



BORN WITH ADDICTION TO ILLEGAL DRUGS – RISK FACTORS FOR NEONATAL MORBIDITY AND MORTALITY

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The perinatal period can be marked by risks, defined as the probability of dangerous situations, more or less predictable, with an impact on maternal, fetal, or neonatal morbidity and mortality. Drug addiction, and especially the use of illicit drugs by injection is an important risk factor for the perinatal period. The effects of drug use in pregnancy are multiple and severe.

Material and Method: The retrospective study in INSMC - “Polizu” Hospital includes newborns during 2002-2020, from mothers consuming illicit drugs during pregnancy. Anamnestic-clinical, paraclinical, toxicological data (urine samples collected after birth from the mother and the newborn) and the case presentation of a newborn from pregnancy marked by polydrug use were used. The data were processed statistically.

Results: The incidence of newborns from addicted mothers is low, but has gradually increased over time. Morbidity was marked in descending order of withdrawal syndrome, the infectious risk for possible congenital and/or perinatal infections (syphilis, hepatitis B, hepatitis C, HIV), low birth weight (≤ 2500 g), prematurity.

Conclusions: The association of illicit drug use with prematurity, low birth weight, are risk factors for neonatal morbidity and mortality.

Keywords: drug addiction, withdrawal, infections, prematurity, low birth weight.

INTRODUCTION

The perinatal period can be marked by risks, defined as the probability of dangerous situations, more or less predictable, with an impact on *maternal, fetal, or neonatal* morbidity and mortality¹.

Risk factors may act with different intensities, alone or in combination, and may have different effects depending on when they occur, the characteristics of the individual on whom they act.

Illicit drugs, depending on the main effects produced on the brain, for which they are consumed, can be classified into²: *narcotics* (heroin, hydro-morphone, methadone, morphine, opium, oxycodone), *stimulants* (amphetamines, methamphetamines, cocaine, khat), *depressants* (barbiturates, benzodiazepines, GHB, Rohypnol), *hallucinogens*

(ecstasy/MDMA, K2/spice, ketamine, LSD, peyote, mescaline, psilocybin, marijuana/cannabis, steroids, inhalants), *risky* drugs (DXM, sage

Divinorum). Volatile inhalants (nitrogen monoxide, ether, chloroform, solvents, isobutyl nitrite, paint spray, glue, cleaning fluids, thinners, toluene) alter perception (cerebral hypoxia).

Natural products (cannabis, etc.), semi-synthetic (heroin, etc.) or synthetic (ecstasy, LSD, etc.), illicit drugs have unpredictable effects, depending on multiple individual factors, especially when consumed the first time, even in small doses.

Abuse, addiction (mental and physical dependence), in addition to the associated infectious diseases, are common in illicit drug users.

Drug addiction, and especially the use of illicit drugs by injection, is usually associated with opiate use (although in some countries amphetamine injection is a major problem)³ affecting approxi-

mately 1.3–1.7 million people in the European Union and Norway⁴ of 34% of whom are women, mostly of childbearing age⁵, is an important risk factor for the perinatal period.

The effects of drug use during pregnancy are multiple and severe (due to their affinity for central nervous system proteins and their late elimination due to fetal enzymatic immaturity⁶), the most common being:

- intrauterine fetal death^{7,8};
- hasty birth and necessary high doses for pain therapy at birth⁹;
- *retroplacental hematoma*, vascular lesions by ischemia, and implicitly diminished oxygenation^{10,11};
- *intrauterine growth restriction* (by the direct action of the drug on the uteroplacental vascularization but also by the mother's malnutrition, being more frequent in case of cocaine and heroin consumption, than in case of methadone treatment)^{6,8-11};
- *prematurity*⁹⁻¹¹;
- *hematogenous or sexually transmitted infections*: HIV (30% seropositive cases)⁹, hepatitis B and hepatitis C (80% seropositive tests)¹², syphilis, tuberculosis^{3,9,10,12-15};
- *congenital malformations* (genito-urinary, digestive, and limb, especially in case of cocaine use, being apparently secondary to vascular spasms that occurred during embryogenesis)^{8,14};
- *impregnation syndrome* (newborn "asleep" showing from birth for 2–3 days hypotonia, hypothermia, apnea, or shallow breathing that requires artificial ventilation in conditions of accelerated lung maturation in fetuses of heroin-addicted mothers^{8,15} until the elimination of the drug⁶;
- *the newborn's withdrawal syndrome* (in a state of innate dependence on the drug used by his mother during pregnancy) with onset from a few hours to 10⁶ even 15–21 days (methadone which is stored by the fetus in the lung, liver, spleen)⁶ present in 40-90% of cases¹², may be due to mortality from acute dehydration syndrome and morbidity from neurological impairment (including seizures at 2%–7% in exposure to heroin and methadone, respectively)^{6,8,12,13,15-29};
- *brain damage*: microcephaly, cerebral infarction, intracranial hemorrhage⁹, uncertain evolution in a difficult family context with hyperactivity, psychomotor instability^{8,30-35}.

Objectives: Identification of the incidence of newborns from drug-addicted mothers, risk factors, causes of neonatal morbidity, and evaluation of growth parameters (weight, length, skull perimeter, weight index) according to gestational age.

MATERIAL AND METHOD

The retrospective study in INSMC – "Polizu" Hospital includes newborns in the period 2002–2020 (n=57178), from mothers using illicit drugs during pregnancy (n=82). Anamnestic-clinical data (including Finnegan score to assess the severity of withdrawal syndrome), paraclinical, toxicological (urine samples collected from mother and newborn in 61% of cases), and presentation case of a newborn from pregnancy marked by polydrug use were used. Data were statistically processed (Fisher exact-corrected Bonferroni, Mann-Whitney).

RESULTS

The incidence of newborns from addicted mothers was low 0.143% (82 cases out of 57178 in the period 2002–2020). The evolution of the incidence over time recorded a gradual increase from 0.03% (2006) to 0.23% (2017) and a slight decrease to 0.11% in 2020.

Neonatal mortality, however, was high (8 out of 82 cases), representing 9.75%.

Polydrug use has been reported in most cases, and the most commonly used drugs, in descending order, have been heroin (> 90% of cases), methadone, ethnobotanicals (SNPP), amphetamines, cocaine, cannabis (THC), tramadol, ecstasy (MDMA), LSD, volatile substances.

The majority of drug-using mothers were (52%) aged 19–29 years, and 23% were 30–34 years old, 14% were *minors* (14–18 years old) and 9% were > 35 years old.

The domicile of the mothers was in the urban environment (Bucharest sector 5) in most cases, but a percentage of 8.5% were homeless.

The schooling of the responding mothers (40), found illiteracy in 7% of cases, with primary cycle (1–4 classes) 20%, gymnasium (5–8 classes) 38%, high school (12 classes) 25%, college and school post-secondary education 10% of cases. Most mothers were multiparous (58.53%).

Associated with drug use, the mothers studied had infections with a risk of fetal/neonatal transmission, inducing a risk of congenital and/or

perinatal infections. Except for 4 cases of hepatitis C and 3 cases of syphilis, newly detected after birth, all these mothers were pre-natal in the hospital records of infectious diseases, so that the 9 newborns with HIV mothers benefited from antiviral prophylaxis (Epivir and Retrovir) (Figure 1).

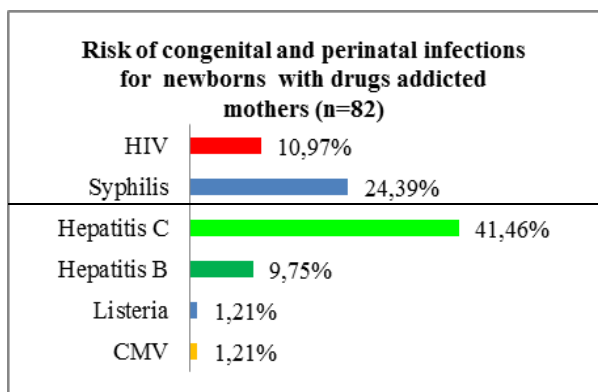


Figure 1. Infections in addicted mothers.

Premature birth (at <37 weeks gestation) was present in 47.56% of mothers (6.09% at <28 weeks (extreme prematurity), 7.31% at 28 and <32 weeks (very high prematurity), 6.09% at 32 and <34 weeks (moderate prematurity) 28.04% at 33–36 weeks (“late” prematurity) (Figure 2).

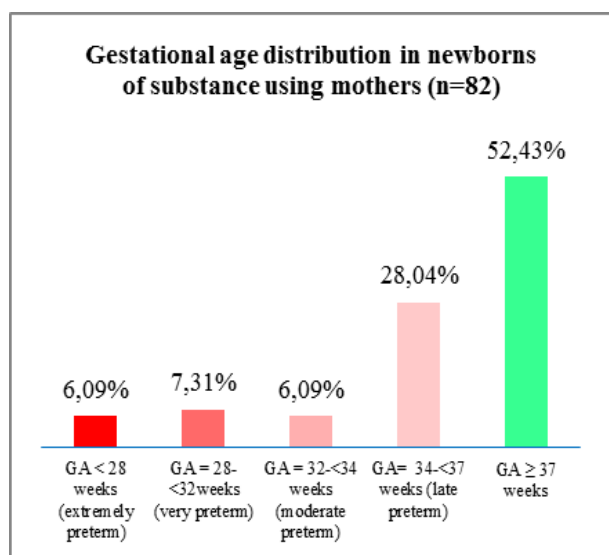


Figure 2. Distribution by gestational age of newborns from addicted mothers.

Newborns had a low weight (≤2500 g) at birth, in 53% of cases (8.53% had <1000 g, 3.65% had 1001–1499 g, 8.53% had 1500–1999 g and 31.70% weighed between 2000–2499 g and only 47.56% weighed ≥ 2500 g (Figure 3).

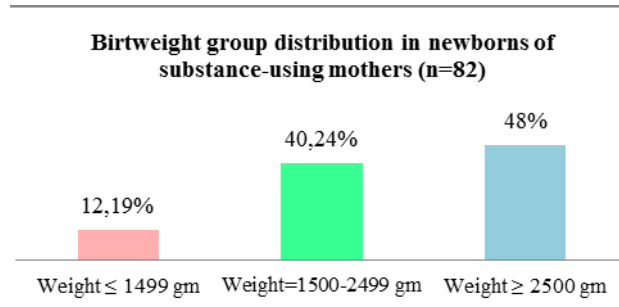


Figure 3. The birth weight distribution of newborns from addicted mothers.

The distribution of newborns by gestational age and birth weight, based on intrauterine growth curves, found cases of low birth weight or *intrauterine growth restriction* in 15.21% of newborns weighing ≤ 2500 g (Figure 4).

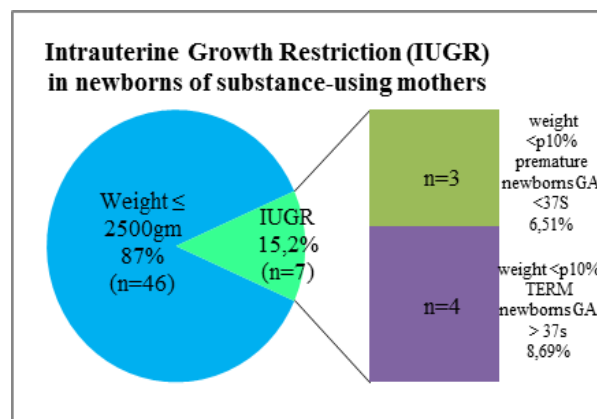


Figure 4. Distribution of newborns with birth weight ≤ 2500 g, with intrauterine growth restriction (IUGR) with weight located at percentile <10%.

Weight index (intrauterine weight-length ratio = 100 × grams/L³ centimeters) > 10% indicated *harmonious (symmetrical)* fetal development with interest in all parameters (weight, length, cranial perimeter) in 58.53%, suggesting a process pathology occurred *early* in pregnancy (cause: genetic, constitutional, first-trimester congenital infections with cytomegalovirus, rubella, toxoplasma gondii³⁵) and the weight index <10% indicated *disharmonious development (asymmetric)* in 41.46%, suggesting an alteration of *late* growth in pregnancy (cause: vascular, drugs³⁵).

Comparison of a group of 72 newborns from drug-addicted mothers with a group of 72 newborns from a control group showed *statistically significant differences (p<0.05)* between the two groups (Figure 5).

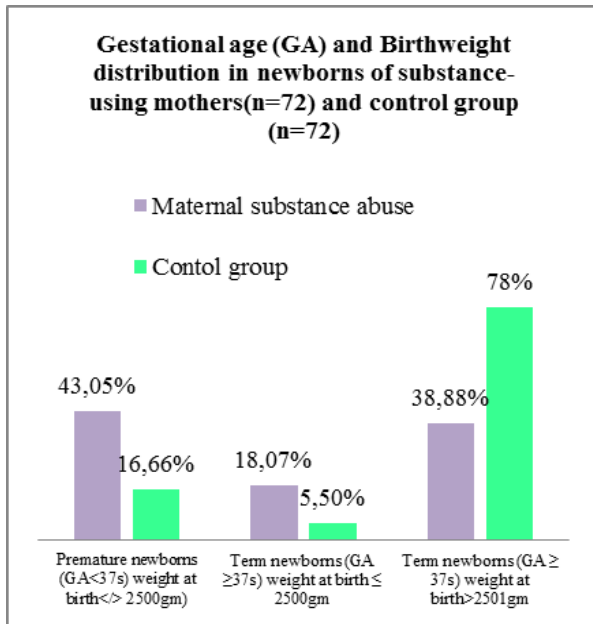


Figure 5. Distribution by gestational age and birth weight in newborns of addicted mothers compared to control group.

Table 1

Comparison of the group of newborns from drug-addicted mothers and the control group, for the incidence of premature and full-term births

	Premature newborns (VG < 37s) GN < / ≥ 2500g	Term newborns (VG ≥ 37s) GN ≥ 3000g
Substance-using mothers	31 [43.05%]	14 [19.44%]
Group control	12 [16.66%]	44 [61.11%]
Odds ratio (OR)	OR=3.78 (1.74, 8.21)	OR=0.15 (0.07, 0.32)
p-value	0.013872 (Fisher exact) corrected Bonferroni	0.000000 (Fisher exact) corrected Bonferroni

Statistically significant differences between the two groups ($p < 0.05$) were also found in terms of growth parameters (weight, length, cranial perimeter, birth weight index) located at the percentile <10%, indicating deficient intrauterine fetal growth in case of drug use in pregnancy (Figure 6).

Neonatal morbidity was marked in descending order of incidence, withdrawal syndrome, the infectious risk for possible congenital and/or perinatal infections, birth weight ≤ 2500 g, prematurity.

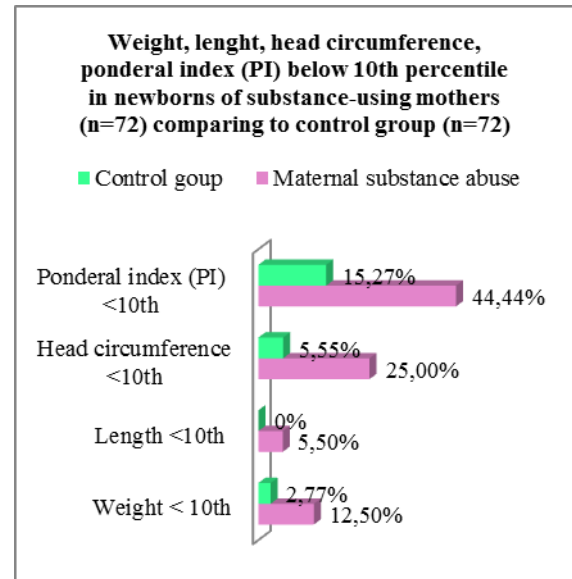


Figure 6. Distribution according to the growth parameters located in the percentile <10% in newborns from drug addicted mothers, compared to control group.

Table 2

Comparison of a batch of newborns from addicted mothers and control batch, for growth parameters located at percentile <10%

IP $\leq 10\%$	p_value = 0.000111 (Fisher exact)
PC $\leq 10\%$	p_value = 0.001009 (Fisher exact)
L $\leq 10\%$	p_value = 0.000001 (Mann-Whitney)
G $\leq 10\%$	p_value = 0.027722 (Fisher exact)

Withdrawal syndrome, present in 60% of cases, was manifested by *clinical neurological signs* (tremors, marked agitation, hypertension, loud, continuous screaming, convulsions in 14% of cases), respiratory, digestive signs (vomiting, bloody stools, dehydration > 15%), fever, abrasions. The severity of withdrawal syndrome was assessed using the Finnegan score (Table 1), which also guided therapeutic conduct by non-pharmacological methods (used exclusively in only 21.95% of cases) and/or pharmacological methods.

The onset of withdrawal syndrome was recorded in most cases on the first day of life, except for newborns from methadone-consuming mothers, in whom the first clinical signs were recorded 4–5 days after birth.

Table 3
Finnegan Score for evaluating the severity of withdrawal syndrome (Cloherty)

Clinical Signs	Score
Excessive High – pitched cry	2
Continuous High – pitched cry	3
Sleeps < 1 Hour After Feeding	3
Sleeps < 2 Hours After Feeding	2
Sleeps < 3 Hours After Feeding	1
Hyperactive Moro Reflex ++	2
Markedly Hyperactive Moro Reflex +++	3
Mild Tremors Disturbed	1
Moderate-Severe Tremors Disturbed	2
Mild Tremors Undisturbed	3
Moderate-Severe Tremors Undisturbed	4
Increased Muscle Tone	2
Excoriation (specify area)	1
Myoclonic Jerks	3
Generalised Convulsions	5
Sweating	1
Fever 37.2-38.2 gr C	1
Fever > 38.4 gr C	2
Frequent Yawning	1
Nasal Stuffiness	1
Frequent Yawning	1
Mottling	1
Sneezing	1
Nasal Flaring	2
Respiratory Rate > 60/min	1
Respiratory Rate > 60/min with Retractions	2
Regurgitation	2
Projectile Vomiting	3
Loose Stools	2
Watery Stools	3
Poor Feeding	2
Excessive Sucking	1
TOTAL	

The Score should be repeated 4–6 times per day (if stable – same treatment, higher – increase doses, lower – decrease doses); Score < 8: non-pharmacologic treatment; Score > 8: for three consecutive scorings indicates the need for pharmacologic intervention.

The duration of withdrawal syndrome was for most cases < 7 days, but in the births of mothers with polydrug addiction, it was longer (Figure 7).

As an example, we present the case of a newborn from the pregnancy of a 30-year-old woman, G IV P IV, heroin addict i.v. (for about 4 years), the last dose she took, being on the very day of his birth. After the vaginal birth, in cranial presentation, at term (38 weeks gestational age), the investigations were within normal limits (VDRL / TPHA, HBsAg, HIV, HCV, etc.), except for urine toxicology examination which found drugs in *Multi-Drug Screen Test* (Opioid,

Methadone, Barbiturics, Benzodiazepines, Tricyclic antidepressants) and *GC-MS analysis* – performed at the “Floreasca” Emergency Hospital (Heroin, Methadone, Diclofenac).

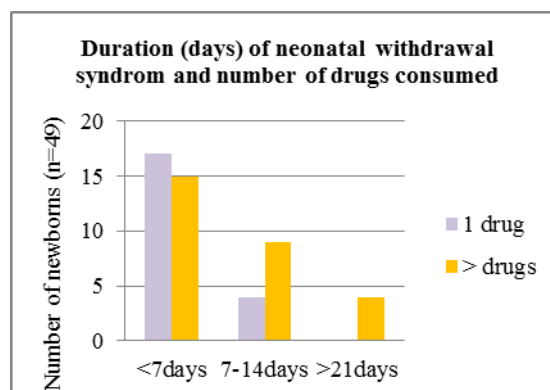


Figure 7. Duration of withdrawal syndrom.

Male newborn, Apgar 8 score, birth weight 3050g (p = 50%), length 52 cm (p=75%), skull perimeter 32 cm (p=25%). Toxicological examination of the first urine after birth, identified by *Multi-Drug Screen Test* Opioid, Methadone, Barbiturics, Benzodiazepines, Tricyclic antidepressants. The evolution of the newborn was marked by withdrawal syndrome with onset from the first day of life with clinical signs of neurology, respectively marked agitation and hypertonia (Finnegan score 12) to which were added from the 3rd day of life, convulsions, confirmed by Continuous EEG monitoring and respiratory disorders – respiratory distress syndrome (Finnegan score 20). The total duration of clinical signs was 15 days, despite intensive therapy which included oro-tracheal intubation and mechanical ventilation for 7 days, administration of anticonvulsant medication (phenobarbital, midazolam), fentanyl in a continuous infusion, antibiotics (penicillin G and gentamicin) prophylactic.

CONCLUSIONS AND DISCUSSIONS

The incidence of newborns from drug-addicted mothers in the studied period (2002-2020) was low (0,143% out of a total of 57178 births), but the evolution of the incidence over time, registered a gradual increase, 10 times, from 0.03% (2006) to 0.23% (2018), and neonatal mortality was high, with deaths recorded in 9.75% of newborns of mothers using illicit drugs.

Neonatal morbidity was marked in descending order of incidence, withdrawal syndrome (manifested

by *major neurological syndrome*, clinical and electroencephalographic seizures in 14% of cases), the infectious risk for *congenital infections* (syphilis, HBV, HCV, HIV), and *infections perinatal* (bacterial), low weight ($\leq 2500\text{g}$) at term or premature birth, prematurity (VG <37 weeks gestation).

Anthropometric values recorded at birth, depending on the intrauterine growth curves, showed in many cases, restriction of intrauterine growth, type I (symmetrical or harmonic) or type II (asymmetric or disharmonious – 41.3% for newborns with weight at birth $\leq 2500\text{g}$), indicating an early and/or late impairment, depending on the maternal pathology associated with the use of illicit drugs.

Table 4

Psycho-social problems in drug-addicted mothers

Psycho-social problems at drug-addicted mothers	No., % cases
Social case – in the records of the Social Assistance service	22 (26%)
Escape from hospital after birth (possible to buy drugs)	19 (23%)
Newborn abandonment in hospital, after birth, taken over as a maternity assistant or social assistance center	14 (17%)
Newborn death	8 (9,75%)
Hospital transfer of infectious diseases for HIV-positive mother, newborn with CMV infection	8 (9,75%)
Homeless	7 (8,53%)
Admission to psychiatry for detoxification, behavioral disorders	5 (6,09%)
The father of the newborn drug addict	5 (6,09%)
Suicide attempt	4 (4,87%)
No documents – mother identified by police	3 (3,65%)
Mother detained in prison for drug trafficking, homicide	3 (3,65%)
The father was detained in the penitentiary	2 (2,43%)
Maternal death after running away from the hospital one day after birth	1 (1,21%)
Prostitution	1 (1,21%)
Birth at home	1 (1,21%)
Transfer to psychiatry	1 (1,21%)
Psychologist request for aggression	1 (1,21%)

The use of illicit drugs during pregnancy (in the context of food deficiencies, infectious diseases, poor socio-economic conditions) associated with prematurity and/or low birth weight for gestational age, are risk factors for neonatal morbidity and mortality.

Psycho-social problems (multiple and miscellaneous) of addicted mothers (in order of

incidence: request for help from the Social Assistance service, running away from the hospital after birth, abandonment of the newborn in the maternity ward, and taking over as a maternity assistant or social assistance center, hospitalization for HIV infectious diseases, mothers with a history of psychiatric hospitalization for detoxification, addicted father, history of suicide attempt, undocumented mothers, mothers and fathers detained in prison, maternal death after running away from hospital, prostitution), present at in most cases, they can have an impact not only on the pregnancy (medically unattended in most cases) but also on the postpartum evolution, in the short and long term, from a somatic, neuro-psychic and social point of view (Fig. 3).

To help the newborn of the addicted mother, the mother must firstly be helped, avoiding the neonatal risks in case of maternal addiction, imposing a multidisciplinary medical-psycho-social approach (Figure 8).



Figure 8. Medical partnership.

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