



## Investigating Alcohol Consumption during Pregnancy for the Prevention of Fetal Alcohol Spectrum Disorders (FASD)

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### Abstract

The term FASD (Fetal Alcohol Spectrum Disorders) is used to describe the entire spectrum of pathologies and disorders caused by alcohol exposure in uterus. Alcohol assumed in pregnancy passes directly through the placental barrier causing a broad range of symptoms whose severity can greatly vary in degree. The alcohol teratogenic effect may result in physical damage and specific facial anomalies, growth delays, neurological defects along with intellectual disabilities and behavioral problems. Children affected show difficulties in verbal learning, memory, visual-spatial abilities, attention, logic and math abilities, information processing, executive functions as well as in many other domains and in general coping with daily life. Total abstention from alcohol during pregnancy is strongly recommended, as a safe threshold of consumption has not been established yet. Hence, the early identification of alcohol consumption in pregnancy is crucial. Specific methodologies to overcome difficulties related to the identification of alcohol behavior in pregnant women are needed and intervention protocols should be implemented to prevent damage in offsprings. This paper gives an overview on this pathology, from clinical delineation to epidemiology and risk factors with a special focus to promote alcohol-free pregnancy.

### Introduction

Reference to the effects of alcohol on newborns prenatally exposed to it can be traced in ancient time in Aristotle and even in the Bible [1] but was only in 1968 that they were described in a scientific paper titled "Anomalies in 121 children of alcoholics" by Lemoine et al. [2]. Then Jones et al. [3,4] published several papers where a clear association between alcohol consumption in pregnancy and a specific syndrome in exposed newborns was defined. Since then, over 3500 papers have been published on this issue [5] and nowadays alcohol is a very well known and recognized teratogen for the fetus. Lifelong consequences of this pathology include brain damage and cognitive impairments with high costs for individuals and society [6,7].

A review of the international guidelines on alcohol consumption

during pregnancy shows that many Countries all over the world officially released recommendations on the safest drinking behavior during pregnancy, from total abstention to no more than 1 or 2 drinks<sup>1</sup> once or twice a week (i.e. the United Kingdom)<sup>2</sup>. Some countries made health warning labels on alcoholic beverages mandatory: the US enacted such a law in 1989, China in 2005, France in 2006, Russian Federation and South Africa in 2007<sup>3</sup>. But still a percentage of women drink during pregnancy and professionals during prenatal care suggest avoiding alcohol not as much as needed [8,9]. Professionals' recommendations and early identification of at-risk women are crucial, as fetal alcohol effects are 100% preventable just suspending consumption during pre-conception time and pregnancy. Thus, the role of obstetrics and gynecologists for prevention is essential.

### Fetal Alcohol Spectrum Disorders (FASD)

Even if differences may exist in the main description of the syndrome, the following features are commonly recognized in children prenatally exposed to alcohol [10]:

- specific facial anomalies
- growth delay
- central nervous system (CNS) problems and intellectual disabilities and behavioral problems

Four are the main codes utilized for diagnosing alcohol-related damages: the American Institute of Medicine (IOM) criteria [11], The Canadian guidelines [12], the Four Digit Code [13] and the Center for Disease Control National Task force code [14,15].

All of these codes agree on describing the main altered facial features: short palpebral fissures, smooth philtrum and thin upper lip; growth deficiencies are generally identified as prenatal or postnatal birth weight or height below the tenth percentile, CNS dysfunctions include brain structural anomalies, small head circumference (below

<sup>1</sup>Standard drink =14 grams of alcohol (i.e. 330 ml of beer or 125ml of wine)

<sup>2</sup><http://www.iard.org/policy-tables/drinking-guidelines-pregnancy-breastfeeding/>

<sup>3</sup><http://www.iard.org/policy-tables/Health-Warning-Labeling-Requirements/>

**Citation:** Ceccanti M, Fiorentino D, Ciolfi P, Coriale G, Messina MP, et al. (2016) Investigating Alcohol Consumption during Pregnancy for the Prevention of Fetal Alcohol Spectrum Disorders (FASD). *Obstet Gynecol Cases Rev* 3:076

**Received:** December 10, 2015: **Accepted:** February 23, 2016: **Published:** February 26, 2016

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the tenth percentile) and a pervasive neurological deficit. Potentially, children affected may experience difficulties in verbal learning, memory, visual-spatial abilities, attention, logic and math abilities, information processing, executive functions as well as in other domains [16-20].

The IOM describes the following revised diagnostic criteria [11]:

1. A full syndrome (FAS) that includes, at least, two of the above-mentioned facial features; growth deficiencies (height or weight equal or below the tenth percentile) and CNS problems, including structural brain anomalies or head circumference equal or below the tenth percentile. This syndrome can be diagnosed in the presence of a confirmed history of maternal alcohol abuse or without it.

2. A partial syndrome (Partial FAS; PFAS), with the presence of at least two of the three facial features described above; one among the following evidences: growth deficiencies, brain structural anomalies or small head circumference (equal or below the tenth percentile) and a pattern of behavioral or cognitive impairments not attributable to genetic, family history or environmental influence alone.

This diagnosis can be made with or without a confirmed history of maternal consumption in pregnancy.

3. The IOM criteria include also two other clusters of symptoms: Alcohol-Related Birth Defects (ARBD) and Alcohol Related Neurodevelopmental Defects (ARND) but this diagnosis can be made only in the presence of a confirmed exposition to alcohol in utero.

The term FASD has recently been introduced as a nondiagnostic term [15,21] to comprehend the whole range of possible alcohol-related damage in children exposed, including also effects like abortion [22,23].

Alcohol exposure causes cognitive and behavioral impairments affecting individuals all their lifelong. Cognitive and behavioral main affected domains include global functioning, executive functioning, memory, verbal learning, language, visual-spatial ability, motor functioning, attention and arousal levels, scholastic proficiency, mathematic, adaptive skills, emotional functioning [10,24,25]. As a consequence, individuals exposed may develop several secondary disabilities. It has been estimated that during adolescence the following secondary disabilities may occur: mental health problems (90%), trouble with the law (60%), low school proficiency and dropout (60%), inappropriate sexual behavior (49%), alcohol and drug problems (33%) [26,27].

It should be noted that FASD arises also from a complex interplay of genetic and epigenetic factors [28]. Indeed, several studies have suggested a significant epigenetic FASD etiology and supporting evidence for such a mechanism is accumulating [29]. Gene expression disturbances can be caused by changes in DNA methylation, molecular modification of histones and through RNA interference. These mechanisms work together to produce a unique, and reversible epigenetic signature that regulates gene expression through chromatin remodeling. DNA methylation has been investigated extensively as a mechanism of alcohol teratogenesis too [28].

## Fasd Prevalence

Most of the prevalence studies were performed in the United States, mainly registry or clinic based. Registry-based studies rely on reviewing existing registries, such as clinical records, disabilities registries and at birth diagnosis records [30]. Thus far nearly 15 studies of this kind have been conducted, producing a mean FAS prevalence of 0.85 per 1,000 (median 0.27) while information on FASD are not provided [30].

Clinic studies consist in following pregnant women during pregnancy, collecting data on their alcohol consumption and then evaluating the newborns, very often in the form of prospective studies [30].

In literature, more than 50 clinical studies are reported [30],

showing a mean prevalence rate of 1.8 for FAS (median = 1.9) and of 6 per 1000 for FASD (median = 5). These rates are consistently higher than those obtained through surveillance systems.

A minority of studies were performed on nonclinical population, based on an active case ascertainment methodology, where researchers actively evaluate a population in the field to individuate cases. These early studies have been conducted among native population in the US and Canada [31-33]. As this population, with low socio-economic status, may be considered at risk for alcohol consumption during gestation with elevated percentages of binge drinkers the prevalence obtained were high and not easily generalizable. May [30] resumes prevalence rates obtained from such a kind of studies: mean rate of FAS prevalence = 38.0 per 1000 (median = 9.0) and mean rate of FASD prevalence = 16.9 per 1000 (median = 19.0). A recent meta-analysis of active case ascertainment studies among children in child-care setting showed a prevalence of 6.0% for FAS and 16.9% for FASD [34]. The active case ascertainment method has been utilized also to highlight prevalence in the correctional system, leading to an estimate of the prevalence of 1.04% for FAS, 10% for PFAS and 4.1 to 8.7% for ARND [35]. But also in this case, results are not generalizable because of the at-risk condition of the selected settings.

This problem can be partially overcome by a particular kind of active strategy: the in-school active case ascertainment studies, where a normal population of children attending school (usually 6-7 years old) is screened. The process of evaluation goes from the first screening for height, weight and head circumference, to an evaluation of behavioral problems and pre-learning skills, to the final dysmorphic exam and neuropsychological testing. An accurate interview of drinking patterns and health conditions of the mother is performed as well [30].

The main part of these studies has been performed in South Africa: due to low socioeconomic conditions, they showed very high percentages of FASD occurrence [36-39] for the extremely poor condition of life in the areas chosen for the studies. But recently active ascertainment in schools in the Western world revealed prevalence higher than what was expected. Table 1 resumes the prevalence rates found in in-school studies from around the world. Furthermore, a recent meta-analysis by Ospina [35], not including studies performed in South Africa, resumed prevalence rates as follows: FAS = 3.6 per 1000, PFAS 29 per 1000, ARND = 2.3 per 1000.

## Risk Factors

It has been estimated that the full syndrome occurs in nearly 40% of heavily exposed pregnancies [49]. The range and the severity

**Table 1:** Prevalence rates from in school studies by countries.

	FAS	FASD
	Rate per 1000	Rate per 1000
South Africa [36-39]	50.0	72.3
Whashington, US [40] (Only results obtained in one of the two screened counties are showed, due to low consent rate in the second county)	3.1	
US [41]	4.3*	
Italy, Europe [42,43]	4.0-8.2*	23.1-47.1*
US City 1 [30]	1.4-2.5*	9.5-17.4*
US city 2 [30]	6.4 -11.3*	14.1-24.8*
Plains Head Start School (US) [30]	10.2	20.3
Croatia, Europe, [44]	6.4*	40.7*
Taiwan, [45]	1.83*	5.76*
Korea, [46] General school, Institutions for intellectual disabilities	2.8*	14.9 *
Croatia, Europe [47] rural	16.9*	66.7*
Rocky Mountain Region, US [48]	2.9-5.5*	10.9-20.3*

Re-elaborated from May [30].

\*These percentages do not include children without parental consent: they are rated only based on sample. The other percentages are rated including also those children not enrolled in the study because without parental consent, theoretically assumed as not affected.

of damage in children exposed are wide, depending on different variables, including dose and timing of exposition, genetic factors and the nutritional status of the mother.

The amount of alcohol consumed represents the most important risk factor for FASD. Even if a safe threshold of consumption has not been established yet, an average consumption of more than 1 drink per day (14 grams of alcohol) may be considered at risk [50]. But the main dangerous behavior is the consumption of great quantities in short time, as the damage on the fetus is directly related to the level of blood alcohol concentration (BAC) [38]. This behavior is commonly referred to as “binge drinking”, defined by the US NIAAA (National Institute on Alcohol Abuse and Alcoholism) as the consumption causing a BAC of 0.08 grams per liter or more. An adult woman reaches this level after the consumption of 4 or more drinks in two hours [51]. Pointing at what can be considered a binge episode in pregnancy, several studies showed that the consumption of three or more drinks per single occasion is highly related to morphological and behavioral damage in children exposed [38].

Based on the well demonstrated association between heavy episodic drinking or chronic drinking and negative outcomes in offspring's [52-55], studies aimed at evaluating the effects of light consumption gave opposite results over the years, but evidences exist that even small amount of alcohol ingestion can affect the fetus, i.e. 0.5 alcohol units (nearly half of a standard drink) [56]. The number of alcoholic beverages assumed is also correlated with heavier consumptions and could, therefore, be used as an indicator of at-risk drinking [57].

Active-case ascertainment epidemiological studies performed in Italy [42-43,58] showed that in a retrospective interview, the current mean number of drinks consumed per week in mothers with FASD children was higher compared to that of control mothers (FASD Mean = 10.37, standard deviation 18.92; Controls, Mean = 1.52, standard deviation = 2.80,  $p < 0.001$ ). It was suggested that current drinking could represent a more reliable measure of drinking because less susceptible to social stigma. Similar effects can be observed for self-report of drinking out of pregnancy.

The kind of alcoholic beverage consumed should be taken into consideration as well. Animal model studies [59-62] investigated damage differences due to gestational exposure to alcohol when comparing wine and other alcoholic beverage. The papers compared mice prenatally exposed to 11% ethanol or to the same concentration of red wine. It was shown that administration in utero of ethanol-induced long-lasting changes in offspring behavior, brain areas, endocrine tissues and liver, while in mice exposed to red wine changes were evident mostly in the peripheral tissues but not in brain structures. These findings suggested that differences in toxicity can be due to putative neuroprotective antioxidant compounds present in the red wine as polyphenols [63,64]. An Italian survey among 992 pregnant women identified the following risk factors for alcohol-exposed pregnancies: being younger (under 30), having an unplanned pregnancy, being unemployed, having a lower educational qualification and being single [65].

Other factors may have effects on offspring's as mother's age, parity, body size, nutritional status, socioeconomic status and other drugs use, as well as genetic and epigenetic factors [66-69].

Paternal alcohol exposure (PAE) only may also elicit changes in the newborns comparable to those observed with gestational ethanol exposure as shown in both animal model and human studies [70-72]. Indeed, contrary to the large attention given to the roles that maternal factors have on the outcome of pregnancy, little is presently known about the possible function played by paternal factors, especially about the influence of PAE on the neurobehavioral and developmental characteristics of offspring [71]. It has been suggested that about 75 percent of children with FAS have heavy drinkers or alcoholic biological fathers [71]. These findings suggest that the anomalies in the newborns attributed to the influence of the teratogenic effects of maternal drinking are also the consequence of the PAE, so the

anomalies could be due to or are exacerbated by paternal drinking.

The occurring of alcohol problems in the family environment also should be taken into consideration as a risk factor. An Italian active case ascertainment study [58] showed that alcohol problems in the child's family were the most significant risk factor for FASD and sequential multiple regression analysis of the neuropsychological performance of tested children identified family's alcohol problems as the only significant risk variable in mothers.

## Alcoholic Anamnesis and Detection of at Risk Women

Prevalence of women drinking during pregnancy in the US decreased over the last decade, from 20% prior to 2001 [73] to 10.2% in 2011-2013 [74] while in Europe rates range from 25% in Spain to 79% in the United Kingdom and Ireland [75]. However, in Italy, a multicenter analysis indicated considerable variability in the prevalence of fetal exposure to ethanol in different Italian cities, as determined by the objective measurement of biomarkers in meconium. These data, together with those obtained in Barcelona, Spain, indicate that gestational ethanol exposure is widespread, at least in parts of Europe [76]. Thus, the identification of women still drinking during pregnancy has main implications for prevention.

When investigating about alcohol consumption issues arise as very often inaccurate reports of self-drinking were reported. One of the main issues is the social stigma attached to alcohol consumption: especially during pregnancy the perception of a stigma can create embarrassment in giving honest answers and determining underestimation of the personal consumption [77].

Several methods and instruments have been developed to standardize the assessment to enhance the chance of a realistic evaluation of consumption. A commonly used method is the quantity/frequency/variability that evaluates mean amounts consumed per day, their frequency and whether peaks of consumption may occur [78]. According to this method, questions may be: on a typical day when you drink, how many drinks do you have? On average, how many days per week do you drink alcohol? What is the maximum number of drinks you had on any given occasion during the last month?

The Timeline Follow-Back is another commonly used method [79], where questions are made anchoring them to important events in the past such as holidays and parties to facilitate recollection of personal drinking behavior. Questions can be asked also referring to the last week. This method may increase the chances of a more accurate personal consumption recalling but it lacks to evaluate consumption in less regular drinkers, especially during pregnancy [80].

In general, it is recommended to imbibe questions about drinking in the context of a diet diary, always on the purpose of avoiding social stigma [81].

Moreover, persons may not be able to exactly evaluate amounts and frequency of their drinking because of the several different sizes of existing glasses. People can be helped in correctly identifying quantities by showing them visual aid such as pictures depicting standard drinks and glass sizes of different kind of alcoholic beverages [82].

Many screening tests have been developed to identify at risk consumption in the general population but they often fail when used to identify pregnant women at risk [83] because they target men's patterns of consumption more than women and because they are aimed at identifying addiction, that is not a very common situation in prenatal care (Table 2). However, specific screening instruments for pregnant women have been developed. A review [84] compared 7 different screening tests and 3 of them showed more sensitivity and higher specificity: the TWEAK [85], the AUDIT-C [86] and the T-ACE [87] (Figure 1). Particularly, the AUDIT-C showed the highest sensitivity in identifying pathologic abuse. Chang [83] compared the T-ACE with three widely used screening tests: the AUDIT [88], the SMAST [89] and medical records of patients. The T-ACE resulted the

**Table 2:** Questions from T-ACE, TWEAK and AUDIT-C.

<b>T-ACE [73]</b>	
<b>T</b>	Tolerance: How many drinks does it take to make you feel high?
<b>A</b>	Have people Annoyed you by criticizing your drinking?
<b>C</b>	Have you ever felt you ought to Cut down on your drinking?
<b>E</b>	Eye opener: Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?
<b>TWEAK [71]</b>	
<b>T</b>	Tolerance: How many drinks can you hold?
<b>W</b>	Have close friends or relatives Worried or complained about your drinking in the past year?
<b>E</b>	Eye Opener: Do you sometimes take a drink in the morning when you get up?
<b>A</b>	Amnesia: Has a friend or family member ever told you about things you said or did while you were drinking that you could not remember?
<b>K(C)</b>	Do you sometimes feel the need to Cut down on your drinking?
<b>AUDIT-C [72]</b>	
1)	How often do you have a drink containing alcohol?
2)	How many units of alcohol do you drink on a typical day when you are drinking?
3)	How often have you had 6 or more units if female, or 8 or more if male, on a single occasion in the last year?

#### Questions from T-ACE, TWEAK and AUDIT-C

##### T-ACE [73]

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##### TWEAK [71]

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- A** Amnesia: Has a friend or family member ever told you about things you said or did while you were drinking that you could not remember?
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##### AUDIT-C [72]

- 1) How often do you have a drink containing alcohol?
- 2) How many units of alcohol do you drink on a typical day when you are drinking?
- 3) How often have you had 6 or more units if female, or 8 or more if male, on a single occasion in the last year?

**Figure 1:** Questions from T-ACE, TWEAK and AUDIT-C.

more sensitive in the detection of current alcohol consumption, risky drinking, and diagnoses of alcohol problems according to DSM-III-R during lifetime [69, now DSM-V].

Data from a recent pilot study among an Italian nonclinical population of 123 pregnant women who volunteered to be interviewed, compared the efficacy of three different methods to investigate alcohol consumption during pregnancy [90]. The first one was a weekly diary evaluating both food and beverage consumption, the second one was the WHO's AUDIT test for the detection of problematic drinking and the T-ACE screening test was the third one. Results showed that the weekly diary identified more drinking women compared to the AUDIT ( $p < 0.01$ ). Also, any of the screened women scored positive values for risky drinking through the AUDIT, while the T-ACE identified 2.2% of the screened women as at risk. These women answered they needed more than 2 drinks before feeling high (the cut-off point to the T-ACE question about tolerance; it scores 2 points, thus identifying the at-risk drinker). None of them scored positive values to the T-ACE because of positive answers to the other questions, thus showing the ability of the tolerance question alone, to screen at risk consumption. This question, in fact, is less sensitive to social stigma and has more chances to get honest answers, and at the same time it tells a lot about habits of consumption, as tolerance represents the diminished response to alcohol-induced by repeated

or prolonged exposure to it.

Biomarkers also can be used in order to identify at-risk women and children. Fatty acid ethyl esters (FAEEs) traced in the meconium can be a marker of alcohol consumption occurred during the second and the third trimester of pregnancy, as this non-oxidative metabolite accumulates in the meconium when alcohol is metabolized [91]. It has been shown that in Spain the 45% of the meconium samples exceeded the cut-off limit ( $> 2 \text{ nmol/g}$ ) [92] while in the above mentioned Italian multicentric study different rates of alcohol exposition were discovered, ranging from 0% to 29.4% [76]. This method could be considered useful to identify high-risk children, even if it does not allow prenatal identification. To overcome this limitation, FAEEs can be traced also in maternal hair [93]. At present, other biomarkers are studied such as micro-RNA and potential proteomic and metabolic markers [94].

#### Intervention Protocols

According to official statements by governmental agencies and medical boards, the best practice is to suggest total abstention from drinking during pregnancy. The American College of Obstetricians and Gynecologists and the American Academy of Pediatrics, as well as the U.S. Office of the Surgeon General and the U.S. Department of Health and Human Services, underlined the crucial role that

health care providers can play in informing, counseling and referring women at risk for an alcohol-exposed pregnancy [95].

Prevention efforts should start before pre-conceptual period to target women of childbearing age [96]. The American Center for Disease Control and Prevention (CDC) in 2008 recommended to screen for alcohol use all childbearing-aged women. Undergoing a screening for alcohol use can itself induce a reduction in alcohol consumption [97]. CDC also strongly recommended giving information on the consequences of alcohol use during pregnancy. A pilot prevention study showed that in a general population of pregnant women those who were informed about the risks related to alcohol consumption in pregnancy drank less than those who could not correctly identify them, as well as women who had been exposed to preventive leaflets compared to those not exposed [57]. Pregnancy, in fact, is believed to be a moment in which women are very motivated to protect baby's and their own health [98].

However, the only information on alcohol related consequences may not be effective in heavier drinkers. Handmaker et al. [99] showed that mailing a letter or delivering a motivational session were both effective in reducing alcohol use in a group of pregnant women, but only the motivational session was effective in reducing consumption in heavy drinkers.

Hence, it is important to identify women at higher risk to deliver affected children. Taking into consideration literature-based risk factors discussed above can be helpful in the process of identification of at-risk patients. Pregnant women consuming more than one drink per day and/or binging must be considered at risk, but also heavy drinking women before pregnancy, or showing a high tolerance or also preferring a variety of alcoholic beverages should be addressed for preventive interventions.

Motivational sessions [100] and brief interventions [101,102] have been proved to be effective in reducing alcohol use in at-risk women. Both interventions can be used by professionals not specialized in alcohol abuse treatment and are low-cost not time-consuming interventions [95]. The Acronym FRAMES is used to resume key elements in effective interventions: feedback on personal risk; personal responsibility, advise for a change; a menu of strategies to cut on drinking; empathic communication style; focus on self-efficacy [103].

The highest at-risk women are those consuming both alcohol and drugs and those who have already delivered a FASD child. Chances to have another affected child may be as high as 75% [104,105]. When facing these cases, treatment is complex and includes intensive case management and deep collaboration among several agencies and health services. Also, effective contraceptive counseling is needed and women abusing alcohol should be referred for an addiction treatment program in specialized units [19,95].

Based on these considerations, a standardized protocol is recommended, to prevent alcohol-exposed pregnancies. First, universal preventive actions to prevent alcohol-exposed pregnancies targeting all the women of childbearing age have to be undertaken: questions inquiring alcohol consumption should be routinely included in patient's anamnesis. Alcohol anamnesis should be performed in the context of a general investigation about eating habits. Whether they drink or not, all the women have to be informed about consequences linked to alcohol use in pregnancy and be suggested to suspend consumption if planning a pregnancy. Second, when targeting pregnant women, detection of alcohol consumption and screening tests are needed. After having carried out the alcohol anamnesis, patients can be grouped in four categories, each requiring specific interventions.

1. Not at-risk women: women who do not drink during pregnancy. Reaffirming the importance of total abstention can be useful to reinforce behavior and to have women spreading the health message in their personal environment.
2. Mild risk women: women consuming alcohol occasionally

or less than one drink per day and not binging. As a safe threshold has not been established yet, all women consuming any amount of alcohol in pregnancy is considered potentially at risk and should be informed about the risks for the babies; total abstention from alcohol has to be recommended. In this case, a single brief counseling session could be enough to ensure a safe pregnancy.

3. At-risk women: women presenting one or more among risk factors. The following risk factors should be considered: consumption of more than one drink per day or three or more in a single occasion; variety of beverages consumed; positive answer to the T-ACE question about tolerance (two drinks or more needed to experience some alcohol effects), presence of heavy drinking before pregnancy, partner's problematic alcohol consumption and alcohol problems in family environment. These women may need more structured counseling sessions following the FRAMES model cited above, to enhance chances of a behavioral change.

4. High-risk women: when there are clear evidence of abuse and addiction or women with established heavy alcohol-exposed pregnancy or women who have already delivered an affected child, it is strongly recommended to refer the patient to a proper alcohol treatment units, and work together to maximize chances of a safe pregnancy.

Early detection of alcohol consumption during pregnancy is essential both for its preventive and therapeutic implications. While a simple suggestion by professionals' can persuade mild drinkers to give up consumption, when damage has not occurred yet, the knowledge that a pregnancy is at risk for alcohol consumption allows particular interventions also through nutritional supplementation. Indeed, optimal maternal nutritional status is of utmost value for proper fetal development frequently altered with alcohol consumption. Indeed several investigations in animal models and humans addressed the role of prenatal nutrition as possible interventions for FASD throughout several nutrients supplementation (vitamin A, docosahexaenoic acid, folic acid, zinc, choline, vitamin E, and selenium) that may prevent or counteract the development of FASD [106].

## Conclusion

The burden of lifelong disabilities caused by alcohol exposure during pregnancy is extreme at individual, familial and societal level. In latest years the adoption of active case ascertainment methods for establishing prevalence in general population revealed higher rates than those estimated through passive surveillance methods or clinic studies. Public agencies all over the world underline the crucial importance of prevention through the enactment of laws on labeling alcoholic beverages and the release of health statements recommending total abstinence from alcohol during pregnancy and lactation as the unique way of prevention. As far as a safe consumption behavior cannot be established, for the extremely individual conditions of susceptibility to alcohol, risk factors should be screened and addressed in women of child bearing age. Furthermore, the early detection of alcohol drinking during pregnancy may be mostly helpful in therapeutic interventions rather than prevention of FASD. This is because in most cases, the embryos exposed to alcohol during the first trimester of pregnancy may have higher tendency to develop FASD. Obstetrics and gynecologists are in the first line to face the issue and can do a lot in preventing FASD by routinely performing an alcohol anamnesis during prenatal care and before it. Gaining a realistic estimation of patient's alcohol intake is possible if validated instruments and methods are adopted. Professionals dealing with women health can be trained to perform accurate alcohol anamnesis, screening and brief counseling interventions. Fostering these skills will permit them to adopt protocols matching risky conditions with proper interventions to maximize the possibility of a healthy pregnancy.

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