

# Fetal alcohol syndrome disorders: experience on the field. The Lazio study preliminary report

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**Summary.** In Italy, little is known about the problems related to alcohol drinking during pregnancy. In this paper, the Italian literature about this subject is briefly reviewed. This first Italian experience of a field study, aimed to the assessment of the prevalence of fetal alcohol syndrome (FAS) and fetal alcohol spectrum disorders (FASD) in an area in the Rome province (Lazio region) is reported. This in-field study was performed in the school years 2003-2004 and 2004-2005 in cooperation with American researchers, most from University of New Mexico (Albuquerque), and Italian researchers from University "la Sapienza" of Rome. First grade children ( $n^{\circ} = 1086$ ) of primary school were contacted to enter in the in-school study for the detection of FAS and FASD and were examined by the experts team of clinicians, pediatrics, psychologists. Preliminary consideration and the implications of this study for FASD prevention are discussed.

*Key words:* fetal alcohol syndrome, epidemiological clinical study, Italy.

**Riassunto** (*Sindrome fetoalcolica: dati preliminari dello studio svolto nel Lazio*). In Italia, la conoscenza delle problematiche connesse al consumo di alcol in gravidanza è ancora scarsa. Dopo una breve rassegna della letteratura italiana sull'argomento, questo lavoro descrive l'esperienza effettuata sul campo durante uno screening (il primo studio italiano) volto ad individuare la prevalenza della sindrome fetoalcolica e, più globalmente, dei disordini legati ad esposizione fetale ad alcol in 15 comuni del Lazio nell'area della provincia di Roma. Lo studio è stato effettuato negli anni scolastici 2003-2004 e 2004-2005 ed è stato svolto in collaborazione tra ricercatori americani, molti dell'Università del New Mexico (Albuquerque), e italiani dell'Università "La Sapienza" (Roma). Sono stati contattati 1086 alunni delle classi di prima elementare delle scuole presenti nel territorio. Vengono discusse le considerazioni circa la percentuale di risposte e le implicazioni in termini di prevenzione dovute al processo attivato da tale studio.

*Parole chiave:* sindrome fetoalcolica, studio clinico epidemiologico, Italia.

## INTRODUCTION

Fetal alcohol spectrum disorders (FASD) is a cluster of abnormalities occurring in children born to mothers with histories of alcohol drinking during pregnancy, while fetal alcohol syndrome (FAS) is the full-blown syndrome. The diagnosis of FAS needs the existence of specific signs in each of the following categories: growth retardation, central nervous system involvement and the characteristic face.

In Italy, little is known about FAS and FASD. The teratogenic effects of alcohol were first reported in France in by Lemoine in the 1968 [1] but it remained substantially ignored until, in the '70, it was described by Jones *et al.* in 1973 [2-3]. Up to today, the awareness of FAS problem is poor in Italy both among experts (doctors, psychologists, social operators and teachers) and laymen.

In US, the prevalence of FAS is 1-3‰ [4] and the highest prevalence in the world was found in South Africa, where 46‰ of children were affected by FAS even if the real prevalence could be even higher, according to studies in progress [5]. High prevalence was found also in ethnic minorities.

No reliable estimate of FAS prevalence in Italy: epidemiological studies using active case ascertainment are lacking, as in the other countries of Western Europe. Indeed, while in ICD-9 the 760.71 code for FAS was introduced in 1976, the prevalence of FAS was severely underestimated in hospital diagnosis at birth, since most of the abnormalities may be related to other birth defects or other mechanisms (malnutrition, genetic disorders), or may be detected only when the child ages.

Only few case reports were published about children born to Italian mothers, with symptoms like microcephaly, hypoplasia of corpus callosum, hyperactivity, low IQ, not different from FAS symptoms registered in other countries [6-10].

Conflicting results are reported in the few Italian studies about the effect of prenatal exposure to alcohol: in some studies, negative effects are reported, as spontaneous miscarriage, low weight at birth, jaundice, premature delivery; in other studies, no harmful effects of alcohol drinking during pregnancy was reported. This last finding is very surprising, since in the study of Primatesta *et al.* [11], 9% of women enrolled used to have more than 11.5 drinks a week, at risk drinking during pregnancy for most scientists.

Unfortunately, this finding is perfectly in agreement with the alcohol-drinking pattern for most Italian people. In Italy, binge drinking is fairly rare, while a steady moderate drinking at meals is very common, and several women do not change their habits during pregnancy, which is often unplanned: thus, some women (mostly poorly educated) drink alcohol during the first months of pregnancy, since they are not aware of their condition. The spread of this dangerous behavior in Italy is confirmed by a transversal study performed by our group in Rome in 2003. Drinking habits were investigated in 122 pregnant women by a semi-structured interview: 62.1% of the women used to drink alcohol before pregnancy, and 52.6% during pregnancy; thus, only 10% of the women quit drinking when pregnant. While the 68.4% of the women reduced or quit smoking, only 21.5% reduced or quit drinking. The 11.7% of pregnant women on study used to have more than 7 drinks a week. Moreover, 2 women started alcohol drinking during pregnancy, probably because popular ideas about safety and even usefulness of moderate alcohol drinking during pregnancy are still widespread in Italy where, several years ago, beer drinking was considered a lactation-enhancer by common people, and this idea is still present, mostly in uneducated people [12].

In this situation, a nation-wide effort for prevention is needed. Whereas in US the National Health Institute officially advised women that drinking alcohol (any amount) during pregnancy is highly dangerous for the fetus and must be avoided, in Italy FAS prevention from official health agencies is lacking and the risk of fetal damage related to prenatal alcohol exposure is under-evaluated.

This lack of correct information about FAS risk is present even among midwives and obstetricians, who should be the advisers of pregnant women, and even in some manuals for medical and nursing schools.

Taking into account the lack of awareness of the FAS risk, the popular ideas about drinking in pregnancy, the behavior of pregnant women and the large number of alcohol abusers and alcoholics (about 4 000 000 out of 57 000 000 inhabitants), the actual prevalence of FAS in Italy could be relevant. A successful prevention needs a careful assessment of the real prevalence of FAS and FASD, using extensive outreach methods.

## EXPERIENCE IN THE FIELD. THE LAZIO STUDY

This in-field study was performed in the years 2003-2004 and 2004-2005 in cooperation with American researchers, mainly from University of New Mexico, Albuquerque, and Italian researchers University "La Sapienza", Rome. It was aimed to the assessment of the prevalence of FAS and FASD in the area on study, and the evaluation of the drinking pattern of mothers of the enrolled children. The study was approved by the Ethic Committees of the Aziende Sanitarie Territoriali (ASL) involved in the study, and by the Ethic Committee of the University of New Mexico. The schools of the districts of two Territorial Health Agencies (in Italy, Aziende Sanitarie Locali, ASL), including several small towns and rural areas, were selected for the study. Many people were commuters to Rome, while others were local agriculture workers. Among the primary schools that volunteered to participate to the study, 25 schools were randomly selected. The first grade students of these schools were enrolled if permission was granted by their guardians by signing a permission form. Only 543 children out of 1086 participated in the study and underwent the screening protocol.

As the cooperation of the schoolteachers and the children's mothers was crucial, several informative meetings with the Italian researchers were needed. Briefly, the questionnaire for the mothers' interview employed in the South-African study was translated and modified for the needs of the Italian study, and was used to assess the life-style of the mothers, before and during pregnancy and at present. The questions about alcohol drinking were included in a large series of questions about health, food consumption and life-style, to increase the reliability of the answers. The one week - day by day method was used. The areas investigated in the questionnaire are reported in *Table 1*.

**Table 1** | *Maternal interview. Areas investigated*

1. Social and demographic variables
2. Mother's health lifelong: general aspects
3. Mother's conditions during the pregnancy and after delivery, regarding physical, psychological and behavioral problems.
4. Food intake at present and during the pregnancy. The three trimesters of pregnancy were investigated separately
5. Alcohol intake at present and during the pregnancy. The three trimesters of pregnancy were investigated separately
6. Use of tobacco and other psycho-active drugs at present and during the pregnancy. The three trimesters of pregnancy were investigated separately
7. Information, suggestion, advises received during the pregnancy
8. Quality of the family environment where the child is living
9. Information about any disease, inherited or not, present in the child's family

*Anything noteworthy observed by the interviewer was reported. "Pregnancy" is referred to the pregnancy which gave birth to the child on study.*

In the screening first step, the children with impaired growth (height, weight, cranial circumference  $\leq 10\%$ ) or impaired performance at school (learning deficit and/or attention and hyperactivity, assessed by the Parent/Teacher Disruptive Behavior Disorder Rating Scale Pelham's test [13] and the Problem Behavior Checklist (PBLC) test [14], in Italian translation), were selected for further tests. School performance and behavior were assessed by the teachers, previously briefed by the psychologists of the team, filling a form based on the tests employed. Also the children's parents were asked to fill the same form about attention and hyperactivity.

In the second step, the children were examined by two American dysmorphologists and by two Italian pediatricians, working blinded to child's history. The children with FAS-related morphological abnormalities were tested with the Ravens Coloured Progressive Matrices [15] and the Rustioni Test of Language Comprehension [16], to assess their psychological and developmental levels.

In the diagnosis step, at present still in progress, each case is discussed by the whole team, collecting and discussing all the information obtained by different sources: the parent's questionnaire, the report from the teachers, the mother's interview, the morphological assessment and the neuro-psychological testing. The diagnosis of FAS or FASD was established, according to the diagnostic criteria of the Institute of Medicine (IOM) [17].

The parents of each child were informed about the results of the screening in a meeting with the psychologists: the problems of the child, if any, were discussed with the parents, as well as the guidelines of following interventions, if needed.

### PRELIMINARY RESULTS

At present, only data about the compliance of the family are available, suggesting some considerations about the feasibility of these studies, and of their implications for prevention and health promotion.

Among the schools in the chosen districts, 70% voluntarily agreed to enter the study.

A limit of the study is the low participation rate of the families: only 50% of parents agreed the participation of their children to the study. During preparatory meetings with the parents, most of them were reluctant to submit their children to an unnecessary medical visit; many parents said they were perfectly satisfied with the state-granted pediatric care, which in Italy is free and capillary widespread in the field. On the contrary, the parents who thereafter accepted the study found useful a further check of the psycho-physical health of their children, and liked the idea of helping the scientific progress in this field. Moreover, the poor cooperation of families may be related to the choice of the study design, as suggested by the study of Clarren *et al.* [18], in two US counties: when passive parental recruitment was employed, the participation rate was very high, whereas was low when active recruitment (the parents

had to sign an acceptance form) was employed. In Italy, because of legislation and high sensitivity about privacy and human rights, only active parental recruitment was possible.

During the first year of the study, the teachers were questioned about the possibility that a problematic child was not included in the study (because of the parents' refusal), and 71.4 of the teachers gave a positive answer. This fact raises several doubts about the efficacy of in-school studies in reaching all the population worth of interest, but an easy solution of this problem is difficult to find. According to the preliminary data available, 33.0% of the children participating to the first screening had low weight or height, or reduced cranial circumference, or learning and behavioral problems.

### IMPLICATION OF THE STUDY FOR FAS PREVENTION

As the effect of prenatal exposure to alcohol on the psycho-physical development of the child is dramatic, and no effective treatment is available, FAS prevention is a worthwhile task. In our country, the risk of FAS is increased by the common pattern of alcohol drinking (a large number of reproductive women drinking moderately during meals, even when pregnant), by the poor awareness and the under-evaluation of the FAS risk. The awareness of the risk may be increased only by a careful assessment of FAS and FASD risk in our country, which is unknown, and by a nation-wide effort for a campaign of information and education, for the promotion of the health of pregnant woman and unborn child.

Thus, this first Italian study in a large group of children is a significant step for FAS prevention. Moreover, the awareness of the problem among the teachers and the health workers (doctors, psychologists, staff) employed in the study and the children's families is increased. The awareness of the of the behavior disorders in problematic children is certainly increased among the teachers participating in the study, beyond the FASD children, and their effectiveness in coping with problematic children is further enhanced. All the activities for people information and for involvement of the whole community will be passed to common people in the neighborhood, further increasing the awareness in the area interested by the FASD Lazio project, obtaining an effective health promotion.

The data from the interviews of 519 mothers may be very helpful for understanding the drinking habits of Italian women, during and after pregnancy. Nearly all of them were drinkers at present: 100% of the mothers of control health children, but, surprisingly, about 90% of mothers of FASD children; the veracity of their answers seems questionable, as some of the answers were false, because of the guilty feeling and the fear of social blame in heavy drinkers. The same mechanisms may be responsible of the low participation rate, as discussed before. An alternative explanation of the relatively high rate of non drinkers among the FASD mothers may be that some of them were heavy drinkers, and they quit drinking, after the birth of the child on study,

being worried about their health. Two-thirds of women reported alcohol drinking during pregnancy, without difference between the mothers of FASD children and of controls; the veracity of these answers seems even more questionable.

Also the formation of an Italian team able in diagnosing FAS and FASD subjects is a crucial step for the treatment, but is helpful also for prevention, since the awareness of the problem will be further increased. Moreover, the parents of a FASD child will be informed of the risks of prenatal exposure to alcohol in a further pregnancy: this is a relevant goal, since the probability of FASD in children from further pregnancies is increased in mothers of a FASD child, if they do not quit drinking.

More relevant is the opportunity of helping the children resulting affected by disorders related to prenatal exposure to alcohol, as happened for the two children evaluated in this screening. The Medicina Scolastica (School Medicine) Service accepted the indication from the University team, and both the children have a support teacher. According to the most recent research, this is not the best approach for the needs of a FAS child: if he is placed with age peers, he may have a wide range of abilities that may not all fall in the range of abilities compared to his classroom peers [19]. Unfortunately, personalized teaching is not available at present in Italian school.

A crucial point for the prevention of FAS/FASD is to avoid unintended pregnancies in heavy-drinking women: obviously, women, ignoring that they are pregnant, drink as usually and alcohol can cause fetal damage. Unfortunately, at-risk sexual intercourse is common in alcoholics, and unwanted pregnancies are frequent in female alcoholics and are an increasing problem in general people.

An interesting, positive side-effect of this study is the improvement of the teachers' and parents' awareness of behavioral and learning problems of the children. In the first year of the study, 11.4% of the children seemed affected by attention deficit, 13.4% by hyperactivity, 13.4% seemed to have a delay in the acquisition of learning abilities. The diagnosis of FASD was not confirmed in all the cases, but in most cases the awareness of the child's problems lead to a modification of the family and school environment and to an improvement of the attitude of the parents toward their child. Indeed, the teachers found a support in their evaluation of children's behavior and

could improve their attitude towards problematic children. The final meeting with the parents was performed according to the basal principles of professional counseling.

All the information obtained in the study are available from the Territorial Health Services participating in the study, and may be used for the implementation of further projects in the field. The institutions and services participating in the study could acquire a new experience about a poorly known problem, and this information will be shared with the whole institutions. Thus, the improvement of the awareness and the knowledge of the effects of prenatal exposure to alcohol are more far-reaching than the present results.

## CONCLUSIONS

At present, FAS is the more frequent syndrome of mental impairment completely preventable. We hope that in Italy clinicians and psychologists will be advised of the need of taking a thorough history to determine alcohol use in all women of childbearing age and to provide information regarding FASD prevention.

Screening tests to detect at risk pregnancies may be helpful, and also some biological markers of alcoholism may be useful [20]: moreover, the assessment of fatty acid ethyl esters (FAEE) in the newborn meconium seems the most reliable test [21]. Programs and interventions to help the women to quit drinking in pregnancy may be implemented. Some experimental studies suggest that the administration of antioxidants and free-radicals scavengers to pregnant women unable or unwilling to quit drinking may reduce fetal damage, but further research in humans is needed [22].

Moreover, the procedures for an early diagnosis of FAS should be improved, to obtain a FAS/FASD diagnosis in the newborn, to set up an early treatment, if possible, and to prevent further at risk pregnancies in the same family.

FAS primary prevention is a major target, since no effective treatment is at present available for the effects of prenatal exposure to alcohol. Also the formation of skilled health operators may be very useful for a better care of FASD children.

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