DRUG ADDICTION DURING PREGNANCY – RISK FACTOR FOR PERINATAL INFECTIONS

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ABSTRACT

Introduction. Neonatal infections are a major causes of neonatal morbidity and mortality. Pregnancy complicated by illicit drug abuse is a risk for perinatal infection.
Objective. To assess the incidence of early-onset neonatal sepsis (the first 7 days of life) in newborns from high-risk pregnancies for perinatal infections: the ones affected by drug abuse, without medical assistance versus clinical and fully investigated pregnancies.
Material and methods. Retrospective study on newborns from "IOMC – Emergency Clinical Hospital of Obstetrics and Gynaecology Gh Polizu", Bucharest, sorted in two separate groups: one of 25 newborns, from 2005 to 2012, coming from uninvestigated pregnancies in women with illicit drug dependencies and another of 50 newborns from properly managed pregnancies from the clinical and anamnestic point of view, but with known risk factors for perinatal infections. The data has been statistically analysed (correlation tests: Student T, Fisher exact, chi-square)
Results. The incidence of newborns from pregnancies affected by drug abuse was 0,09% in all 28489 newborns, the highest percentage of 0,2% being recorded in 2011. Statistically significant differences between the two groups of newborns with risk factors for perinatal infections (emerged from uninvestigated pregnancies with drug abuse and respectively from investigated pregnancies) were: the age of the mothers – lower in drug addicted mothers (p_value 0,0002), the percentage of congenital infections (p_value 0,00003; OR 0,03; 95%CI) and respectively the mean length of hospital stay-days (p_value0,0180) higher in dug addicted mothers. On the other hand: the delivery by cesarean section (p_value 0,0010), urogenital colonisation (p_value 0,0016) were more frequent in newborns from investigated pregnancies. A percent of 22 of all investigated women were positive for Group B Streptococcus and the most frequent type was I b type. The share of perinatal infections among neonatal morbidity was 33% for the newborns from drug addicted mothers and 27% for the newborns from investigated mothers. The incidence of neonatal infections was 52% for the newborns from drug addicted mothers (a risk of 1 in 1,9 cases) and 18% for the newborns from investigated mothers (a risk of 1 in 5,5 cases)
Conclusions. Drug addiction during pregnancy represents a high risk factor for perinatal infections due to sexual and blood transmitted diseases associated with lack of hygiene, precarious nutrition and low immunological status and leads to high medical and social costs. The correct medical management of pregnancies, through early diagnosis and treatment of neonatal infections may lower the incidence and the consequences of perinatal infections.

Keywords: risk factors, perinatal infection, fallow up of pregnancy, maternal drug abuse

INTRODUCTION

Neonatal infections still are (in an era of imposing medical achievements like in vitro fertilisation – assisted human reproduction technology and the survival of foetuses of lower and lower gestational ages and birth weights) major causes of neonatal morbidity and mortality.

Acknowledging the risk factors for the perinatal infections (between 22 weeks of gestation or 154 days of pregnancy and day 7 after birth – W.H.O. definition (1)) enhance the prevention of their oc-

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currence and/or augments the diagnose and efficient treatment.

Both medical factors, like the mother's precarious health state, often with untreated infections, and social-cultural factors, like the lack of medical surveillance of the pregnancies, are indirectly *contributing factors* to the morbidity and mortality through perinatal infections. It is a widely known fact that medical science can improve the mother-child health status only when supported by an effective program of social actions (2).

Drug addiction, especially for injected illicit drugs usually related to opiates use (although in some countries amphetamines injection represents a major problem), affects 1,3 to 1,7 million persons in EU and Norway (4), from which 34% are women, most of them at fertile age (5) and that constitutes an important risk factor for perinatal infections.

These infections are acquired via parenteral or sexual way before and/or during pregnancy and they are transferred to the foetus/the newborn before or during delivery, the most frequent ones being caused by hepatitis B or C virus, human immunodeficiency virus or treponema pallidum(6,7,8,9).

The determining factors of perinatal infections are micro-organisms passed from mother to foetus *in utero* (congenital infections), frequently identified as TORCH group (T = toxoplasma gondii, O = other agents, R = rubella virus, C = cytomegalovirus or CMV, H = herpes simplex virus or HSV), TORCHES CLAP group (TORCH and E = enterovirus, S = syphilis, C = chickenpox - varicella - zoster virus or VZV, L = Lyme disease – Borrelia burgdorferi, A = AIDS or HIV, P = parvovirus B19) or CHEAP TORCHES (H = B and C hepatitis - hepatitic B (VHB) or C (VHC) virus and E = any other sexually transmitted disease like gonorrhoea, Chlamydia, Ureaplasma and papillomavirus). The infections passed from mother to foetus/newborn *during delivery or immediately after* are produced by micro-organisms located within the vagina and are frequently (*Grup B streptococci, Enterococcus, Escherichia coli, Neisseria gonorrhoeae, Listeria monocytogenes, Candida albicans, hlamydia trachomatis*), seldom (*Staphylococcus aureus, Alfahaemolytic streptococci, Proteus species, Klebsiella species, Pseudomonas species, Salmonella species, Shigella species, Alkaligenes faecalis, Neisseria meningitidis, Haemophilus influenzae, Vibrio fetus, Bacteroides, Clostridium species, Mycoplasma hominis, Ureaplasma urealyticum, Trichomonas vaginalis*) or extremely rare (*Lactobacillus, Staphylococcus epidermidis, Gardnerella vaginalis*, *Corynebacterium, Bacillus subtilis, Peptostreptococcus, Veillonella, Bifidobacterium, Eubacterium, Mycobacterium tuberculosis*) associated with neonatal sepsis (10).

The correct management of the pregnancy with infectious hazards, early diagnosis and treatment of maternal infections can diminish the incidence and ameliorate the outcome of perinatal infections.

In Romania, the consequences of drug abuse during pregnancy for the newborn have been reported for the first time in a written paper in the year 2005 (11).

MATERIAL AND METHODS

Retrospective study on newborns from "IOMC – Emergency Clinical Hospital of Obstetrics and Gynaecology Gh Polizu", Bucharest, sorted in two separate groups: one of 25 newborns, from 2005 to 2012, coming from uninvestigated pregnancies in women with illicit drug addictions and another of 50 newborns from properly managed pregnancies from the clinical and anamnestic point of view, but with known risk factors for perinatal infections.

For the group of newborns from drug addicted mothers a clinical exam was performed (including assessment by FINNEGAN score) and toxicological (urine testing for 68% of the couples newborn – mother), serological, bacteriological and biochemical tests were accomplished, along with radiologic and echographic exams and psycho-social inquiries made by the social workers and the psychologist.

For the group of newborns with risk factors for perinatal infections coming from investigated pregnancies we have selected some of the cases already included in a prospective study realised during 2007-2008 with The National Institute for Research and Development in Microbiology and Immunology "Cantacuzino", Bucharest. The laboratory work-up performed to identify the risk factors for perinatal infections (toxoplasmosis, rubella, cytomegalovirus infection, herpes, B or C hepatitis, parvovirus infection, syphilis, listeriosis, chlamydia and B group streptococcus) in the stage of symptomatic or asymptomatic infections/healthy carrier subjected women in various points of their pregnancies and 28% of the newborns carried by them, who presented clinical signs suggestive for perinatal infections. To detect the *Group B Streptococcus* (*Streptococcus agalactiae)* vaginal samples were taken (from the inferior third) during week 35-37 and the lochia were tested after delivery. Bacterial culture identification was achieved with serological methods (se-

rotyping the specific antigen of group B streptococcus).

The data has been statistically analysed (correlation tests: Student T, Fisher exact, chi-square). The significance level of the test was compared to $p = 0,05$.

RESULTS AND DISCUSSIONS

Drug addiction during pregnancy was described in 0,09% of all women (28 489) who delivered live babies in Polizu Hospital between 2005 and 2012, with a peak of incidence in 2011 (0,2%).

The illicit drugs were in the vast majority of intra-venous type, fact that was alone a risk factor for perinatal infections, in addition to the overlooking of preventive measures for sexually transmitted diseases. More than one drug was consumed in 36% of cases.

12% of the drug addicted mothers were underaged (< 18 years), 40% had between 21 and 29 years and 24% between 30 and 34 years. 84% of them resided in urban environment, 12% in rural one, 4% had no residence and for 8% we had no available data.

Drug addicted mothers were known for or they tested positive for *Treponema pallidum* (8 cases), hepatitis C virus (5 cases), hepatitis B virus (1 case) and human immunodeficiency virus – HIV (1 case), representing altogether a total of 60% of the cases. Medical monitoring during pregnancy was widely absent in the group of drug addicted mothers. In addition to medical issues many of them also had psycho-social difficulties: psychosis (2 cases), attempted suicide (2 cases), penal detention (1 case), decease (1 case) and child abandonment (6 cases).

Most of the investigations completed in mothers from the second group (preponderantly aged between 21 and 35 years – 85% and with urban residence – 70%) revealed the immunisation for rubella (97.95%), cytomegalovirus (92.68%), toxoplasmosis (41.46%) and parvovirus B (31.25%). The most frequent identified risk factors for perinatal infection were urogenital bacterial/*Group B Streptococcus* colonisation (14%), abnormal amniotic fluid (6%), ruptured membranes for more than 18 hours (3%), cervical cerclage (3%) and fever in labour (2%). *The Group B Streptococcus,* which may transitory, chronically or intermittently colonise the maternal vagina, was found in 22% of investigated mothers, therefore representing a risk factor for infections in newborn (vertical transmission leads to colonisation and/or early or late-onset neonatal sepsis). *Group B Streptococcus* typing**,** based on capsular polysaccharides identification, has shown a prominence of Ib type (34%) followed by type III (22%) and type IV (22%) and associations between type III and IV and respectively type IV and V.

The newborns from this study had the following characteristics: male sex was preponderant in newborns from drug addicted mothers (68%) versus 50% in the group of newborns from investigated mothers; 72% were term babies (≥ 37 weeks of gestation) in the group with drug addicted mothers and 70% in the second one; premature birth (gestational age ≤ 36 weeks and 6 days) affected 28% from newborns with drug addicted, uninvestigated mothers and 30% of those with investigated mothers during pregnancy. Low birth weight ≤ 2,500 g was a more frequent finding (48% versus 36%) in the group of newborns from drug addicted mothers, whereas birth weight ≥ 2,501 g was preponderant in the other group (64% versus 54%)

The distribution of the newborns by gestational age and birth weight emphasised the following: prematurity was more frequent in babies from investigated pregnancies (34% versus 28%), intra-

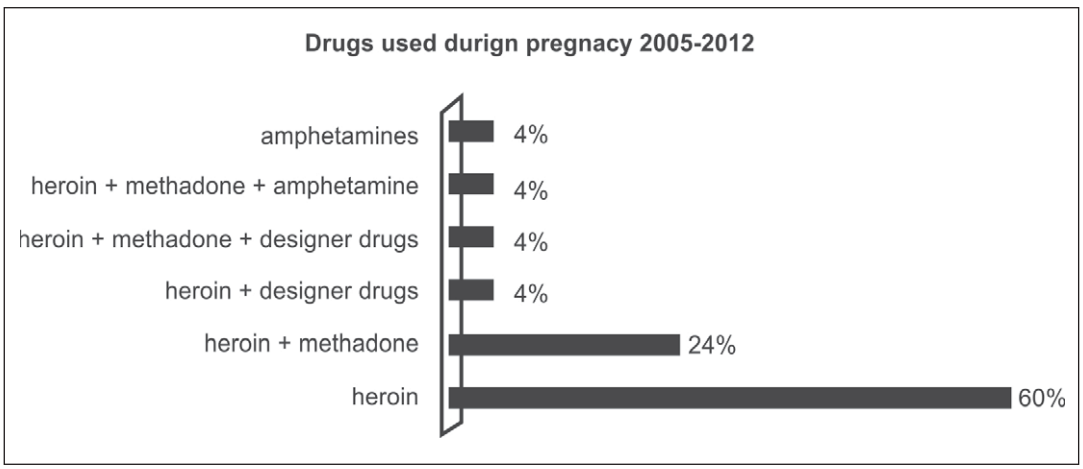
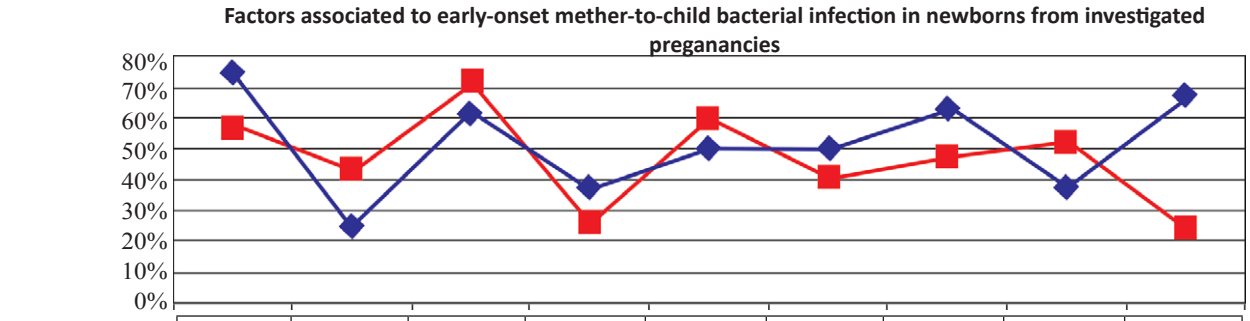


***FIGURE 1**. Illicit drugs consumed during pregnancy and no. of drug abusing mothers*



	primiparity	> parity	urban	rural	cesarean section	vaginal delivery	males	females	prematurity
Infection +	75%	25%	62.50%	37.50%	50%	50%	63%	37.50%	66.66%
Infection -	57.15%	42.85%	71.40%	26.10%	59.50%	40.47%	47.60%	52.30%	24.39%

FIGURE 2. *Associated factors to early-onset mother-to-child bacterial infection in newborns from investigated pregnancies*

uterine growth restriction (IUGR) occurred twice as frequent in newborns from drug addicted mothers (20% versus 10%) and term babies from this group had often weighted under 3000 g at birth (24% versus 18% in the group with investigated mothers). The delivery was mainly vaginal (80%) for the drug addicted mothers and by cesarean section (58%) for the investigated mother with infectious risk factors in addition to other obstetrical risk factors.

Neonatal morbidity was 88% for the newborns from drug addicted mothers and 34% for the ones from investigated pregnancies.

For the newborns from uninvestigated, drug addicted mothers the incidence of *perinatal infections* was of 52% (13 cases out of 25) namely a risk for infection of 1 in 1,9 cases; interestingly, 9 cases out of this group had 1 type of perinatal infection – bacterial mother-to-child infection (3 cases) or congenital infection (6 cases: 5 with syphilis and 1 with HIV) and 4 cases counted 2 types of infection: congenital (syphilis in 3 cases and CMV in 1 case) associated to bacterial gram-negative neonatal sepsis (*Escherichia coli* in 3 cases and Enterobacter, 1 case). Syphilitic infection was confirmed in 2 cases (both VDRL and TPHA positive testing) and suspected in 3 cases (only TPHA positive).

In the group of newborns from investigated pregnancies the incidence of *perinatal infections* was of 18% (9 cases: 8 diagnosed with early-onset bacterial sepsis and 1 with congenital infection) representing an infection risk of 1 in 5,5 cases. Maternal bacterial colonisation as a risk factor for perinatal infection was not constantly associated to neonatal infection. From 9 cases (22,22%) of *Group B Streptococcus* maternal colonisation only 2 counted for neonatal sepsis (but the pathogen agent was not identified in the newborn). A reasonable explanation for this lack of identification of causal agents might be the antibiotic treatment provided for mothers with urogenital colonisation, other risk factors for infections or suspected/confirmed infection before delivery (in labour) for prophylactic reasons – in order to prevent the early-onset neonatal sepsis. The prematurity was frequently linked to perinatal infection. Male sex was more often relat-

TABLE 1. *Results*

Variable	Uninvestigated. drug abusing pregnancies n = 25 (%)	Investigated pregnancies. with infectious risk factors n = 50 (%)	p_ value
Mother's age (years)	24.40 ± 6.0553 (14-34)	29.7 ± 5.2598 (19- 40)	0.0002 *
Male sex	17 (68%)	25 (50%)	0.138 **
Gestational age (weeks)	37.36 ± 2.9704 (29-41)	36.86 ± 3.3807 (27-42)	0.5321 *
Birth weight (g)	2510.00 ± 639.49 (900-3850)	2772.80 ± 861.18 (900-4200)	0.1814 *
Cesarean section	5 (20%)	29 (58%)	0.0010 **
Birth asphyxia	2 (8%)	8 (16%)	0.2822 ***
Congenital infection	10 (40%)	1 (2%)	0.00003***
Bacterial mother-to-child infection	7 (28%)	8 (16%)	0.2206 **
Mean duration of antibiotic treatment (days)	12.56	7.1	0.1191 *
Mean duration of hospital stay (days)	22.16	11.7	0.0180 *

*Student T. **Chi-square. *** Fisher exact

ed to the risk factors' presence and to neonatal infection.

The amount of congenital infections in the group of newborns from uninvestigated, drug abusing mothers was significantly higher from statistical point of view than in the group of newborns from pregnancies with infectious risk factors but with proper medical assistance.

CONCLUSIONS

Drug addiction during pregnancy represents a high risk factor for perinatal infections, especially for the congenital ones, due to sexual and blood transmitted diseases associated with lack of hygiene, precarious nutrition and low immunological status. The incidence of drug abuse during pregnancy might seam small but the effect is double, both on mother and her child. Perinatal infection was 2,88 times more frequent in newborns from uninvestigated, drug addicted mothers than in those born from pregnancies with infectious risk factors but correct medical management. Proper medical assistance during pregnancies, through early diagnosis and treatment of neonatal infections may lower both the incidence and the consequences of perinatal infections and the human and financial costs on short and long term.

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