NAS)	10	32.3%	All among opioid-exposed index pregnancies
Fetal growth restriction	7	22.6%	–
Major malformations	3	9.7%	
Conflictual/unstable partner relationship	14	45.2%	14 Conflictual/unstable; 9 Satisfactory; 8 Good
Breastfeeding following index pregnancy	13	41.9%	–
Education: High	8	25.8%	–
Education: Medium-high	12	38.7%	–
Education: Medium-low	11	35.5%	–

4. Discussion

In this selected multicenter clinical sample, opioid exposure was the most frequently documented substance-related condition during pregnancy. However, because participants were recruited from tertiary clinical and addiction-treatment settings, the observed proportions should not be interpreted as prevalence estimates for pregnant women in Italy. The observed proportion of NAS was within the range previously reported among opioid-exposed infants [11,12,36,37]. Cocaine/crack use was also frequently documented, likely reflecting the specialized clinical settings rather than patterns in the general population. Prenatal cocaine exposure has been associated with preterm birth, impaired fetal growth, and placental complications [17,18,38]. The known mechanisms underlying these complications include placental vasoconstriction, impaired nutrient transfer, and increased risk of placental abruption [17–19,38]. Prematurity was documented in 13 of the 31 index pregnancies (41.9%). However, because of the descriptive design, frequent polysubstance use, absence of an unexposed comparison group, and small sample size, prematurity and the other obstetric outcomes observed in this study cannot be attributed specifically to cocaine or stimulant exposure.

The frequent polysubstance use observed in this cohort is consistent with previous evidence from pregnant individuals with opioid use disorder [32,33,39,40]. Polysubstance use may increase clinical complexity and make it difficult to attribute maternal and neonatal outcomes to individual substances [33,39,40]. Nevertheless, the present descriptive study was not designed to compare outcomes between single-substance and polysubstance exposure groups.

Cannabis exposure represents a growing concern as its use during pregnancy increases in some settings, partly because of changing legal frameworks and evolving social perceptions [20,21]. While the teratogenic potential of cannabis remains uncertain, emerging evidence suggests associations with neurodevelopmental outcomes in exposed children, including modest but statistically significant increased risk of attention-deficit/hyperactivity disorder and offspring cannabis use [23–26]. However, findings remain heterogeneous, and effect sizes are generally small, making it difficult to disentangle the effects of cannabis from those of other substance exposures and co-occurring risk factors [22,23,26]. Because cannabis was also used in combination with other substances in this cohort, no independent association between cannabis exposure and the observed neonatal outcomes can be inferred.

Infectious comorbidities were frequent in this selected clinical cohort. However, the route of opioid administration was not systematically available; therefore, the presence of HIV and HCV among women with opioid exposure cannot be interpreted as evidence of a specific transmission pathway. These findings nevertheless reinforce the importance of screening for blood-borne infections and linkage to appropriate treatment during pregnancy and postpartum [8,41,42].

Conflictual or unstable partner relationships were frequently documented, supporting the importance of assessing relational and psychosocial vulnerability alongside substance use. Previous research has linked SUDs during pregnancy with psychiatric comorbidity, intimate partner violence, socioeconomic instability, and inadequate social support [27–31]. Adverse childhood experiences and other psychosocial vulnerabilities have also been frequently documented in populations affected by prenatal substance use [27,28,43]. However, relationship quality in this study was derived from routine clinical documentation rather than a standardized instrument, and should therefore be interpreted cautiously.

4.1. Implications for the Italian Health System (Sistema Sanitario Nazionale, SSN)

In the Italian healthcare context, the clinical complexity observed in this cohort supports integrated pathways connecting obstetric services, SerD, psychiatric care, infectious disease units, neonatal and pediatric services, and social support. Although the present study did not evaluate healthcare pathways directly, standardized regional coordination between hospital-based and territorial services may improve continuity from pregnancy through the postpartum period [15,35]. Care should be family-centered and non-punitive, while maintaining appropriate safeguarding procedures. Staff training, clearly defined referral pathways, and access to psychosocial and intimate partner violence services may support earlier identification and more consistent care.

4.2. Multidisciplinary Care Implementation and Strategic Roadmap for Perinatal Substance Use in Italy: An Ambitious but Feasible Frontier

Integrated pathways should coordinate obstetric, addiction, psychiatric, infectious disease, neonatal, and social care, with continuity from pregnancy through the postpartum period [15,35]. Appropriate infrastructure should connect addiction treatment with obstetric, maternal–fetal, neonatal, pediatric, and social care, while ensuring continuity throughout pregnancy and the postpartum period [15,34,35].

Care should be coordinated, family-centered, and non-punitive, while maintaining appropriate safeguarding procedures when maternal or infant safety concerns are identified [35,44,45]. Staff training and clearly defined referral pathways may support earlier identification and more consistent coordination across services [15,34,35]. Follow-up should include medical, developmental, and psychosocial support for both mother and infant, together with specific pathways for intimate partner violence screening and referral to dedicated anti-violence services [1,35,46].

4.3. Outstanding Knowledge Gaps and Future Directions for Perinatal Substance Use Care in Italy

Significant knowledge gaps remain that require systematic investigation. Epidemiological research should characterize the prevalence, patterns, and trends of SUDs during pregnancy in Italy. National surveillance and multicenter epidemiological studies covering both urban and rural settings are needed to guide service planning and resource allocation.

Evaluation of SerD programs for pregnant and postpartum women should assess accessibility, treatment retention, integration with obstetric and neonatal services, and outcomes for mothers and infants. Prospective

studies should use standardized assessments of substance type, dose, frequency, timing, route of administration, psychiatric comorbidity, psychosocial vulnerability, and maternal and neonatal outcomes. Such studies should also identify sustainable staffing and infrastructure requirements while protecting patient autonomy [15].

Longitudinal investigation of exposed children remains important because prenatal substance exposure may be associated with developmental, behavioral, and neuropsychological difficulties over time [47–51]. Collaboration among Italian centers and participation in European research networks could support standardized data collection, comparison of different care models, and development of evidence-based, treatment-focused, and non-punitive policies.

4.4. Limitations

Limitations of this study include the retrospective design, small sample size, descriptive nature without inferential statistical testing, and potential selection bias inherent in tertiary center populations. Consequently, the proportions observed in this cohort should not be generalized to pregnant women using substances in Italy. Substance-use information was obtained from clinical records, including patient self-report, and was not systematically confirmed using standardized toxicological testing. Exposure may therefore have been underestimated or misclassified because of recall difficulties, stigma, fear of legal or social consequences, and variability in clinical documentation. Information regarding substance dose, frequency, timing, route of administration, and changes in exposure during pregnancy was also not consistently available.

The high frequency of polysubstance use and the absence of an unexposed comparison group prevented attribution of maternal or neonatal outcomes to individual substances. Psychiatric diagnoses and partner relationship quality were derived from routine clinical documentation rather than from standardized research assessments. In particular, relationship quality was not evaluated using a validated instrument.

Additionally, the study did not capture longitudinal outcomes for mothers and infants, limiting conclusions about the effectiveness of interventions and longer-term maternal and child outcomes. Future prospective studies with larger, more diverse samples, standardized exposure assessments, appropriate comparison groups, and standardized outcome measures are encouraged to further characterize this population and evaluate the effectiveness of integrated care models in the Italian healthcare context.

5. Conclusions

In this selected Italian multicenter cohort, substance use during pregnancy was frequently accompanied by medical, psychiatric, infectious, and psychosocial vulnerability. Opioid and polysubstance use predominated, and all documented cases of NAS occurred among opioid-exposed index pregnancies. However, the small sample, retrospective design, overlapping exposures, and absence of a comparison group preclude causal or population-level conclusions. The findings support coordinated, multidisciplinary, and non-punitive care pathways linking obstetric, addiction, psychiatric, infectious disease, neonatal, and social services. Larger prospective studies using standardized exposure and outcome assessments are needed to characterize this population and evaluate integrated care models in Italy.

Author Contributions

A.I.: methodology, formal analysis, data curation, visualization, writing—original draft preparation, writing—review and editing; F.D.C.: methodology, investigation, data curation, writing—review and editing; V.M.: conceptualization, methodology, supervision, funding acquisition, writing—review and editing; C.D.A.: conceptualization, supervision, funding acquisition, writing—review and editing; A.D.C.: investigation, data curation, writing—review and editing; R.M.: investigation, data curation, writing—review and editing; G.M. (Giulio Marasca): investigation, data curation, writing—review and editing; G.F.: investigation, data curation, writing—review and editing; R.V.: investigation, data curation, writing—review and editing; L.M.: investigation, data curation, writing—review and editing; U.V.: investigation, resources, supervision, writing—review and editing; M.P.: conceptualization, supervision, writing—review and editing; G.M. (Giovanni Martinotti): conceptualization, methodology, supervision, project administration, funding acquisition, writing—review and editing. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

This study was based on a retrospective analysis of anonymized clinical records collected during routine clinical care. Each participating center extracted and anonymized the relevant data before sharing them with the investigators. According to the institutional regulations of the participating centers, formal ethics committee approval was not required.

Informed Consent Statement

Individual informed consent was waived because this retrospective study used only anonymized data extracted from clinical records collected during routine care, in accordance with the institutional regulations of the participating centers.

Data Availability Statement

The datasets generated and/or analyzed during the current study are not publicly available due to the sensitive nature of the clinical data and the risk of participant identification, but de-identified data may be made available from the corresponding author upon reasonable request and subject to approval by the relevant ethics committees.

Conflicts of Interest

The authors declare no conflict of interest. Given the role as Editor-in-Chief, Giovanni Martinotti had no involvement in the peer review of this paper and had no access to information regarding its peer-review process. Full responsibility for the editorial process of this paper was delegated to another editor of the journal.

Use of AI and AI-Assisted Technologies

During the preparation of this work, the authors used OpenAI's ChatGPT (GPT-5.6 Sol) for language checking and to improve clarity and readability. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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