Fetal-maternal toxicology: fetal somatic consequences of noxious habits in pregnant women

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Abstract: Consumption of noxious substances (alcohol, tobacco or drugs, even “the light” ones) is harmful during pregnancy. Nevertheless, in the contemporary Romania many pregnant women do not drop out on these habits, on the contrary they even associate them. The goal of our study consists in the identification of these habits’ effects on the pregnancy and we carried on in the Department of Obstetrics-Gynecology “Sf. Pantelimon” Emergency Clinical Hospital Bucharest a prospective study based on the anonymous interviewing of 169 patients who got birth between March and April 2016. A number of 97 patients out of 169 patients declared that they referred to at least one out of three noxious habits (57.40%). Smoking is the best represented vice in the studied test sample, having a weight of 42.01% (71/169), followed by alcohol consumption - 30.17% (51/169) and by the associated consumption of alcohol and smoking - 15.38% (26/169). The least representative in the test sample was the drugs consumption, having a weight of 1.77% (3/169) but with an association of 100% with smoking (3/3 cases) and of 66.66% (2/3 cases) with alcohol consumption, fact that shows a great risk behaviour. Smoking associated with alcohol consumption, followed by smoking with no other associations had the negative effects on the average gestation age, average weight and average APGAR score. All categories of studied vices registered variable fetal somatic damages.

Key Words: alcohol, smoking, drugs, pregnancy, premature birth, restriction of intrauterine growth.

Consumption of noxious substances (as alcohol or drugs, even “the light” ones) or smoking is harmful during pregnancy. In spite of that, in 2016 Romania- as a UE member state, many of these pregnant women don’t drop out of these vices.

According to “Centers for Disease Control and Prevention” from USA, the side effects of smoking, alcohol consumption or drugs – on pregnancy - can be abortion, premature birth, intrauterine growth restriction, fetal death in utero, fetal malformations. It can’t be specified yet the precise incidence of the phenomenon and either the true impact on the pregnancy [1].

There are studies which were addressed to the association between smoking and abortion, but there isn’t yet certain evidence concerning the influence of smoking or alcohol on the pregnancy development. Other studies carried on lab animals underlined the negative effect of smoking and alcohol on the embryo and fertility, but studies concerning the effects of active or passive smoking on feminine fertility, on premature birth...
or on intrauterine growth restriction are still insufficient [2]. In the case of the active smoking patients, but also in some situations of passive smoking, the potentially toxic substances for pregnancy and fertility would be: carbon monoxide, benzene, cadmium, ethylbenzene, formaldehyde, methylamine, nicotine, cotinine and toluene [3].

Active smoking is associated with spontaneous abortion, premature birth, abnormal placentation, intrauterine growth restriction, perinatal death rate, fetal malformations [4], but also with the growth of cotinine (nicotine metabolite) concentration in the follicular liquid (it has a negative effect on the quality of oocyte, blastocyst and nidation)[5]. There are less data concerned the influence of passive smoking on the pregnancy, but the presence of nicotine and cotinine was distinguished in the fetal blood of the pregnant exposed to the passive smoking, and the concentration of these compounds was superior to the concentration from the maternal blood [6].

Alcohol consumption of the reproductive age women is frequent in Europe. The negative effects of the alcohol on the pregnancy are varied: congenital malformations, isolated fetal neurological disorders, specific fetal neural-behavioural disorders (in alcohol abuse) that can evolve till an entity called alcholoic fetal syndrome (AFS), with severe consequences [7-10]. AFS is characterised by: intrauterine growth restriction, alterations of central nervous system and behavioural disorders. Even ASF incidence is 1%, the effects of alcohol consumption in pregnancy are bigger and they comprise a large spectrum of diseases (Diseases of Alcoholic Fetal Spectrum - DAFS) [11].

According to the Romanian authors, AFS (Alcoholic Fetal Syndrome) associates in different degrees: low weight at birth, facial dysmorphism, growth deficiencies, dysfunctions of central nervous system, very high frequency of the attention in childhood, hypotonia and irritability at early ages, microcephaly, articular anomalies, affections of spinal column curvature, urogenital affections (cryptorchidism, hypospadias, labial hypoplasia), cardiac anomalies, mental retardation, aberrant palm patterns, nail hypoplasia, syndactyly, Klippel – Feil syndrome, skin hemangioma, hirsutism, pectus excavatus, xiphoid bifid [12].

Nicotine and carbon monoxide from the cigarette smoke would be the most involved ones (out of more than 30 noxae) in the affection of the fetal development. The carbon monoxide would be responsible for the appearance of the cerebral atrophy of a new born baby, for the mental retardation and microcephaly, and the cyanides would affect the calcium metabolism, that of B12 vitamin, C vitamin [12, 13].

Fetal effects of cocaine maternal consumption is characterised by: abortion to a high gestation age, premature birth, premature bursting of the membranes, malformations of the central nervous system, microcephaly, porencephalia, ventricular hemorrhage, cerebral infarcts, urogenital malformations, fetal hypotrophy, cardiovascular malformations, limbs malformations, the increase of the risk of premature getting apart of the normally fixed placenta [12, 14], modifications of the fetal electrocardiogram, convulsions, ulceronecrotic enterocolitis, intestinal atresia and prune-belly syndrome, unexpected death, the delay of the cognitive and motor development in the first years, cocaine neonatal addiction syndrome ("Crack baby syndrome") [12, 15]. The consumption of Opioids increases the risk for an intrauterine fetal death, fetal hypotrophy, premature birth, chorioamnionitis and severe withdrawal of the new born baby, and the consumption of Marihuana increases the risk for premature birth, fetal hypotrophy, behaviour disorders, trembling, hypoxia intrapartum, hypocalcemia, hypoglycemia [12].

The identification of the women of reproductive age who are at the risk of alcohol abuse and the risk of having a baby with the ASF specific elements is essential in the fight with the consumption of these substances. It must be accompanied of pregnancy prevention methods and interventions which reduce the risk of consuming alcohol and tobacco. Without such a prophylaxis, the exposure to alcohol and tobacco will be kept to the subsequent pregnancies [16, 17].

Some studies show an increased prevalence of the alcohol and tobacco consumption during the pregnancy, especially in young persons (15-21 years old), the causes not being elucidated yet [18]. There were elaborated theories which explain the increase of alcohol and tobacco in young pregnant, but they did not reach a precise conclusion. The absence of a biological parent, alcohol consumption and smoking in the company of the pregnant or by the partner can be possible explanations [19].

According to these data, the main goal of our study was that of quantifying as exactly as possible the incidence of the patients who have such a behaviour, a part of the causes, but especially the consequences of this phenomenon and improper behaviour towards the pregnancy, which have medico-legal implications. Accomplishing a "robot portrait" of the pregnant who smoke and/or consume alcohol and/or drugs during pregnancy, as well as the identification of the consequences of these habits reflected in the main somatic and functional characteristics of the fetus born from these pregnancies (gestation age at birth, weight at birth and APGAR score) take part also of the main goal. Secondary objective of our study was the educational one, that of sensitizing the patients of the study to the risks of these habits and to inform them about these risks.
MATERIAL AND METHODS

We elaborated a prospective observational study (based on a voluntary and anonymous action) which included a number of 169 patients (N=169), who were hospitalised in Obstetrics-Gynecology Clinic of “Sf. Pantelimon” Emergency Clinical Hospital Bucharest between 1st of March 2016 – 30th of April 2016.

The 169 patients who got birth in the clinic represent 11.46% out of 1474 patients who got birth in 2016. The results were 172 new-born babies (3 patients with twins pregnancies with 2 fetus each), meaning 11.48% (out of 1497 babies born in 2016).

The study meant the anonymous, voluntarily and unpayed or rewarded in any way interviewing of the patients – by an anonymous opinion questionnaire, which included 14 statistic questions. The questions had an unique answer and they meant the ticking off with a simple “X” by the respondent; and the fulfilling of the opinion questionnaire was also the informed consent for the participation to the study and for the publishing of its results in scientific papers. In order to keep the anonymity, the data from the data base can not reach us to the identification of the respondent or the fetus.

The inclusion criteria were: a patient who got birth (or who ended the birth in the clinic) in Obstetrics-Gynecology Clinic of “Sf. Pantelimon” Emergency Clinical Hospital Bucharest and wanted to answer voluntarily, anonymously and not rewarded (material or any other type) to the opinion questionnaire and to participate to the study; patients who agreed for their data to be used in the study (and also the scientific works resulted from them); there are data referred to their born fetus from these pregnancies (number of fetus, gestation age, fetus weight, APGAR score), as well as data from their obstetrical antecedents). Inclusion criteria did not allow at all the discrimination of the study participants (depending on the education, schooling, ethnical community, nationality, age, social origin, marital status, economical status, religion, political convictions, profession, race etc.). The work had the acceptance of the Ethical Committee.

In order to accomplish this goal- after it was explained to them which the objectives, the use and the stages of the study are- any patient who wanted to participate at the study voluntarily, anonymously and not rewarded- was accepted, after they expressed freely their consent to the participation. The only exclusion criterion from the study (immediately applied) was that of their verbal refuse to participate.

The first question of the questionnaire mentioned patient age group (years old already reached at): 13-17 years old, 18-20 years old, 21-24 years old, 25-29 years old, 30-34 years old, 35-39 years old, 40-44 years old and 45 years old or more.

The second question referred to the level of schooling (graduation): 0 (zero grades), 1-4 grades (primary ones), 5-8 grades (secondary ones), 9-12 grades (high school level), post high school, university studies or more.

Question no. 3 was questioning the patient about her previous pregnancies (“Yes”/ “No”).

The following three questions (4, 5, 6) were interviewing the patient as regards of the characteristic of prenatal visit during the pregnancy she had just ended. Question no. 4 asked the respondent to mention if she came for prenatal visit during the pregnancy and the options of the response were “Yes”/ “No”. Question no. 5 mentioned the approximate number of medical visits during the pregnancy: no one, 1-5, 6-9, 10 visits ore more. Question no. 6 mentioned the type of medical visits: medical visits had not been done, visits to the obstetrics doctor, visits to the family (generalist) doctor, visits to both categories of doctors.

Question no. 7 asked the patient to answer “Yes” or “No” if she consumed alcohol during the pregnancy she had just finalised. Question no. 8 asked the respondent to mention by “Yes” or “No” if she smoked (tobacco products) during the pregnancy she had just finalised. Question no. 9 asked the interviewed one to specify by “Yes” or “No” if she took drugs (illicit substances popular named “drugs”) at any kind during the pregnancy she had just finalised. Question no. 7, 8 and 9 did not specify the regularity or intensity of these habits. Question no. 10 - "Did you know that the consumption of these types of substances can harm you and/or your baby?" had as options for answers “Yes” or “No”. Question no. 11: "Did the doctor explicitly talked to you- during the prenatal visits- about the consumption of these substances in the pregnancy and their pernicious effects on the pregnancy?" (“Yes”/ “No”). Question no. 12: "Do you consider that if they had been explained you more detailed the harmful effects of these substances on the pregnancy would you not have been used them anymore?" (“Yes”/ “No”). Question no. 13: "Do you consider that the prenatal visits of the pregnancy is useful?" (“Yes”), “No”). Last question (14): "Do you consider that the organised education as “School of Pregnant” and/or "School of Parents" could have been useful to you? (“Yes”) “No”).

The analysed medical data (parity, gestation age at birth – as weeks reached at, the number of fetus, the weight at birth, the APGAR score) were taken from the birth register and were introduced in the data base and analysed so not to lead to the identification of the patients or of their children.

The data analysis was accomplished with the SPSS software version 23 and EpiInfo 3.5.4.

RESULTS AND DISCUSSION

The sample had the following characteristics: in the studied sample (N=169 patient) we had 51 patients (30.17%) who declared that they consumed alcohol...
during pregnancy, 71 who declared that they smoked during pregnancy (42.01%) and 3 patients who declared that they consumed drugs during pregnancy (1.77%).

Among 51 patients who declared that they consumed alcohol, 27 declared that they smoked, too (27/51 = 52.94%) and 2 of them that they consumed drugs during pregnancy (2/51 = 3.92%). Among 71 patients who declared that they smoked, 27 declared that they consumed alcohol, too (27/71 = 38.02%), and 3 of them declared that they consumed drugs, too (3/71 = 4.22%). Among 3 patients who declared that they consumed drugs, all of them declared that they smoked, too (3/3 = 100%) and 2 of them declared that they consumed alcohol, too (2/3 = 66.66%).

The ratio of the patients who declared that they used all the three types of noxious habits during pregnancy is of 2 out of 169 (1.18%). The ratio of the patients who declared that they used 2 of these habits was of 28 out of 169 (16.56%), and the weight of patients who declared that they used just one of these was of 67 out of 169 (39.64%). In the sample there were just 72 out of 169 patients who declared that they did not use any of these noxious habits during pregnancy (42.60%).

The general characteristics of the patients sample included in the study are the following: Age of patient: 13-17 years old -12/169 (7.1%), 18-20 years old - 20/169 (11.8%), 21-24 years old-26/169 (15.4%), 25-29 years old-53/169 (31.4%), 30-34 years old-41/169 (24.3%), 35-39 years old-14/169 (8.3%), 40-44 years old -3/169 (1.8%), Primiparas-90/169 (53.2%), Overunitary parity-79/169 (46.7%). No. of medical visits: 0 25/169 (14.8%), 1-5 visits 33/169 (19.5%), 6-9 visits 22/169 (13.0%), 10 visits or more 89/169 (52.7%). Type of medical visit No one 25/169 (14.8%), Family doctor, 5/169 - (3.0%), Obstetrician 51/169 (30.2%), Both 88/169 (52.1%).

Alcohol Yes 51/169 (30.17%) Alcohol No. 118/169 (69.82%), Smoking Yes 71/169 (42.01%)Smoking No 98/169 (57.98%). Drugs Yes 3/169 (1.8%), Drugs No 166/169 (98.1%).

Main characteristics of the patients sample who declared they consumed alcohol during pregnancy (N=51) are shown in Table 1, opposite the characteristics of the patients who declared they did not consume alcohol during pregnancy, having a significantly statistic difference.

Main characteristics of the patients sample who declared they smoked during pregnancy (N=71) are shown in Table 2, opposite patients who declared they did not smoke, with a significantly statistic difference.

The characteristics of the sample of 3/169 patients (1.77%) who declared that they consumed drugs during pregnancy are the following ones: (p_value test comparing to non-consumers of drugs): 2/3 patients declared they consumed alcohol, too (66.6%) (0.216737 Fisher’s Exact Test), and all three (100%) declared they smoked, too (0.072326 Fisher’s Exact Test); 2/3 patients (66.6%) said...
that they knew the risks of these habits (0.244659 Fisher’s Exact Test); 1 patient said that the doctor explicitly told about risks (33.3%), 1 said that the doctor did not explicitly tell her anything (33.3%) și 1 (33.3%) refused the answer (1.000000 Fisher’s Exact Test); all 3 (100%) said that the additional explanations would not have determined them to drop out the vices (0.549913 Fisher’s Exact Test); all 3 (100%) said that they did not consume alcohol (0.244659 Fisher’s Exact Test). We do not have a significantly statistic association between the smoking and the gestation age under 37 weeks fetus (23.1% from the total of smokers) differs significantly statistic from the percentage of the non-smokers who got birth under 2500 grams weigh fetus (23.5% from the total of smokers) and 13% of the smoker pregnants who got birth to premature children (7.1%).

Also a significantly statistic difference exist for the weight at birth of the children resulted from pregnant who consumed alcohol opposite to that of the children resulted from the pregnant who did not consume alcohol (0.031276 Student T). The pregnant who consumed alcohol got birth to children with 203.4 grams smaller- on average- than the pregnant who did not consume alcohol (a weigh 6.59% smaller).

We have a significant statistic association between the smoking and the under 2500 grams weigh of the fetus (0.000491 Pearson Chi-Square) because the percentage of the smoker pregnant who got birth to under 2500 grams weigh fetus (23.5% from the total of smokers) differs significantly statistic from the percentage of the non-smokers who got birth under 2500 grams weigh fetus (23.5% from the total of smokers). We have a significant statistic association between the smoking and the gestation age under 37 weeks (prematurity) (0.005280 Pearson Chi-Square) as the percentage of the smoker pregnant who got birth under 37 weeks fetus (23.1% from the total of smokers) differs significantly statistic from the percentage of the non-smokers who got birth to premature children (7.1%).

For the average gestation age and the average APGAR score we do not have statistic significantly differences in the sample, but we notice an average gestation age with 0.55 weeks lower (for the pregnancies who said that they consumed alcohol (0.031276 Student T). The pregnant who consumed alcohol got birth to children with 203.4 grams smaller- on average- than the pregnant who did not consume alcohol (a weigh 6.59% smaller).

We do not have a significantly statistic association between the alcohol consumption and the

<table>
<thead>
<tr>
<th>Alcohol consumer</th>
<th>Smoker</th>
<th>Non-smoker</th>
<th>p_value (test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation average age (weeks)</td>
<td>37.56 ± 3.163</td>
<td>38.0 [37.0. 39.0]</td>
<td>0.867267 (Student T)</td>
</tr>
<tr>
<td>Average weight (g)</td>
<td>2882.85 ± 637.772</td>
<td>3068.25 ± 508.194</td>
<td>0.031276 (Student T)</td>
</tr>
<tr>
<td>Average APGAR score</td>
<td>8.58 ± 1.217</td>
<td>8.85 ± 1.053</td>
<td>0.158305 (Student T)</td>
</tr>
</tbody>
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<thead>
<tr>
<th>Druggs consumer</th>
<th>Smoker</th>
<th>Non-smoker</th>
<th>p_value (test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation average age (weeks)</td>
<td>36.0 ± 3.011</td>
<td>37.98 ± 2.223</td>
<td>0.210750 (Student T)</td>
</tr>
<tr>
<td>Average weight (g)</td>
<td>2566.66 ± 46.188</td>
<td>3035.09 ± 556.629</td>
<td>0.036451 (Mann-Whitney U)</td>
</tr>
<tr>
<td>Average APGAR score</td>
<td>9.0 [8.0. 9.0]</td>
<td>8.78 ± 1.115</td>
<td>0.867267 (Student T)</td>
</tr>
</tbody>
</table>
Table 4. The main somatic characteristics of the fetus resulted from the pregnant who declared they smoked and consumed alcohol during the pregnancy

<table>
<thead>
<tr>
<th>Smoking alcohol simultaneously (N=26)</th>
<th>Just smoking (N=43)</th>
<th>Just alcohol (N=24)</th>
<th>Neither smoking nor alcohol consumption (N=74)</th>
<th>p_value (test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average gestation age (weeks)</td>
<td>37.65 ± 2.057</td>
<td>37.65 ± 2.057</td>
<td>38.67 ± 1.464</td>
<td>38.38 ± 1.141</td>
</tr>
<tr>
<td>Average weight (grams)</td>
<td>2618.00 ± 690.832</td>
<td>2937.79 ± 542.310</td>
<td>3158.75 ± 441.817</td>
<td>3173.698 ± 469.069</td>
</tr>
<tr>
<td>Average APGAR</td>
<td>8.17 ± 1.523</td>
<td>8.55 ± 1.400</td>
<td>9.00 ± 0.590</td>
<td>9.03 ± 0.745</td>
</tr>
</tbody>
</table>

We drew up a similar statistic analysis for the patients who declared they smoked and consumed alcohol during the pregnancy (simultaneous vices), and the characteristics of these fetus are given in Table 4.

There were significantly statistic differences of the average fetal weight between the patients who smoked and consumed alcohol and those who did not have any of these vices and between the patients who consumed just alcohol and those who consumed alcohol and smoked, too (0.000059 ANOVA).

The patients who cumulated the two vices got birth to fetus with a 555.69 g lower average weight (17.50% less) than the patients who did not have any of these vices. The patients who cumulated the two vices got birth to fetus with the following deficiencies of these parameters (comparing with the same parameters of the fetus from the non-consumer patients): average gestation age 1.65 weeks lower (4.34% lower), and average APGAR score was 0.11 lower comparing to that of the fetus from the non-consumer sample.

We have a significantly statistic difference for the fetal weight between the patients who said they consumed drugs and those who said they did not consume drugs during pregnancy (0.036451 Mann-Whitney U). The consumer patients got birth- on average- to children with a weight with 508.43 g lower (16.75% less), average APGAR score 0.11 points lower (9.22% less) than the patients who consumed just alcohol (p-value = 0.000).

**CONCLUSION**

Smoking is the best represented vice in the studied sample, with a weight of 42.01% (71/169), followed by alcohol consumption - 30.17% (51/169) and by the associated consumption of alcohol and smoking - 15.38% (26/169). The worst represented vice in the sample was drug consumption, with a weight of 1.77% (3/169) but with an association of 100% with smoking (3/3 cases) and of 66.66% (2/3 cases) with alcohol consumption, fact that represents a great risk behaviour.

Smoking determined the birth of some fetus with the following characteristics of the general somatic parameters, analysed in the moment of birth (comparing with the same parameters of the fetus from non-smoking pregnant): average gestation age 1.22 weeks lower (3.17% less), average weight 350.0 g lower (11.04% less), average APGAR score 0.62 points lower (6.87% less).

Alcohol consumption led to the birth of some fetus with the following somatic parameters: average gestation age 0.55 weeks lower (1.44% less), average weight 203.4 g lower (6.59% less), average APGAR score 0.27 points lower (3.05% less).

Drug consumption led to the birth of some fetus with the following deficiencies of these parameters (comparing with the same parameters of the fetus from the sample of the non-consumer patients): average gestation age 1.65 weeks lower (4.34% less), average weight 508.43 g lower (16.75% less), average APGAR score 0.11 points lower (1.25% less).

Smoking associated with alcohol consumption led to the birth of some fetus with the following deficiencies of these parameters (comparing with the same parameters of the fetus from the sample of no vices patients): average gestation age 0.73 weeks lower (1.90% less), average weight 555.69 g lower (17.50% less), average APGAR score 0.83 points lower (9.22% less) than the patients who consumed just alcohol (p-value = 0.000).

**Conflict of interest.** The authors deny any conflict of interests.

fetal hypotrophy (0.437583 Fisher’s Exact Test), and the percentage of the alcohol consumer mothers who got birth to hypotrophy fetus was of 2.0%, comparing to a percentage of 5.9% mothers who got birth to hypotrophy fetus from the non-consumers sample.

There were significantly statistic differences of the average APGAR score 0.86 points (9.52% less).
Ionescu C. et al.  Fetal-maternal toxicology: fetal somatic consequences of noxious habits in pregnant women

References