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ORIGINAL PAPER

Establishing normative values for palpebral fissure length in Polish children: implications for foetal alcohol syndrome diagnosis

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ABSTRACT

Introduction: Foetal alcohol syndrome (FAS) is a serious condition resulting from prenatal alcohol exposure, often characterised by distinct facial features. The goal of this study is to demonstrate the need to develop reference distributions for the width of the palpebral fissure in the Polish population, as this is one of the most important characteristics applicable to the diagnostic FAS syndrome.

Material and methods: The research involved 210 children (102 girls and 108 boys) aged 3–16 years (mean age 9.57 years). The palpebral fissure lengths were measured using a computerised method applied to digital photographs. The images were labelled solely by the child's sex and birth date. The study participants were primarily recruited from patients admitted to the Children's Memorial Health Institute and their siblings. An additional sample of 38 children was recruited from scientific events. The study took place between 2019–2023.

Results: The measurements were grouped into two-year age categories. A statistical hypothesis test was performed to assess the assumption that the palpebral fissure length (PFL) of the right eye is equal to that of the left eye. The mean values of PFL were classified by age and gender groups. The analysis revealed that PFL increases with age, and there is a slight, though not statistically significant, difference between boys and girls in each age group

Conclusions: These data have important implications for the accurate diagnosis and management of FAS and related disorders. By addressing the identified limitations and expanding research efforts, future studies can build on this foundation, ultimately enhancing clinical outcomes and supporting public health initiatives.

KEY WORDS:

foetal alcohol syndrome (FAS), foetal alcohol spectrum disorders (FASD), palpebral fissure length.

INTRODUCTION

Foetal alcohol syndrome (FAS) is one of the most severe consequences of alcohol exposure during pregnancy. It was first described by Lemoine in 1968. Five years later, Jones *et al*. [1] established a link between alcohol abuse in pregnant women and specific birth defects [2].

Prenatal alcohol exposure can lead to a range of negative effects on foetal development, collectively known as foetal alcohol spectrum disorders (FASD). These effects can manifest as structural, neurocognitive, and behavioural anomalies. The following categories of disorders related to alcohol exposure are recognized [2]:

- FAS,
- partial FAS,
- alcohol-related neurodevelopmental disorders,
- alcohol-related birth defects,
- prenatal alcohol exposure.

Foetal alcohol spectrum disorders are recognized as primary developmental issues in children and they can oc-

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cur in any society and among all social and ethnic groups. A 2018 report from the World Health Organization reported that the global prevalence of alcohol consumption during pregnancy is 9.8% [3]. Binge drinking during pregnancy varies by country, with rates ranging 0.2–13.9% [4]. It is estimated that drinking alcohol during pregnancy results in a prevalence of FAS of 1.46 per 1,000 people and a prevalence of FASD of 7.73 per 1,000 people [5]. For comparison, the incidence of Down syndrome is reported in approximately 1 in 700 births [5, 6].

Additionally, it is reported that one in three women of childbearing age (18–40 years old) consumes alcohol during pregnancy. Among these women, younger individuals (19%), those with higher education (33%), and those who drink more than six litres of pure alcohol annually (57%) are more likely to drink during pregnancy. It is estimated that the negative consequences of foetal alcohol exposure may affect about 1% of all newborns [7].

Foetal alcohol syndrome is marked by a specific set of symptoms and signs that commonly occur together. The impact of prenatal alcohol exposure can differ from one child to another. Timely and accurate diagnosis is crucial as it allows for the implementation of appropriate interventions. While these actions may not erase the existing damage caused by alcohol exposure, they can help minimise its effects. This support can significantly enhance the quality of life and lead to better social and professional functioning for individuals with FAS.

The most common health problems in children with FAS and FASD stem from alcohol's impact on brain development. Alcohol disrupts the migration of brain cells, preventing them from reaching their proper destinations. This can lead to difficulties in remembering and processing information. Additionally, alcohol can cause brain cell death, resulting in a reduced number of brain cells at birth [8].

The areas of the brain most affected by alcohol include the corpus callosum, cerebellum, basal ganglia, hippocampus, and frontal lobes. In some children with severe FAS, hypoplasia (or complete absence) of the corpus callosum is observed. This lack of connections between the brain's hemispheres can cause slow and ineffective information processing. As a result, affected children may struggle with distinguishing left from right or performing alternating movements, leading to awkward motions.

Damage to the cerebellum can also result in specific difficulties, such as trouble climbing and descending stairs, jumping on one leg, and maintaining balance during changes in position [9].

The basal ganglia play a crucial role in memory and cognitive processes. The hippocampus, a key brain structure, is essential for memory formation and learning. Damage to the hippocampus can weaken spatial memory and hinder the learning process [10]. In contrast, the frontal lobes are responsible for executive functions, impulse control, and judgment. When there is damage to the frontal lobes, it can lead to a decline in executive functions. This decline in children with FAS may result in difficulties such as an inability to navigate social situations, struggle with spontaneous problem-solving, lack of control over sexual impulses, and challenges in understanding the consequences of past behaviours [9, 10].

Prenatal alcohol exposure also affects parts of the forebrain and associated optic structures. It leads to eye abnormalities such as short palpebral fissure length (PFL) and problems with eye-opening [11, 12]. Disorders within the FAS are characterised by several features, as shown in Table 1. While some children may experience gradual improvement of certain features over time, many of these characteristics persist into adulthood. These children often experience delays in physical development, even when they receive adequate nutrition and are in supportive environments. When FAS is not diagnosed early and appropriate care is not provided, it can lead to secondary complications. These secondary issues may include anxiety, anger, social withdrawal, adopting victim or persecutor roles, isolation, school dropout, unemployment, homelessness, dependence on others, mental health challenges (such as depression and self-harm), violent behaviours, impulsivity, tendencies towards addiction, and suicidal thoughts or actions [9, 10].

To address the limitations of subjective assessments by examiners, the 4-digit FASD diagnostic questionnaire, commonly known as the Washington questionnaire, was developed in 1997. This tool evaluates the severity of four key diagnostic features of FASD [13]:

- weight and length deficiency,
- characteristic facial phenotype,
- central nervous system abnormalities,
- prenatal alcohol exposure.

The severity of each trait associated with FAS is evaluated using a 4-point Likert scale, in which 1 indicates the complete absence of a feature typical of FAS and 4 signifies its definite presence. The result is a 4-digit diagnostic code, e.g., code 4444 indicates FAS of the highest severity. An objective assessment of the phenotype is crucial for diagnosing FAS. Classic features of facial dysmorphism include microcephaly, short palpebral fissures, smoothing of the nasal gutter (philtrum), and thinning of the upper lip. Over the past 20 years, research has confirmed the sensitivity and specificity of several characteristics as indicators of FAS syndrome, particularly the palpebral fissure width, the degree of smoothness of the nasal gutter, and the level of upper lip thinning [14]. Clinical screening, epidemiological, and experimental studies have supported the use of these features, demonstrating a correlation between these characteristics and brain damage [15, 16]. The assessment methods for the nasal gutter and upper lip are internationally standardised, utilisinge a 5-point Likert scale. In this process, the appearance of a child's nasal gutter and upper lip is compared with photographic templates represented on the scale [13]. However, mea-

TABLE 1. Key diagnostic features for differential classification of foetal alcohol syndrome disorders categories (foetal alcohol syndrome, partial foetal alcohol syndrome, ND-prenatal alcohol exposure, and rFASD)

Category (diagnosis)	Prenatal alcohol exposure	Growth restriction (pre-/postnatal)	Key facial dysmorphology	Neurodevelopmental impairment (required)
FAS (ICD-10: Q86.0)	Yes or unknown (may be unconfirmed)	Yes	3/3: short palpebral fissures + thin upper lip + smooth philtrum	Yes: ≥ 3 cognitive deficits (or ≥ 2 + neurological signs) and ≥ 3 abnormalities in emotional–social/adaptive/psychopathological domains and significant impact on daily functioning
pFAS (ICD-10: G96.8)	Yes (variant with confirmed exposure)	Not required	2/3 facial features	Yes: 1 key neurological symptom or deficits in ≥3 neurocognitive domains or ≥1 abnormality in each of 3 domains (neurocognition, self-regulation, adaptive functioning)
pFAS (ICD-10: G96.8)	Unconfirmed/no data (variant without confirmed exposure)	Yes	2/3 facial features	Yes: same as above (neurological symptom or 3-domain profile)
ND-PAE (ICD-10: G96.8)	Yes (confirmed exposure required)	Not required	None (not a criterion)	Yes: ≥ 3 cognitive deficits (or ≥ 2 + neurological signs) and ≥ 3 abnormalities in emotional–social/adaptive/psychopathological domains and significant impact on daily functioning
rFASD (risk of FASD – non-diagnostic category)	Unknown/suspected or yes, but full assessment currently not possible	Monitoring/ observation	Monitoring/ observation	Cannot be determined or still under evaluation/differential diagnosis

FAS – foetal alcohol syndrome, FASD – foetal alcohol syndrome disorders, ND-PAE – neurodevelopmental disorder associated with prenatal alcohol exposure, PAE – prenatal alcohol exposure, pFAS – partial foetal alcohol syndrome, rFASD – risk of fetal alcohol spectrum disorder

suring the width of the palpebral fissure presents some challenges. Currently, three methods are employed worldwide: using computer software with 3D imaging, utilising a ruler or caliper, and measuring from photographs. The most accurate method is to take a digital photograph and measure the width of the palpebral fissure using FAS Facial Photographic Analysis Software. After obtaining the measurement, the researcher compares it to reference values for that trait.

At present, there are no reference values for the width of the palpebral fissure specific to the Polish population. Therefore, potential diagnostics must rely on reference values available in the literature. Anthropometric research, including the measurement of children and adolescents, is periodically conducted across various academic centres in Poland. Due to the specificity, complexity, and requirement for specialised measurement techniques, only a few centres include head and facial measurements alongside general body measurements [17–20]. However, none of these studies have directly measured the width of the palpebral fissure.

The goal of this study is to demonstrate the need to develop reference distributions for the width of the palpebral fissure in the Polish population, because this is one of the most important characteristics applicable to the diagnostics of FAS syndrome.

MATERIAL AND METHODS

The study participants were primarily recruited from patients admitted to the Children's Memorial Health Institute and their siblings, totalling 172 children. An additional sample of 38 children was recruited from scientific events. The study took place between 2019–2023. The inclusion and exclusion criteria are detailed in Table 2.

The research involved 210 children (102 girls and 108 boys) aged 3–16 years (mean age 9.57 years). The palpebral fissure lengths were measured using a computerised method applied to digital photographs. To ensure the subjects' identities were further protected, only the eyes were captured in the photos rather than the full face (Figure 1). The images were labelled solely by the child's sex and birth date.

The study was approved by the Bioethics Committee. Participants whose parents consented to the study and completed the research questionnaire were given three digital photographs of the eye area. A scaling sticker was applied to the forehead following the guidelines of the University of Washington's Foetal Alcohol Syndrome Diagnostic and Prevention Network. The width of the palpebral fissure was measured using the FAS Facial Photographic Analysis Software. During the measurement process, we assessed the diameter of the scaling

TABLE 2. Criteria of participation in the study

Criteria type	Description
Inclusion criteria	
Normal range of growth	Head circumference and body height within the range of ±2 SDS or 10th to 90th percentile
Exclusion criteria	
FASD	Diagnosed cases
Microcephaly	Significantly smaller head circumference
Serve growth deficiency	Clinically diagnosed significant growth impairment
Suspected or recognised genetic syndromes and diseases associated with facial dysmorphia	Silver-Russel syndrome, Turner syndrome, Beckwith-Wiedemann syndrome, Prader-Willy syndrome, Down syndrome, Louis-Bar syndrome, mucopolysaccharidoses, FACES syndrome

FASD – foetal alcohol syndrome disorders, SDS – standard deviation score

sticker and the distance between the outer (A) and inner (B) palpebral fissure angles. The correct width of the palpebral fissure was calculated using the following formula:

PFL [mm] = (diameter of the scaling sticker in mm × width of the palpebral fissure in pixels) × 1.07 [21].

The final measurement was based on the average of the three photographs.

FIGURE 1. Photographic region of participants with landmarks identified

RESULTS

The measurements were grouped into two-year age categories. A statistical hypothesis test was performed to assess the assumption that the PFL of the right eye is equal to that of the left eye.

The mean values of PFL were classified by age and gender groups. The analysis revealed that PFL increases with age, and there is a slight, though not statistically significant, difference between boys and girls in each age group ($p = 0.57$). We opted for separate graphs to avoid inflated detection rates in girls (Table 3). The palpebral fissure length results are presented in Table 4 and Figure 2.

TABLE 3. Basic statistical characteristics for distinguished age groups for girls and boys

Age group	GIRLS				
	n	Mean	Min	Max	SD
3–4	9	22.57	20.19	24.53	1.64
5–6	16	23.25	14.35	26.75	3.06
7–8	15	24.65	20.14	26.44	1.89
9–10	21	24.25	20.36	29.43	2.10
11–12	15	25.65	24.08	27.98	1.05
13–14	14	26.98	25.15	29.13	1.41
15–16	11	26.99	23.78	29.72	1.70
Age group	**BOYS**				
	n	Mean	Min	Max	SD
3–4	8	21.49	20.30	23.71	1.29
5–6	11	24.31	21.40	26.47	2.02
7–8	27	24.69	18.93	31.39	2.35
9–10	17	25.23	21.40	28.81	1.60
11–12	14	26.26	23.54	29.33	1.70
13–14	18	25.90	20.96	28.53	2.44
15–16	13	26.92	22.05	29.52	1.90

SD – standard deviation

DISCUSSION

This study aimed to establish reference distributions for the PFL specific to the Polish population. The obtained data might be a useful tool to recognise the consequences of prenatal alcohol exposure (FAS or FASD). Although the study is exploratory, several findings and limitations deserve in-depth discussion. The pilot nature of this study significantly limits its scope and generalisability. The sample comprised 210 participants aged 3–16 years, all recruited from a single institution. As such, it does not accurately represent the broader Polish population. The small sample size resulted from the challenges posed by the COVID-19 pandemic, which severely restricted patient attendance and led to a notable decrease in the number of patients accompanied by healthy siblings – an essen-

TABLE 4. Mean and standard deviation values of palpebral fissure length for girls and boys

GIRLS							
Age group	*n*	SD	−2 SD	−1 SD	Mean	+1 SD	+2 SD
3–4	11	1.64	19.28	20.92	22.57	24.21	25.85
5–6	15	3.06	17.13	20.19	23.25	26.31	29.38
7–8	16	1.89	20.87	22.76	24.65	26.54	28.43
9–10	21	2.10	20.06	22.15	24.25	26.34	28.44
11–12	15	1.05	23.54	24.60	25.65	26.70	27.75
13–14	13	1.41	24.17	25.58	26.98	28.39	29.79
15–16	11	1.70	23.59	25.29	26.99	28.69	30.39

BOYS							
Age group	n	SD	−2 SD	−1 SD	Mean	+1 SD	+2 SD
3–4	8	1.29	18.91	20.20	21.49	22.79	24.08
5–6	11	2.02	20.27	22.29	24.31	26.33	28.34
7–8	27	2.35	20.00	22.35	24.69	27.04	29.39
9–10	17	1.60	22.03	23.63	25.23	26.83	28.44
11–12	14	1.70	22.86	24.56	26.26	27.96	29.67
13–14	18	2.44	21.02	23.46	25.90	28.34	30.78
15–16	13	1.90	23.12	25.02	26.92	28.82	30.72

SD – standard deviation

tial subgroup for generating normative data. Furthermore, many participants over 14 years of age opted out of having their photographs taken, further constraining the dataset for older age groups. These factors necessitate cautious interpretation of the findings while affirming the study's importance as a foundational basis for future research.

The results indicate a clear trend of increasing PFL with age, aligning with expected developmental patterns. The narrow range of variation in PFL values (from −2 standard deviation [SD] to +2 SD, spanning 5–6 mm depending on age) highlights the importance of precise measurement techniques and standardized reference systems. Current methods for measuring the width of the palpebral fissure have significant limitations when applied to the Polish population. Growth charts by Hall *et al.* [21] are based on aggregate data collected over 50 years from various researchers employing different methods and equipment. Additionally, studies measuring the palpebral fissure focused exclusively on a group of newborns with gestational ages 25–43 weeks [22]. The Canadian Growth Charts [23] are based on an extensive research group but include a high degree of ethnic diversity, which may limit their relevance to specific populations. In Poland, using the growth charts developed by Strömland *et al.* is recommended [24, 25] until regional percentile charts become available. The variations among the cited standards underscore the need for developing and improving local standards, as shown by this study's findings.

The main strength of this study is its methodological rigor. By utilising digital photography and the FAS Facial Photographic Analysis Software, the researchers achieved high measurement accuracy. They focused specifically on the eye region, which minimised variability and enhanced attention to the palpebral fissure. Additionally, because the tests were conducted in a single centre by one research team, this approach helped to eliminate measurement errors.

The limitations of the study need to be acknowledged. First, the sample size was small and not representative of the general population. Additionally, the recruitment strategy may have caused selection bias, as participants were mostly sourced from a clinical setting. This could result in skewed findings, primarily reflecting individuals with more frequent interactions with healthcare services. Lastly, the need for parental consent and cooperation may lead to social desirability bias.

Future studies should recruit larger, more diverse cohorts from various regions in Poland to enhance the representativeness of findings. It is also important to address

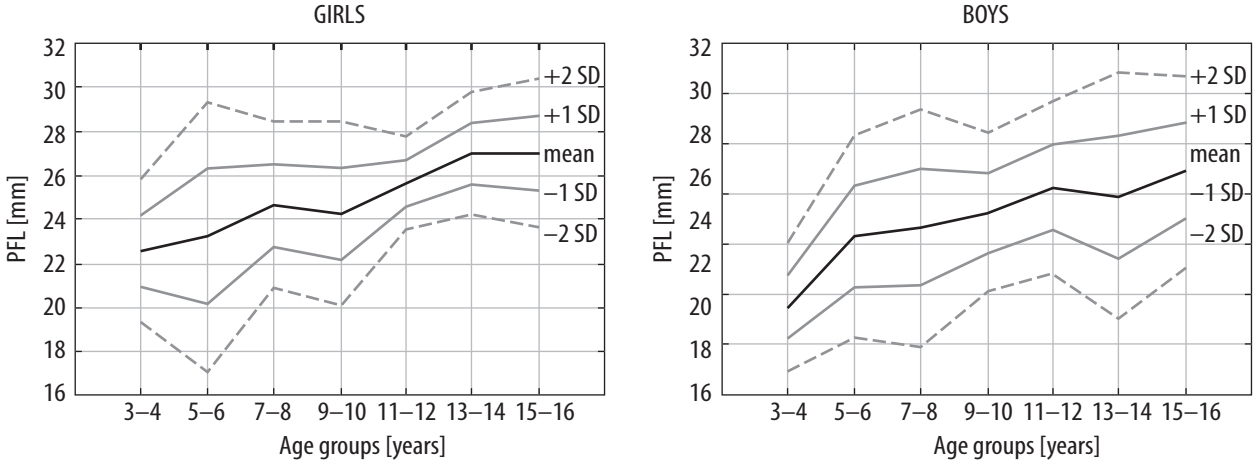

FIGURE 2. The palpebral fissure length for Polish girls and boys aged 3–16 years

logistical challenges to better engage older children and adolescents in research. Further research should explore longitudinal designs to track changes in PFL over time, providing dynamic insights into developmental patterns. Integrating advanced imaging technologies like 3D facial scanning could enhance measurement precision and reliability.

CONCLUSIONS

Although the findings of this study are preliminary, they are an essential step toward establishing reference norms for PFL that are specific to Poland. These data have important implications for the accurate diagnosis and management of FAS and related disorders. By addressing the identified limitations and expanding research efforts, future studies can build on this foundation, ultimately enhancing clinical outcomes and supporting public health initiatives.

DISCLOSURES

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2. Assistance with the article: None.
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