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Italian Guidelines for the diagnosis and treatment of Fetal Alcohol Spectrum Disorders: international diagnostic criteria - differences and similarities

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Summary. The umbrella term Fetal Alcohol Spectrum Disorders (FASD) brings together under its definition a heterogeneous continuum of disabilities linked by a common etiology and pathogenesis: exposure to alcohol during intrauterine life. Despite extensive research, definitive toxic thresholds remain elusive, underscoring the recommendation for complete alcohol abstinence during pregnancy and lactation. FASD poses diagnostic challenges due to its varied presentations and heterogeneous phenotype. Consequently, no singular diagnostic guideline exists, with multiple expert-driven diagnostic systems globally available. This review aims to synthesize recent and notable guidelines facilitating FASD diagnosis. While efforts were made to include the latest diagnostic systems, determining which scheme is best applied to each individual patient population necessitates clinician discretion. In Italy, the guidelines proposed by Hoyme, revised in 2016, are commonly utilized, yet comparative analysis among guidelines offers valuable insights into their historical context and diagnostic utility. Our discussion explores both similarities and discrepancies among systems for diagnosing FASD, shedding light on their evolution and practical application. The objective of our work was to compare in a practical and precise manner the various existing guidelines used globally regarding the diagnosis of FAS. Our review therefore proposes the diagnostic criteria used by the various working groups and compares them, trying to create a practical comparison between the various guidelines, identifying differences and similarities.

Key words. Alcohol, children, diagnostic criteria, FASD, guidelines, pediatrician.

Linee guida italiane per la diagnosi e il trattamento dei disturbi dello spettro feto-alcolico: criteri diagnostici internazionali: differenze e somiglianze.

Riassunto. Il disturbo dello spettro feto-alcolico (FASD) riunisce sotto la sua definizione un quadro eterogeneo di patologie accomunate dalla comune eziopatogenesi: l'esposizione fetale all'alcol. Nonostante ricerche approfondite, la soglia tossica non è stata ancora definita, obbligando alla raccomandazione di una completa astinenza dall'alcol durante la gravidanza e l'allattamento. La FASD pone anche sfide diagnostiche a causa della sua presentazione clinica varia e del fenotipo eterogeneo. Di conseguenza, non esiste una singola linea guida diagnostica, ma molteplici linee guida, disponibili a livello globale, redatte in base alle competenze prevalenti degli estensori. Questa revisione mira a sintetizzare le linee guida più utilizzate che consentono la diagnosi di FASD. Sebbene siano stati compiuti notevoli sforzi per sintetizzare le linee guida più recenti, non ne esiste ancora una che racchiuda tutti i criteri contenuti nelle precedenti, pertanto la diagnosi contiene ancora elementi di discrezionalità del medico che la pone. In Italia, le linee guida proposte da Hoyme et al., riviste nel 2016, sono comunemente utilizzate, ma l'analisi comparativa tra le linee guida offre preziosi spunti sul loro contesto storico e sull'utilità diagnostica, ponendo le basi per un'ulteriore proposta che le riassuma tutte. Questo lavoro esplora sia le somiglianze che le differenze tra le varie linee guida esistenti, facendo luce sulla loro evoluzione e applicazione pratica.

Parole chiave. Alcol, bambini, criteri diagnostici, FASD, linee guida, pediatra.

Introduction

The umbrella term fetal alcohol spectrum disorders (FASD) is used to describe the range of possible physical, behavioral and neurodevelopmental effects in individuals with prenatal alcohol exposure (PAE)[1]. In a meta-analysis of 24 studies, which used active case ascertainment or clinic-based methods specifying the diagnostic guideline or case definition adopted, the global prevalence of FASD among children

and youth in the general population was estimated to be 7.7 per 1000, and 1 of 13 pregnant women who consumed alcohol during pregnancy was estimated to deliver a child with FASD[2,3].

Alcohol is a teratogen with significant adverse effects on central nervous system (CNS) development[4-10]. During pregnancy, a safe threshold of amount or time of alcohol consumption has not been established; it is therefore recommended that women completely avoid drinking alcohol while pregnant or trying to conceive, since FASD is the most frequent, totally avoidable and preventable cause of acquired intellectual disability in childhood[4,11-14].

There are no unique physical or neurodevelopmental features that are individually specific or sensitive enough to confirm FASD diagnoses, nor is there a diagnostic laboratory test. Several diagnostic schemes exist. However, despite some shared characteristics, they differ in terminology, sensitivity and specificity, leading to confusion and lower confidence in obtaining a valid diagnosis[15,16].

Here, we briefly review the nomenclature and criteria used by the various diagnostic systems adopted internationally. The main differences usually involve the number of sentinel facial features required to diagnose FASD, cutoffs for inclusion of any specific clinical feature, the inclusion or exclusion of growth deficit as a diagnostic criterion, the type of neurodevelopmental evaluation employed in the diagnostic approach, and the methods to confirm PAE[17,18]. The diagnostic systems discussed in this paper are set forth in table 1.

Historical overview of FASD diagnosis

Despite ancient references to the harmful effects of PAE, the associated physical malformations and neurodevelopmental disabilities were first described in the medical literature in 1968[13,19]. In France, after a 1957 thesis dissertation by Jacqueline Rouquette (describing what was later termed FAS)[20], Paul Lemoine et al. reported on 127 cases of children born to alcoholic women with a singular pattern of morphological and cognitive characteristics[21]. Subsequently, in the USA, in 1973 Jones and Smith analyzed the recurrent pattern of structural alterations in the children of drinking women and coined the term "Fetal Alcohol Syndrome (FAS)"[18,22-25]. More recently, given the wide variety and degree of severity with which the teratogenic effects of PAE can present, and as pediatricians became more familiar with the clinical presentation of PAE, experts in the field advocated for assignment of distinct PAE-related diagnostic categories within a continuum (FASD), from mild to severe[2].

International guidelines and variations

Institute of Medicine Criteria

In 1996, the US Institute of Medicine (IOM) published seminal guidelines for the identification and classification of children prenatally exposed to alcohol. The IOM broadly set forth four distinct diagnostic categories within FASD: FAS (with or without

Table 1. Diagnostic categories and overlap of nomenclature used by the FASD diagnostic systems[28-30,71,84,85].

Center for Disease Control and Prevention 2004	4-Digit Code 2004	Hoyme et al. 2016	Canadian 2015	Australian 2016	Scottish Intercollegiate Guidelines Network 2019	Guidelines of Interdisciplinary Group of Polish Professionals 2021
FAS Alcohol Exposed or Unknown	FAS Alcohol Exposed or Unknown	FAS Alcohol Exposed or Unknown	FASD with the Face - Alcohol Exposed or Unknown	FASD with the Face - Alcohol Exposed or Unknown	FASD with the Face - Alcohol Exposed or Unknown	FAS Alcohol Exposed or Unknown
Not present	pFAS- Alcohol Exposed or Unknown	pFAS- Alcohol Exposed or Unknown	FASD without the Face - High Alcohol Exposure	FASD without the Face - Alcohol Exposed	Not present	Not present
Not present	SE/AE Static Encephalopathy Alcohol Exposed ND/AE Neurobehavioral Disorder Alcohol Exposed	ARND High Alcohol Exposure Must be ≥ 3 years old	Not present	Not present	ND-PAE neurodevelopmental disorders associated with prenatal alcohol exposure	ND-PAE neurodevelopmental disorders associated with prenatal alcohol exposure
Not present	Not present	ARBD-High Alcohol Exposure	Not present	Not present	Not present	Not present

confirmed maternal alcohol exposure), partial fetal alcohol syndrome (PFAS), alcohol-related neurodevelopmental disorder (ARND), and alcohol-related birth defects (ARBD). However, the 1996 IOM report did not offer practical guidance to clinicians about how to assign children with PAE to the diagnostic categories. In 2005, Hoyme et al. operationalized the IOM classification by describing specific clinical recommendations to be used to assign diagnoses within the 1996 IOM rubric[26-29].

In 2016, as part of an NIAAA sponsored effort to define the prevalence of FASD in the US (CoFASP, the Collaboration on Fetal Alcohol Spectrum Disorders Prevalence), updated guidelines were published, clarifying and expanding the original Hoyme 2005 classification. In particular, the authors set forth the following: precise definitions for documented PAE; neurobehavioral criteria for FAS, PFAS, and ARND diagnoses; revised diagnostic criteria for ARBD; an updated the dysmorphology scoring system; and a new lip/philtrum guide for the white population[28,30].

The evaluation of maternal prenatal alcohol consumption constitutes an essential component of the diagnostic process, serving as the initial stage in evaluating children with reported PAE[31]. As mentioned previously, a consensus definition of significant PAE was defined by Hoyme et al in 2016; this is fundamental, since affirmative validation of alcohol exposure is imperative for the assignment of a diagnosis of ARND or ARBD; whereas, according to the Hoyme criteria, certain situations allow for the diagnosis of FAS or PFAS in the absence of definitive documentation of prenatal alcohol use[5,19,24].

According to the CoFASP guidelines, once alcohol exposure has been established, characteristic structural features of FASD must subsequently be assessed. Growth deficiency (with respect to stature and/or weight) and small head circumference are defined as ≤10th centile. A complete dysmorphology examination follows, with criteria for sentinel facial features being met if at least two of the three specific facial characteristics of FASD are present: short palpebral fissures (≤10th centile), smooth philtrum and thin vermilion border of the upper lip (rank 4 or 5 on a racially normed lip/philtrum guide, if available)[26,28,32-35].

The initial 2005 Hoyme guidelines permitted the assignment of FASD diagnoses in children exhibiting the requisite facial features, growth restriction, and/or microcephaly, even in the absence of substantial neurobehavioral impairment[14,25,36]. The updated 2016 guidelines mandate that all children designated with FASD diagnoses, excluding those with ARBD, must display neurobehavioral impairment, specifically defined as cognitive impairment or behavioral impairment without concurrent cognitive deficits (cutoffs for neuropsychological testing are ≤–1.5 SD). For children aged ≤3 years, a diagnosis of FAS and PFAS may be established when there is observable evidence of developmental delay ≤1.5 SD below the mean; however, a conclusive diagnosis of ARND cannot be assigned before the age of 3 years[37].

ARBD diagnosis requires both documented PAE and ≥1 specific major malformation (cardiac, skeletal, renal, ocular, and ear-related) demonstrated in animal models and human studies to be the result of PAE[3,38,39]. The approach by Hoyme et al recommends assignment of an FASD diagnosis only after considering genetic disorders or conditions stemming from prenatal exposure to other teratogens among possible differential diagnoses[15,40].

The authors assert that the assessment of individuals prenatally exposed to alcohol requires a multidisciplinary team approach with medical assessment and team leadership by a pediatrician or clinical geneticist with expertise in the full range of human malformation syndromes and the dysmorphology evaluation of children with FASD. In addition, exposed children should have expert psychological/neuropsychological assessment, and a skilled interviewer should evaluate prenatal maternal alcohol intake. Other team members may include developmental behavioral pediatricians, psychiatrists, speech pathologists, occupational therapists, physical therapists, special educators, audiologists, and/or ophthalmologists, among others[12,14,17].

The ideal team members, in part, will be determined by the age of the individual being assessed (infant, child, adolescent or adult). In small or isolated communities where essential team members are not available, the community team must collaborate and consult with larger centers that have a more comprehensive diagnostic team. Access to diagnosis can also be enhanced by telemedicine[41,42]. Unfortunately, MDTs are not universally available, and children at-risk often present to primary care providers who may not be sufficiently educated in the diagnosis of FASD. Thus, education of primary care providers in this field is an urgent priority[17]. It should be noted that the Hoyme et al diagnostic criteria are the most extensively used in international FASD prevalence studies.

4-DIGIT DIAGNOSTIC CODE (2004, 3RD EDITION)

The 4-digit code is another diagnostic tool for diagnosing the full spectrum of outcomes observed among individuals with prenatal alcohol exposure[43,44]. The first edition of the FASD 4-digit diagnostic code was developed by the Washington State FAS Diagnostic and Prevention Network (FAS DPN) in 1997 and published in peer-reviewed form in 2000[45,46]. The 4-digit diagnostic code allows clinicians to make diagnoses by assigning Likert-scaled numerical ratings for four key clinical parameters assessed in

the evaluation of a potential FASD. The method uses case-specific and non-operator-dependent definitions[3,34,47]. The four digits of the code reflect the variability of the four key diagnostic features of FASD. The following terms are used in various combinations to name the 22 diagnostic categories:

1. Growth deficit;
2. Morphological facial characteristics of FAS;
3. Central nervous system (CNS) abnormalities;
4. Prenatal exposure to alcohol.

The expression of each characteristic is classified independently from the others on a 4-point Likert scale where 1 reflects the complete absence of the anomaly connected to FASD and 4 coincides with the presence of a pathological trait typical of FASD[28,44]. There are 256 possible 4-digit diagnostic codes ranging from 1111 to 4444 based on the combination of the various clinical characteristics observed in the patient[45,48,49]. Each 4-digit diagnostic code falls into one of 22 unique clinical diagnostic categories (labeled A through V).

The 4-Digit Code also documents and classifies all other prenatal and postnatal risk factors that often accompany prenatal alcohol exposure. The authors suggest that this is a diagnostic methodology valid for all age groups, from birth to adulthood[13,25].

Like the Hoyme criteria, the 4-digit code is designed to be used in a multidisciplinary team setting (which may include a physician, a psychologist, an occupational therapist, a speech pathologist, a social worker, a family advocate and a public health professional, among others)[50,51].

The names assigned to each diagnostic category reflect the patient's clinical outcome and alcohol exposure. The first three categories (A through C) meet the criteria for a clinical diagnosis of FAS and are named as such. The fourth category (D) applies to the patient who presents with all of the features of FAS but has a confirmed *absence* of prenatal alcohol exposure from conception to birth. This category is referred to as an FAS Phenocopy. The remaining 19 categories (E through V) do not meet the minimum criteria for FAS or partial FAS. These are subsequently named to reflect the Likert ranking of each digit in the 4-digit Diagnostic Code. Many of these patients might have previously been referred to variably as having PFAE, ARBD, or ARND[15,44,52]. Diagnostic categories E-I would have previously been referred to as 'fetal alcohol effects', 'alcohol-related birth defects', or 'alcohol-related neurobehavioral disorder'. Categories J–V are new categories that describe a large number of patient groups that have never been adequately classified or described in the past. The Likert ranks for the four digits of the code are case-defined for consistent application[1,2,53].

The 4-Digit Diagnostic Code offers another objective evidence-based approach to reporting outcomes and exposure that reflects the diversity of disability associated with prenatal alcohol exposure. Preliminary assessments of precision, accuracy and power appear to be increased over the 'gestalt' method of diagnosis[54-56]. This can be attributed, in large part, to the use of objective continuous measurement scales, specific, comprehensive case definitions and the use of a multidisciplinary clinical team approach[57-59].

The 4-Digit Diagnostic Code is fully comprehensive; similar to the Hoyme criteria, it can be used to diagnose individuals of all ages and races who present across the full spectrum of exposure and outcomes. This is achieved by directing the clinician to age-, gender-, and ethnically-adjusted anthropometric and psychometric measures when available and appropriate[16,51,60]. This method can be taught to a wide array of healthcare and social service providers and has been adopted in many multidisciplinary FASD diagnostic clinics in the US and Canada[61,62].

The 4-Digit Diagnostic Code has been criticized as being excessively difficult to deploy in a clinical setting[26]. It differs from the 2005 and 2016 Hoyme criteria by requiring all three sentinel facial features to be present to make a diagnosis of FAS (as opposed to two of three in the Hoyme guidelines). In addition, cut-offs for growth deficiency and microcephaly are set at the 3rd centile in the 4-digit code as opposed to the 10th centile in the Hoyme guidelines. Both require accurate assessment of growth, development and prenatal alcohol exposure. The Hoyme guidelines are therefore likely to be more sensitive but less specific than the 4-digit code.

Centers for Disease Control and Prevention (2004)

In 2002, the US Congress mandated that the Centers for Disease Control and Prevention (CDC) develop guidelines for FAS diagnosis to be incorporated into standards for medical practice and to be recognized by professional organizations and accrediting boards. These CDC developed guidelines only include diagnostic criteria for FAS and do not incorporate other diagnoses within the FASD continuum[62,63]. The CDC reported that no existing criteria were uniformly accepted and that the 1996 IOM criteria neither provided reliability and accuracy, nor did the IOM classification take into consideration ethnic or differential diagnostic considerations. As other diagnostic systems have been refined, the CDC guidelines have not been updated.

The CDC consensus identified reports that were used as the scientific basis for creating diagnostic recommendations. With this information, and in coordination with the National Taskforce on Fetal Alcohol Syndrome and Fetal Alcohol Effect (NTFFAS/FAE, another US-funded FAS program), and non-

governmental organizations concerned with FAS, CDC formed a scientific working group (SWG) of persons with expertise in research and clinical practice regarding prenatal alcohol exposure to develop diagnostic guidelines for FAS[2,64]. Guidelines were formulated based on consensus among SWG members and NTFFAS/FAE[40,65].

The CDC diagnostic guidelines for FAS (not intended to represent the entire clinical continuum of FASD), published in 2005, are as follows:

- *Facial dysmorphia*: on the basis of racial norms, an affected individual must exhibit all three of the following facial features: smooth philtrum (University of Washington Lip-Philtrum Guide rank 4 or 5); thin vermilion border (University of Washington Lip-Philtrum Guide rank 4 or 5); short palpebral fissures (≤10th centile).
- *Gro*wth deficiency: prenatal or postnatal height, weight, or both ≤10th centile, adjusted for age, sex, gestational age, and race or ethnicity.
- Central nervous system (CNS) abnormalities: structural CNS anomalies (clinically meaningful brain abnormalities observed through imaging); or, head circumference ≤10th centile, adjusted for age and sex.
- Neurologic: neurologic problems not resulting from a postnatal insult or fever, or other soft neurologic signs outside normal limits.
- Functional: test performance substantially below that expected for an individual's age, educational level, or circumstances, as evidenced by global cognitive or intellectual deficits representing multiple domains of deficit (or substantial developmental delay in younger children), with performance below the third centile (i.e., 2 SDs below the mean for standardized testing); or functional deficits < 16th centile (i.e., 1 SD below the mean for standardized testing) in at least three of the following domains: cognitive or developmental deficits or discrepancies; executive functioning deficits; motor functioning delays; problems with attention or hyperactivity; problems with social skills; other problems (e.g., sensory problems, pragmatic language problems, memory deficits).

The guidelines were developed to assist service providers in making referral decisions[2,17,66]. It was recommended that each case be evaluated individually, and that, when in doubt, providers should refer individuals for a full evaluation by a multidisciplinary team with experience in evaluating prenatal alcohol exposure[28].

The CDC recommended referral for FASD evaluation in the following circumstances:

- When prenatal alcohol exposure is known, a child should be referred for full FAS evaluation when substantial prenatal alcohol use (i.e., seven or more drinks per week, three or more drinks on multiple occasions, or both) has been confirmed. If substantial prenatal alcohol exposure is known, in the absence of any other positive criteria (i.e., dysmorphia, growth deficits, or CNS abnormalities), the primary health-care provider should document this exposure and monitor the child's ongoing growth and development closely.
- When information regarding prenatal alcohol exposure is unknown, a child should be referred for full FAS evaluation for any one of the following:

  – A parent or caregiver (foster or adoptive parent) report that a child has or might have FAS;

  – All three facial features (i.e., smooth philtrum, thin vermillion border, and short palpebral fissures) are present;

  – One or more facial features are present, in addition to growth deficits in height, weight, or both; one or more facial features are present, and one or more CNS abnormalities are documented; or one or more facial features are present, with growth deficits and one or more CNS abnormalities.

Canadian guideline (2005, updated in 2015)

The Canadian guidelines were first developed in 2005 by a multidisciplinary team comprising Canadian and American experts in the diagnosis of FAS and related disabilities[44,67]. Review and feedback were provided by a diverse group of individuals, professional organizations and societies, and provincial, territorial and federal levels of government[68]. The working group endeavored to harmonize existing diagnostic approaches in order to obtain consistent diagnoses of FASD across Canada. The 2005 Canadian guidelines were similar to the Hoyme criteria promulgated in the US, Europe and South Africa, except for the requirement of three (rather than two) sentinel facial features for the diagnosis of FAS and the setting of diagnostic cutoffs at the third (rather than the tenth) centile for growth and neurobehavioral assessments.

The guideline for diagnosis of FASD in Canada underwent significant revision in 2015, resulting in the consolidation of diagnostic categories into two distinct classifications: FASD with sentinel facial features and FASD without sentinel facial features[17,69]. The simplified diagnostic terminology of the revised Canadian guideline for diagnosis differs markedly from that used in the US and in other international settings, which are based on the original 1996 IOM diagnostic categories. Among other differences in the revised Canadian guideline are the exclusion of the consideration of growth deficiency as a major diagnostic criterion in any diagnostic category and the

elimination of ARBD as a diagnostic category, since it is difficult to attribute alcohol as a causative factor of major structural malformations in exposed children, in the absence of other structural or neurobehavioral characteristics of FAS.

Australian guidelines (2016)

In 2013, in response to limited training opportunities in FASD, lack of a nationally adopted diagnostic instrument and confusion about diagnostic criteria, *The Australian Guide to the Diagnosis of Fetal Alcohol Spectrum Disorder* was developed, and funded by the Commonwealth Department of Health (DoH)[47,62]. The Australian Guide to Diagnosis is based on and incorporates modifications of the Canadian Guideline.

A diagnosis of FASD requires evidence of prenatal alcohol exposure and severe impairment in three or more domains of central nervous system structure or function. A diagnosis of FASD can be divided into one of two sub-categories[37,47,62]:

1. *FASD with three sentinel facial features* (FASD with three sentinel facial features replaces the diagnosis of Fetal Alcohol Syndrome, but without a requirement for growth impairment). The etiological role of alcohol is most clearly established in the presence of all three characteristic facial abnormalities. In this situation a diagnosis of FASD with three sentinel facial features can be made even when prenatal alcohol exposure is unknown, provided there is also severe neurodevelopmental impairment.
2. *FASD with less than three sentinel facial features* (FASD with less than three sentinel facial features encompasses the previous categories of Partial Fetal Alcohol Syndrome and Neurodevelopmental Disorder-Alcohol Exposed).

Co-existing or alternative diagnoses including genetic conditions (e.g. microdeletions or duplications), effects of other teratogens and prenatal exposures, as well as the effects of postnatal exposures such as early life trauma and brain injury should be considered[5,14,43,70].

Scottish Intercollegiate Guidelines Network (2019)

These guidelines were developed by a multidisciplinary team of Scottish experts using a combination of standard Scottish Intercollegiate Guidelines Network (SIGN) methodology. It was based on a systematic review of the evidence and adaptation of the Canadian guideline for the diagnosis of FASD; however, some elements of the Australian guide to the diagnosis of FASD have also been incorporated[2,71,72].

The study group created these recommendations, with permission from the Canadian guideline developers, by considering their work and making minor revisions to align the guidance with practice in Scotland. In Scotland, before these new guidelines were drawn up, diagnoses were based on the classification developed by the World Health Organization (ICD-10)[29,62].

The only new recommendations added are from the evidence-based review of the literature on screening for alcohol use during pregnancy. These guidelines were first published in 2019 and were revised in 2022.

Although the Canadian diagnostic categories are: FASD with sentinel facial features and FASD without sentinel facial features, the SIGN prefers to apply the terms 'FASD without sentinel facial features' as a descriptor rather than a diagnostic term[73,74].

An additional diagnostic category of individuals "at risk for neurodevelopmental disorder and FASD, associated with prenatal alcohol exposure" was introduced to describe individuals with confirmed PAE and some indication of neurodevelopmental problems, who did not fit the diagnostic criteria for FASD[40].

Guidelines of Interdisciplinary Group of Polish Professionals (2021)

In 2021, Polish physicians noted several limitations in applying existing diagnostic criteria in the diagnosis of FASD[29,67]. They argued that terms used in the Hoyme diagnostic guidelines, such as ARBD and ARND, are outdated and suggest a cause-and-effect relationship between alcohol exposure and symptoms that was difficult to document in individual cases[3,67]. In addition, according to the Polish working group, a significant diagnostic delay results from the Hoyme criteria for ARND, since ARND cannot be reliably diagnosed in children under 3 years of age[53,75,76].

The Polish working group recommended distinguishing two fundamental diagnostic categories within FASD:

1. FAS;
2. ND-PAE (neurodevelopmental disorder associated with prenatal alcohol exposure).

It was concluded that to fulfill the criterion of neurobehavioral impairment, it is necessary to meet the following three requirements:

- the presence of deficits in at least three cognitive areas. In the case of neurological symptoms and signs, deficits in two areas;
- the occurrence of abnormalities in at least three areas from the emotional and social sphere, adaptation disorders, or psychopathological symptoms;
- significant impact of the identified deficits and symptoms on everyday life activities and school

functioning (in the case of people who have completed their education, the data from the interview are to be taken into account).

The working group reiterated that the evaluation of maternal alcohol consumption during pregnancy is critical for the diagnosis of FASD[54,56,77,78]. The teratogenic effect of alcohol can vary depending on the timing of exposure (the stage of development of the central nervous system, genetics and other individual factors)[77,79]. There is no single dose of alcohol that is equally dangerous in each case and it is essential to evaluate the level of alcohol consumption during pregnancy on a case-by-case basis[32,51,80-82].

Based on previous studies, and taking into account that, in Poland, a standard drink (one dose) is defined as 10 g of pure alcohol, the working group recommended that alcohol exposure criteria for ND-PAE in an affected child be met if the mother had approximately:

- ≥8 standard doses of alcohol per week for ≥2 weeks of pregnancy or
- ≥2 episodes of excessive alcohol consumption (consuming ≥4 doses of alcohol on one occasion).

The Polish guidelines are based on those of the 4-digit code for assessing growth and dysmorphia. Therefore, the fundamental problem to be solved in this regard was the selection of appropriate centile grids for the Polish population[59,83].

Conclusions

Children who are suspected to have FASD should be referred to an expert team of specialists for rigorous assessment, including assessment of prenatal alcohol exposure, facial dysmorphism and a complete neurobehavioral evaluation. For this reason, it is important to recognize possible FASD-related signs and symptoms early.

In this review we presented a historical and practical comparison among the various existing diagnostic guidelines for FASD, explaining the rationale for their creation and use. Although the proposed guidelines differ significantly from one another, we believe that it cannot be empirically indicated which system is the best. The choice of which diagnostic guideline to use must be based on the diagnostic capabilities of the clinician(s) and the multidisciplinary team that uses them. We reiterate that today in Italy the guidelines proposed by Hoyme and last revised in 2016 are used; however, the other guidelines that we have compared in this discussion also appear to have a scientific rationale. We do believe that although the differences are not always significant between the results of clinical evaluation using various guidelines, it would be appropriate in the future to try to create a universally accepted diagnostic rubric to avoid misdiagnosis and to allow comparisons among populations.

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