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Italian Guidelines for the diagnosis and treatment of Fetal Alcohol Spectrum Disorders: epidemiology

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Summary. Fetal alcohol spectrum disorders (FASD) are a significant global challenge characterized by complex diagnosis and research. The diagnostic process is complicated due to overlapping symptoms with other conditions, as well as factors such as maternal nutrition, socioeconomic status, and mental health, which can affect the severity of FASD traits differently in individuals. Risky drinking behaviors are prevalent in young adults, especially those aged 20-24, which coincides with high rates of unplanned pregnancies, increasing the risk of FASD. Specific subpopulations, such as children in care facilities and specialized clinical settings, face higher FASD prevalence. Preventing alcohol consumption during pregnancy is crucial for maternal and fetal well-being. Yet approximately 10% of women worldwide continue to drink during pregnancy, with notably high rates in the European Region. Young adults, especially in countries like Italy, continue to consume alcohol despite legal restrictions, mirroring the drinking patterns of men and raising concerns for fetal health and development. Research findings regarding alcohol's risks during pregnancy vary, emphasizing the need for increased education on this issue. Ethylglucuronide (EtG) is a reliable biomarker for monitoring alcohol intake during pregnancy, suggesting regular urine examinations throughout each trimester. Proactive education campaigns, particularly in educational institutions, and establishing early diagnosis centers are recommended to address FASD effectively.

Key words. Alcohol, disability, epidemiology, FASD, gestation, pregnancy.

Linee guida italiane per la diagnosi e il trattamento dei disturbi dello spettro feto-alcolico: epidemiologia

Riassunto. I disturbi dello spettro feto-alcolico (FASD) rappresentano una sfida globale significativa caratterizzata da diagnosi e ricerca complesse. Il processo diagnostico è complicato a causa della sovrapposizione dei sintomi con altre condizioni, nonché da fattori quali nutrizione materna, stato socio-economico e salute mentale, che possono influenzare la gravità dei tratti FASD in modo diverso negli individui. I comportamenti rischiosi legati al consumo di alcol sono prevalenti nei giovani adulti, in particolare quelli di età compresa tra 20 e 24 anni, il che coincide con alti tassi di gravidanze indesiderate, aumentando il rischio di FASD. Sottopopolazioni specifiche, come i bambini in strutture di assistenza e contesti clinici specializzati, affrontano una maggiore prevalenza di FASD. Prevenire il consumo di alcol durante la gravidanza è fondamentale per il benessere materno e fetale. Tuttavia, circa il 10% delle donne in tutto il mondo continua a bere durante la gravidanza, con tassi notevolmente elevati nella regione europea. I giovani adulti, in particolare in paesi come l'Italia, continuano a consumare alcol nonostante le restrizioni legali, rispecchiando i modelli di consumo di alcol degli uomini e sollevando preoccupazioni per la salute e lo sviluppo fetale. I risultati della ricerca sui rischi dell'alcol durante la gravidanza variano, sottolineando la necessità di una maggiore istruzione su questo tema. L'etilglucuronide (EtG) è un biomarcatore affidabile per monitorare l'assunzione di alcol durante la gravidanza, suggerendo esami regolari delle urine durante ogni trimestre. Sono raccomandate campagne di istruzione proattive, in particolare nelle istituzioni educative, e l'istituzione di centri di diagnosi precoce per affrontare efficacemente la FASD.

Parole chiave. Alcol, disabilità, epidemiologia, FASD, gestazione, gravidanza.

Introduction

Fetal Alcohol Spectrum Disorders (FASD) are a prevalent issue worldwide[1,2]. Prevalence estimates are crucial for various reasons, including setting public health policy priorities, securing funding for public health initiatives, planning healthcare strategies, allocating resources for healthcare and prevention, and planning and delivering healthcare to high-needs populations[3]. Diagnosing the epidemiological aspects of FASD and alcohol consumption during pregnancy is a challenge due to the difficulties of ac-

curate diagnosis. It is crucial to acknowledge that the data currently available on FASD[2,4-10] may not always reflect precisely the actual epidemiological situation due to various methodological and behavioral concerns in the studies.

Methodological and behavioral concerns

Research methods

Currently, FASD is diagnosed by eliminating other genetic pathologies that may cause similar symptoms in children. Furthermore, four common approaches were used to determine the prevalence of FASD. These include: 1) surveillance record systems[11,12]; 2) individual studies in existing prenatal clinics[13]; 3) meta-analyses of multiple individual studies that use various methods[14]; and 4) active case ascertainment in a circumscribed population[15]. One of the most effective ways of identifying cases has been active case ascertainment (ACA), which is typically used in specific and receptive populations[15]. It has been observed that Alcohol-Related Neurodevelopmental Disorder (ARND) cases are more likely to be found in simple random samples when preliminary screening for size or dysmorphic traits is not available[16]. The main guidelines emphasize the importance of conducting a thorough morphological examination of the child and using specific questionnaires to detect complex responses. It is crucial to detect behavioral and cognitive changes related to FASD. Additionally, it is critical to confirm the mother's alcohol intake during the perinatal period. Recent research has shown that some children may exhibit FASD symptoms due to paternal alcohol consumption[17,18].

Additionally, some experts believe that many children with neurodevelopmental issues caused by alcohol may not have the physical features of FASD and may instead present with an ARND diagnosis. Moreover, it is still uncertain today[19,20] what the exact criteria are for Alcohol-Related Birth Defects (ARBD) and ARND, which used to be known as fetal alcohol effects[21].

Different populations

The considerations for studying child development should include differences in the studied populations, methods for identifying cases, sample collection, diagnostic criteria, and coordination of interdisciplinary activities[21]. In addition, it is essential to consider the calendar years/cohorts in which the studies were conducted, age stratification within the samples, and various mental health issues the subjects may be experiencing. The four different diagnostic types of FASD – Fetal Alcohol Syndrome (FAS), partial FAS (pFAS), ARND, and ARBD – vary in their presentation. The severity of these traits among individuals also varies within each type. Most of this variability can be attributed to the effects of alcohol teratogenicity. The amount, frequency, and timing of maternal drinking during pregnancy can significantly affect the physical, cognitive, and behavioral traits associated with FASD[22,23]. It is crucial to acknowledge that pregnant women who consume excessive amounts of alcohol are often observed to use other drugs during pregnancy and even after childbirth[24,25]. Such concurrent substance abuse can result in more severe physical abnormalities, developmental delays, and significant variation in the offspring[24,26].

While there are proximal risk factors like prenatal alcohol and other teratogenic drugs, many different factors beyond genetics and epigenetics of both parents also contribute to the severity and variation of child outcomes[27]. For example, the nutritional status of a pregnant woman significantly impacts the child's development. Several studies have indicated that different dietary deficiencies can lead to physical abnormalities, cognitive and behavioral delays, and even growth restrictions. Therefore, a mother's nutrition during pregnancy is vital for the child's health. Research has also identified various other factors that can increase the risk of FASD. Common risk factors for FASD include socioeconomic status, marital status, religion, number of pregnancies, access to prenatal care, timing of prenatal care, maternal mental health, intimate partner violence, and age at pregnancy[27-31].

Age of the diagnosis

Globally, it's tough to gather systematic data on the prevalence and distribution of FASD and FAS. Studies on their incidence and prevalence are limited, and diagnostic criteria vary across regions. Misdiagnosis or missed diagnosis of FASD can lead to secondary disabilities such as school failure and psychiatric problems[32]. It is worth noting that around 70% of children with FASD have not been diagnosed, and another 7% have been misdiagnosed[32-34]. This is because many neurocognitive domains and functioning domains, such as academic, adaptive, behavioral, emotional, and social, have common symptoms with other disorders, such as Attention-Deficit/Hyperactivity Disorder (ADHD), Intellectual Disability, Oppositional Defiant Disorder, Conduct Disorder, Reactive Attachment Disorder, and Communication Disorders[33,34].

Alcohol consumption during the reproductive age

Numerous international institutions provide valuable insights into alcohol consumption among women of childbearing age and the prevalence of alcohol use disorders and dependence among adult women

(15 years and older). These insights can help us better understand the impact of alcohol on women's health and well-being and guide efforts to promote healthier habits[35]. The most reliable measure of alcohol use is the adult per capita consumption of alcohol (APC). This measure is based on taxation data, production statistics, and population surveys. In 2019, the global APC for women of childbearing age was 2.2 APC, which varied by region, from 0.1[36] in the Eastern Mediterranean to 4.0 l in Europe (table 1).

Countries with high-income economies had the highest APC, followed by upper-middle, lower-middle, and low-income economies. The European region had the highest prevalence of drinking among childbearing-aged women (53.9%), while the Eastern Mediterranean region had the lowest (1.3%). Approximately 8.7% of women of childbearing age worldwide engaged in heavy episodic drinking[6]. This is defined as consuming at least 60 grams of pure alcohol on at least one occasion in the past 30 days[37].

Alcohol consumption during pregnancy

Research shows that pregnant women must avoid alcohol to ensure their health and the health of their babies. Many countries actively educate women of childbearing age about these harmful effects, using clinical guidelines produced by reputable organizations[38-40]. It has not been determined what amount of prenatal alcohol exposure is safe[41]. Therefore, international guidelines recommend that pregnant women should avoid drinking any amount or type of alcohol[42-44].

Despite these efforts, however, around 10% of women worldwide continue to consume alcohol during pregnancy[8,45]. It is essential to spread awareness about the dangers of alcohol consumption during pregnancy to ensure the health and well-being of both mothers and their babies. According to literature reviews and meta-analyses[8], the use of alcohol during pregnancy is most prevalent in the WHO European Region, with an estimated rate of 25.2%[46]. This is not surprising given that the latest Global Status Report on Alcohol and Health[47] ranks the European region has the highest alcohol consumption and alcohol use disorder rates. More than 25% of pregnant women engage in binge drinking, which is concerning. Binge drinking is defined as consuming five or more drinks for men and four or more drinks for women on a single occasion[48,49].

This type of drinking increases the risk of FASD, which is common in early pregnancy and before pregnancy recognition. Unfortunately, many fetuses are inadvertently exposed to alcohol because binge drinking is prevalent in young women[47] who have alcohol-related, unprotected sex or unplanned pregnancies[50,51]. It is a heart-wrenching reality that some Indigenous populations in Australia, South Africa, and Canada suffer from higher rates of alcohol use during pregnancy. The context of disadvantage, violence, and the ongoing traumatic effects of colonization often compounds this issue[52]. We must acknowledge and address these challenges to ensure the health and well-being of these vulnerable communities. According to studies, the percentage of women who binge drink ranged from 10.7% in Europe to 31% in Africa[37].

Table 1. Total per capita (15 years of age and older) consumption (in liters of pure alcohol).

WHO Region	Both sexes	Male	Female
Africa	5.5 [4.8-6.2]	8.7 [7.7-9.9]	2.2 [1.9-2.5]
Americas	7.5 [6.3-8.7]	11.9 [10.1-13.8]	3.3 [2.7-3.8]
South-East Asia	3.8 [2.3-5.6]	6.4 [3.7-9.2]	1.2 [0.7-1.8]
Europe	9.2 [8.4-10.0]	14.9 [13.6-16.2]	4.0 [3.6-4.4]
Eastern Mediterranean	0.3 [0.2-0.5]	0.5 [0.4-0.9]	0.1 [0.0-0.1]
Western Pacific	6.1 [4.3-7.9]	9.6 [6.8-12.5]	2.5 [1.8-3.2]
Global	5.5 [4.8-6.2]	8.7 [7.7-9.9]	2.2 [1.9-2.5]

Modified by: WHO[46].

Prevalence of FAS and FASD in the general population

FASD Prevalence in the World

Fifteen population-based studies on FASD have been conducted in North America and Europe in recent years[53]. The estimated global prevalence of FASD is 7.7 cases per 1,000 individuals[37,54]. FASD prevalence is highest in the WHO European Region (19.8 per 1,000) and lowest in the WHO Eastern Mediterranean Region (0.1 per 1,000)[37,54], which is consistent with rates of alcohol use during pregnancy (table 2). The prevalence of Fetal Alcohol Spectrum Disorder (FASD) varies across different countries. The highest rates are found in South Africa, Croatia, Ireland, Italy, and Belarus, while some countries in the Middle East report no cases. FASD in 76 nations has a prevalence of >1%, more than the prevalence of neurodevelopmental conditions, such as Down syndrome, Edwards syndrome, spina bifida and anencephaly in the USA, and is similar to the prevalence of autism spectrum disorders[55].

It is worth noting that risky drinking is most found among adolescents and young adults, particularly those aged between 20-24 years. This age group also experiences the highest incidence of unplanned

Table 2. FASD prevalence in some countries.

Countries	FASD prevalence ‰
WHO European Region	19.8
WHO Eastern Mediterranean Region	0.1
South Africa	111.1
Croatia	53.3
Ireland	47.5
Belarus	36.6

Modified by: Lange et al.[54].

pregnancies. Consuming alcohol during pregnancy increases the risk of FASD in the child. One in every 13 pregnant women who drink alcohol during pregnancy will deliver a child with FASD, and the probability of providing a child with FAS is estimated to be 1 in 67 women[8].

FASD prevalence in special populations

FASD prevalence can be up to 40 times higher than in the general population in specific subpopulations[56]. A recent systematic review and meta-analysis[2] shows this elevated prevalence in children in out-of-home care, correctional facilities, special education programs, and specialized clinical settings (tables 3 and 4).

Table 3. FASD prevalence in specific subpopulations[2].

Countries	Prevalence %
Canada	
Youth correctional services	> 23
Correctional system[2]	14.7
USA	
Foster care/out-of-home care[2]	25.2
Correctional system	14.7
Psychiatric care	14.0
Chile	
Foster care/out-of-home care[2]	31.2
Special education[2]	8.4
Intellectual disabilities in care[57]	62.0
Eastern Europe	
Adopted[58,59]	> 50
Russia	
Children with developmental abnormalities in orphanages[45]	46-68
Lithuanian	
Orphanages[60]	40
Australia	
Indigenous communities[61]	19
Youth Correctional Service[62]	36

Modified by: Popova et al.[2].

Alcohol consumption in Italy

In Italy, it's illegal to sell or serve alcohol to those under 18 due to the potential health risks associated with alcohol consumption at a young age. This vulnerability is significantly pronounced in ages 12 through 25[84]. The toxic effects of alcohol on neurons can cause irreparable damage to the brain's modulation and functional maturation. According to data from ISTAT in 2022 from individuals aged 11 and above, there is a significant concern in Italy.

According to the ISTAT survey, there has been an increase in alcohol consumption occasionally and between meals in recent years[85]. Risky alcohol consumption habits are particularly prevalent among individuals aged between 18 and 24 years. Among boys, risky alcohol consumption is about twice as high as in girls. Young people are consuming less alcohol compared to the general population. However, the data show that around 1,057,509 young people between ages 11 and 17 (584,212 boys and 473,297 girls) and 3,249,079 young people aged between 18 and 24 (1,788,470 boys and 1,460,609 girls) still consume alcohol[86].

Moreover, the number of young people drinking between meals has increased by 2,295,411. Approximately 10.1% of young people engage in binge drinking. The statistics regarding binge drinking among young people are alarming, especially among those aged 18-24. According to the data, 22.6% of males and 11.1% of females in this age group binge drink. In the 15-17 age group, approximately 421,573 young people engage in binge drinking, out of which 274,803 are boys and 146,770 are girls. In a study by Addolorato et al.[85], a diagnosis of AUD was made in 6-10 % of adolescents. The prevalence of alcohol use disorder (AUD) was higher in adolescents who reported binge drinking (BD) behavior than in those who did not report BD, supporting the conclusion that alcohol consumption with the pattern of BD among adolescents is highly related to the development of AUD[85]. This trend is concerning because the WHO has stated that consuming alcohol before the age of 21 can negatively impact the health and psychophysical development of young individuals. Moreover, in recent years, the drinking habits of young women have become increasingly like those of young men.

Over the past decade, the number of women who occasionally consume alcohol has risen from 38.8% to 45.3%. Furthermore, the number of women who drink alcohol outside of mealtimes has almost doubled, increasing from 14.2% to 22.4%[85]. The consumption of alcoholic beverages among young people remains a critical issue, and it is essential to maintain a high level of attention on this segment of the population.

Table 4. Study Characteristics and Prevalence of FASD Among Children and Youth in the General Population[54].

Source and Refs	Country	Sample size (n)	Prevalence per 1,000	Guideline	Age range (Y)	Method
African Region						
Chersich et al.[63]	South Africa	809	89.0	TOM	9.5-11.0	ACA
Chersich et al.[63] Davies et al.[64] May et al.[65]	South Africa	818	89.2	TOM	6-7	ACA
May et al.[65,66]	South Africa	155	207.5	IOM	6-7	ACA
Olivier et al.[67,68]	South Africa	1830	88.0	IOM	4.8-16	ACA
Urban et al.[69]	South Africa	1503	63.9	IOM	6-7	ACA
European Region						
Petković & Barišić[70]	Croatia (urban)	466	40.8	IOM	6.6-11.1	ACA
Petković & Barišić[71]	Croatia (rural)	824	66.8	IOM	7-11.9	ACA
Bloch et al.[72]	France	45.919	0.4	Case definition	0-1 Newborns	Clinic based
Lange et al.[54]	France	8284	5.4	Case definition	0-1 Newborns	Clinic based
Lange et al.[54]	France	5000	5.6	Guidelines by ASG of RSA		ACA
Serreau et al.[73]	France	1320	66.0	IOM		
May et al.[74]	Italy (Lazio)	543	40.5	IOM	6-7	ACA
May et al.[75]	Italy (Lazio)	976	47.1	IOM	6-7	ACA
Elgen et al.[76]	Norway	29.091	1.1	CDC diagnostic guidelines		ACA
Region of the Americas						
Lange et al.[54]	Canada	33.485	5.3	Guidelines established by ASG of RSA	0-16	ACA
Barr & Streissguth[77]	USA	1439	25.0	Case definition	0-7	Clinic Based
Konstantinidou et al.[20]	USA	3740	7.0	4-Digit Code	6.7	ACA
Lange et al.[54]	USA	1690	21.9	Guidelines established by ASG of RSA		
May et al.[78]	USA	1433	33.5	IOM	6-7	ACA
May et al.[79]	USA	2334	11.1	IOM	6-7	ACA
Poitra et al.[80]	USA	1384	5.1	Criteria by (81)	5-6	ACA
Western Pacific Region						
Elliot et al.[82]	Australia	1.533.333	0.1	IOM	0-15	ACA
Harris & Bucens[83]	Australia	25.209	1.7	Adapted 4-digit code and the criteria by the AAP	0-10	Mixed Methods (passive, surveillance and clinic based)

Legend: AAP= American Academy of Pediatrics; CDC= Centers for Disease Control and Prevention; ACA= Adult Children of Alcoholics; IOM= Institute of Medicine; ASG= Alcohol Solutions Group; RSA= Research Society on Alcoholism.

A report by the Adolescent Observatory of Blue Telephone and DoxaKids (https://lc.cx/CXW5U8) reveals that more than half (50.6%) of teenagers aged 11 to 19 have experimented with alcohol, and nearly half (49.9%) have been drunk at least once. These data are concerning as they apply to both young adults and the future ruling class, who will set an example for many.

Alcohol consumption during pregnancy and FASD in Italy

It is worth noting that many Italian women drink moderate amounts of alcohol on a daily or frequent basis. While some studies have reported cases of children born with fetal alcohol syndrome (FAS) in Italy[87-91], several other studies have found no evidence of a link between maternal alcohol consumption and

Table 5. Several children are potentially exposed per year by the ACA method and ECG evaluation in hair and meconium.

Study	Method	Population	Method	Results ‰ births	Children potentially involved*
May et al.[109]	ACA	First-grade school children	ACA: FASD Tot. (I.C. ± 95%)	47.1 ‰ (33.4-62.6)	17.898 (12.692-23.788)
La Maida et al.[112]	Hair EtG	Women in pregnancy (Italy)	PAE Hair EtG (+)	59.5	22.420
	Meconium EtG	Newborn	PAE Meconium EtG (+)	7.4	2.812
Ceccanti M. (Data not published)	Hair EtG	Women in pregnancy (Rome)	PAE Hair EtG (+)	82.0	31.160
	Meconium EtG	Newborn	PAE Meconium EtG (+)	193.0	73.340
Ceci et al.[113]	EtG Urine	Women in pregnancy (Rome)	PAE Urine EtG (+)	204.0	77.520

Legend: ACA= Adult Children of Alcoholics; PAE= Prenatal Alcohol Exposure; EtG= Ethylglucuronide.
* The data is reported by calculating an average of 380,000 births annually.

pregnancy loss or reduced birth weight[92-95]. However, an article from Italy has suggested that prenatal alcohol use and smoking could lead to low birth weight, highlighting the need for expectant mothers to be cautious about their drinking habits[96]. In Italian hospitals, over one-third of women giving birth are daily drinkers. Even after recognizing their pregnancy, many continue to drink[97,98]. It highlights the need for more education about the risks of alcohol consumption during pregnancy. In the Bonati study[97], maternal drinking did not significantly correlate with lower birth weight. However, birth weight was affected by "abuse" drinking, and alcohol abuse and binge drinking were found to be rare among women. Primatesta et al.[92] reported low rates of pre-pregnancy binge drinking (1.4%) among women in Milan. However, their data indicated that 9% of women reported risk to hazardous average weekly alcohol consumption, and 29% of women drank daily during pregnancy, which was considerably higher rates than those reported in the US recruitment.

Current methods for detecting FAS and FASD can underreport prevalence and only identify the most severe cases[98,99]. It is crucial to identify cases of FAS and FASD in children actively. Without active case ascertainment, many children with FAS and FASD may go undetected, leading to a lack of proper diagnosis and care. Unfortunately, the referral process is selective, and there is a lack of active outreach, resulting in a shortage of defined cases in the literature from FAS to ARND. Active case ascertainment studies are used to identify instances of FASD by conducting structured outreach in a specific population[100,101]. These studies used an active outreach system to refer children to specialized clinics[20,100-104].

FASD prevalence in Italy

Research shows that relying only on maternal self-reports of alcohol consumption during pregnancy can be unreliable due to recall bias, shame, and fear of stigma. Our 2002 research (unpublished data) found that 12% of pregnant women may consume more than 14 drinks per week. Alcohol consumption was measured using dietary information and various questionnaires and tools[105-108].

FASD prevalence first-grade school children, ACA method

Based on this knowledge, Lazio Region sponsored research in agreement with NIH-NIAAA, USA, on first-grade school children six years old living in the nearby Rome area. A study[109] conducted between 2005-2006 using the ACA method and IOM guidelines found the rate of FAS was 8.2 per 1,000 children; the rate of PFAS was four times higher than FAS at 36.9 per 1.000. The overall rate of FASD was 47.1 per 1,000 (95 % CI, 33.4-62.6) or 4.7%[109]. In this same study, an internal random sample was also employed to capture representative control individuals. Within this random sample, nine children were diagnosed with an FASD, which produced a weighted, estimated rate of 59.4 per 1,000 or 5.9%[108].

Prenatal alcohol exposure: ethyl glucuronide in the hair and meconium

Many studies have focused on identifying a specific marker to overcome the underestimation of alcohol consumption during pregnancy. Ethylglucuronide (EtG) is a reliable biomarker that can be used to

assess alcohol consumption during pregnancy[110]. It is a direct by-product of ethanol and can be measured in maternal hair or neonatal meconium to determine prenatal alcohol exposure.

A multicenter study was conducted in 2010 across seven neonatology wards in Italy to determine the extent of prenatal exposure to alcohol in pregnant women[111]. The study measured EtG levels in neonatal meconium and found that 7.9% of the 607 newborns assessed were prenatally exposed to gestational alcohol. While the prevalence of alcohol exposure varied across the Italian peninsula, ranging from 0% to 10%, the country's capital, Rome, had the highest value of 29.4%. Interestingly, between 20% to 30% of pregnant women who reported drinking while pregnant had newborns exposed to gestational alcohol[111]. Recently, a national study was conducted to assess fetal alcohol exposure through meconium EtG testing and verify gestational alcohol consumption with EtG measurement in maternal hair during pregnancy[112]. The same research includes data obtained in Rome: the results are reported in table 5 and deal with the general study[112] and ACA results[109], suggesting exciting observations:

- the data in table 5, particularly in the column "Children potentially involved", show results very close to those obtained with the ACA method and EtG assessments, especially the weighted, estimated rate of 5.9%. However, there is a difference in the case of Meconium EtG in the general population. This difference could be attributed to various factors, such as differences in drinking behaviors across different cities, variances in the consensus for meconium collection, and variations in the methods used to preserve and transport samples to centralized laboratories;
- it should be noted that the study conducted in Lazio[75], which focused on small towns in the countryside of central Italy, may not be representative of alcohol consumption trends throughout the country. However, based on our knowledge, the drinking habits observed in this region represent the average level of alcohol consumption in all Italian regions[86]. These health districts are considered relatively representative of central Italy[75];
- moreover, meconium studies can rarely be used in population health because it is difficult to obtain large representative samples using this technique[3];
- one of the most significant limitations of these studies' prevalence calculations is the consent rate. The fact that consent to participate was obtained for only 50% of the children in the ACA randomly selected schools introduces potential bias, which is difficult to account for. The authors introduced a method of correction described in the manuscript. In EtG studies, we found incomplete responses on drinking habits in most questionnaire items[112].

Discussion and conclusions

The epidemiological data related to alcohol exposure in utero, including the prevalence of alcohol consumption during pregnancy and FASD, are often heterogeneous and underestimated. Detecting alcohol consumption is challenging due to social stigma and is particularly sensitive when interviewing pregnant women. This issue is confirmed by a study comparing consumption questionnaires with measurements of EtG[113-115]. Based on the data we have gathered, we acknowledge the potential of EtG in hair and meconium testing. I believe it's more practical to detect EtG through urine examination twice a week (Mondays and Thursdays) during each trimester of pregnancy to cover a whole week. Hair and meconium testing is expensive and not easily accessible and is only recommended for research. The interviewing method used to gather information on consumption behavior can influence results, with some methods being more sensitive and others potentially exacerbating social stigma.

The methods used also heavily influence prevalence studies of FASD. Passive studies, which seek diagnoses in discharge registries, yield estimates much lower than those obtained through the active case ascertainment method. Furthermore, different diagnostic guidelines lead to different numbers depending on the diagnostic criteria.

Therefore, there is a recognized need for the personnel involved to be increasingly comprehensively trained. There are opportunities to improve interviewer skills in conducting alcohol histories, which should be performed following literature recommendations, using the proper method, and in the appropriate context. Above all, the ability to make a correct diagnosis needs to be improved. We also support the establishment of new centers to enable early diagnosis. Although existing data underestimate the problem, the numbers still show a high prevalence of alcohol consumption during pregnancy and a significant prevalence of FASD (as high as 5.9%), highlighting the need for the implementation of appropriate prevention and health promotion measures.

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