Incontinence in persons with fetal alcohol spectrum disorders: a polish cohort

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Summary

Introduction
Fetal alcohol spectrum disorders (FASD) is an important preventable public health concern, associated to a number of common pediatric problems such as incontinence. Little is known about the prevalence and presentation of incontinence in FASD, which hinders effective management.

Objective
The aim of the present study was to investigate incontinence among people with FASD.

Study design
Parental questionnaires were sent to all eligible FASD participants. To enable comparing the observed prevalence with typically developing, non-prenatally alcohol-exposed individuals, two clinical control groups of patients undergoing immunotherapy for pollen allergy (GKA) and patients diagnosed with celiac disease (GKG) were selected.

Results
A total of 119 participants were included in the study (FAS: $n = 24$, partial fetal alcohol syndrome [pFAS]: $n = 19$, alcohol-related neurodevelopmental disorder [ARND]: $n = 28$, GKA: $n = 34$, and GKG: $n = 14$). Overall incontinence for FASD was estimated to be 24% (confidence interval [CI] ranges from 15 to 36); nocturnal enuresis (NE) was present in 10% (CI ranges from 4 to 19), daytime urinary incontinence (DUI) in 11% (CI ranges from 5 to 21), and fecal incontinence (FI) in 13% (CI ranges from 6 to 23). Symptoms of urgency were present for 52%, voiding postponement for 10%, and straining for 2%. These data are both consistent with higher prevalence in individuals with FASD and with similar prevalence (the CIs overlap).

Conclusion
Children and adolescents with FAS, pFAS, ARND, GKA, and GKG are affected by incontinence. Highest rates were observed in pFAS and ARND. Persons with FAS were mostly affected by DUI, those with pFAS by NE, and those with ARND by FI.
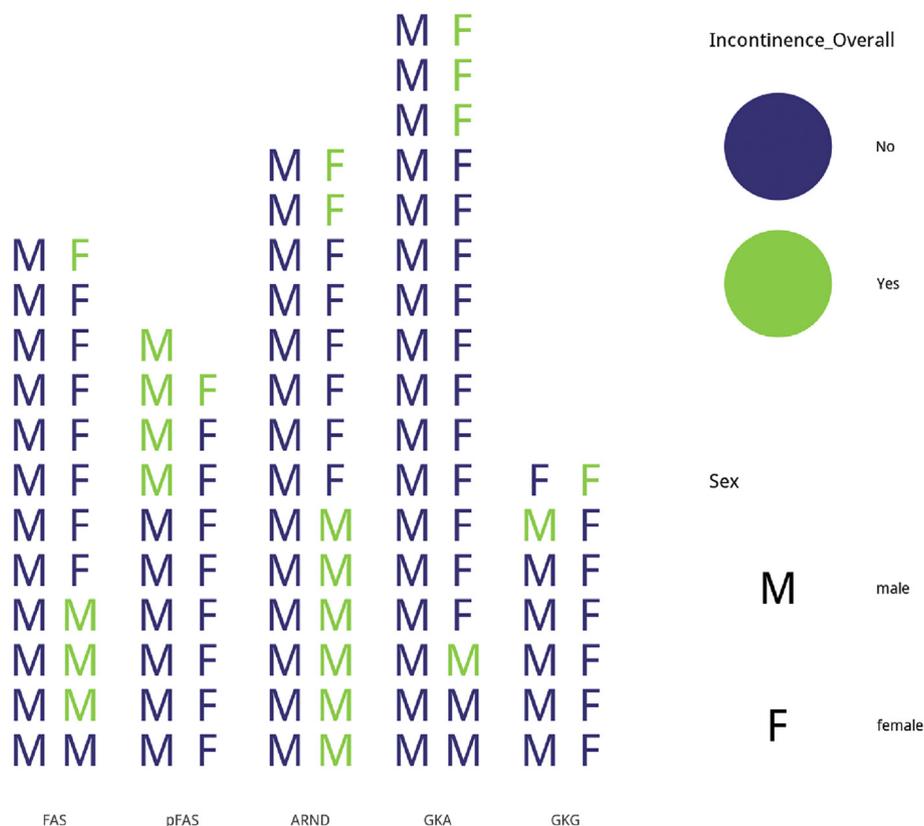
Summary Figure

Introduction

Fetal alcohol spectrum disorders (FASD) encompasses mild to severe disabilities of individuals affected by prenatal alcohol exposure. In accordance with different diagnostic guidelines, FASD includes the following diagnostic categories: fetal alcohol syndrome (FAS), partial fetal alcohol syndrome (pFAS), alcohol-related neurodevelopmental disorder (ARND), alcohol-related birth defects (ARBD), and neurobehavioral disorder with prenatal alcohol exposure [1—3]. Fetal alcohol spectrum disorder has been reported to be one of the leading preventable forms of neurodevelopmental disorders [4,5]. Global FASD prevalence rates have been estimated to range from 0 to 176.77 per 1000 live births [6]. For Poland, these estimates range from 0 to 20 per 1000 live births [7,8]. Fetal alcohol spectrum disorder received international recognition since the first publication on FAS in early infancy by Jones and Smith in 1973 [9]. Since then, extensive research has been published on the adverse outcomes of prenatal alcohol exposure such as facial (e.g. smooth philtrum), structural (e.g. small head circumference), behavioral (e.g. emotional lability), and neurocognitive effects (e.g. complex problem solving), abnormalities, and/or deficits [1,10—12].

However, secondary health problems in persons diagnosed with an FASD (e.g. nutrition, sleep functioning) are not completely understood [13]. Problems of incontinence are common in typically developing children. In 7-year-old children, the prevalence of nocturnal enuresis (NE) is 10%,

daytime urinary incontinence (DUI) is 2—3%, and fecal incontinence (FI) is 1—3% [14—18]. These rates decrease with age to 1—2% for NE and less than 1% for DUI [19—22] in adolescence. In children with special needs, these rates are estimated to be much higher: 38% of 7-year-old children with intellectual disability (ID) had NE, 39% DUI, and 30.5% FI. For 17—20% of children with ID, these problems persist into adulthood (age of 20 years) and are associated with the level of ID [19,23].

Incontinence among individuals with FASD has only been studied in one other study. This first study included children diagnosed with an FASD (aged 6—10 years) in a South African cohort [24]. It was suggested that the problems of incontinence persist during adolescence. Because no comparable studies have been conducted, the aim of the present study was to assess incontinence subtypes and associated conditions among both children and adolescents diagnosed with an FASD in Poland.

Materials and methods

Procedure

All persons who were previously diagnosed within the spectrum of FASD (FAS, pFAS, or ARND) were recruited by a physician through an outpatient and inpatient center at St Louis Children's Hospital in Krakow, Poland. The diagnostic procedures were in accordance with Canadian guidelines [2].

Table 1 Sample characteristics.

Variable	FASD						GKA		GKG		Significance[a]
	FAS		pFAS		ARND						
		N		N		N		N		N	
Sample characteristics											
Male n (%)	16 (66.7)	24	10 (52.6)	19	20 (71.4)	28	20 (58.8)	34	6 (42.9)	14	
Mean age of completion questionnaire in years (SD)	9.35 (2.56)	24	11.1 (4.2)	19	10.15 (3.7)	28	8.29 (2.74)	34	9.85 (3.7)	14	
Mean weight for age in kg (SD)	27.41 (9.39)	19	33.45 (14.7)	15	31.5 (10.9)	26	30.67 (15.17)	34	38.32 (19.39)	14	0.413
Mean height for age in cm (SD)	127.32 (14.52)	19	135.53 (17.7)	15	133.28 (18.4)	24	130.78 (17.65)	34	138.61 (20.56)	14	0.549
Mean BMI[b] (SD)	16.39 (2.83)	19	17.13 (4.27)	14	17.08 (2.6)	24	17.11 (3.53)	34	18.67 (4.5)	14	0.574
Incontinence characteristics											
Any type of incontinence n (%)	4 (16.7)	24	5 (26.3)	19	8 (28.6)	28	4 (11.8)	34	2 (14.3)	14	0.125
Nocturnal enuresis n (%)	2 (8.3)	24	4 (21.1)	19	1 (3.6)	28	1 (2.9)	34	2 (14.3)	14	0.33
Daytime urinary incontinence n (%)	4 (16.7)	24	1 (5.3)	19	3 (10.7)	28	2 (6.1)	33	0	14	0.638
Fecal incontinence n (%)	2 (8.3)	24	1 (5.3)	19	6 (21.4)	28	2 (5.9)	34	0	14	0.33
Any type of incontinence less frequent n (%)	1 (4.2)	24	3 (15.8)	19	5 (17.9)	28	0	34	0	14	0.125
Mean LUTS (SD)	5.75 (3.55)	24	5.84 (3.37)	19	4.89 (3.06)	28	3.21 (2.75)	34	3.43 (1.95)	14	
Straining[c] n (%) Q12. 'Does your child have to push in order to begin urinating'	0	21	1 (6.3)	16	0	23	4 (15.4)	26	0	14	0.413
Urgency[c] n (%) Q13. 'When your child needs to pass urine, does he/she has to rush to the toilet	14 (63.6)	22	8 (47.1)	17	12 (46.2)	26	4 (15.4)	26	1 (7.1)	14	<0.001***

(*continued on next page*)

Table 1 (continued)

Variable	FASD						GKA		GKG		Significance[a]
	FAS	N	pFAS	N	ARND	N		N		N	
Postponement[c] n (%) Q14. 'Does your child try to postpone passing urine by crossing his/her legs, squatting, etc.?'	1 (4.8)	21	2 (12.5)	16	3 (13.0)	23	3 (11.5)	26	1 (7.1)	14	0.811

FASD, fetal alcohol syndrome disorder; FAS, fetal alcohol syndrome; pFAS, partial fetal alcohol syndrome; ARND, alcohol-related neurodevelopmental disorder; BMI, body mass index; SD, standard deviation; LUTS, lower urinary tract symptoms.
Note: Data presented in this table are based on different denominators. [a]Fisher's exact tests for categorical data; univariate analyses of variance (ANOVA) for parametric data; * = p < 0.05; ** = p < 0.01; *** = p < 0.001. [b]BMI was calculated by weight (kg)/(height (m)*height (m)). [c]Rates are based on answers 'all of the time" and 'most of the time.'

Parental questionnaires were sent out by post to all parents and caregivers of individuals with FASD ($n = 198$) between November 2015 and March 2016. At this time, no Polish norm data on incontinence were publicly available.

To be able to compare the observed prevalence rates with prevalence estimates in typically developing, non-prenatally alcohol-exposed individuals, two additional clinical control groups were recruited in December 2017 based on convenience sampling. The first clinical control group consisted of patients of an allergology clinic undergoing immunotherapy for pollen allergy (hereafter referred to as GKA). The second clinical control group included patients diagnosed with celiac disease (hereafter referred to as GKG). The same questionnaire was handed out to these two groups at the clinic (for GKA, $n = 44$; and for GKG, $n = 16$). Questionnaires were completed and returned either by email or at the center during follow-up. Each questionnaire was coded with a unique participant ID number to collect data anonymously and ensure confidentiality.

Instruments

Incontinence and lower urinary tract symptoms (LUTS) were assessed using a combined questionnaire including the 'Parental Questionnaire: Enuresis/Urinary Incontinence' [17], 'Encopresis Questionnaire — Screening Version' [25,26], and 'International-Consultation-on-Incontinence-Questionnaire — Pediatric Lower Urinary Tract Symptom' (ICIQ-CLUTS) modified for the patient group under study [27]. The questionnaire was translated in four languages (English, German, Italian, and South African) but not yet in the Polish language [24,27]. The 10 questions of the ICIQ-CLUTS comprise a LUTS score with clinically relevant scores over 13 (scores lower than 13 indicate that there are no problems in the lower urinary tract). In accordance with the International Children's Continence Society (ICCS), NE and DUI are diagnosed in persons older than 5.0 years when wetting occurs at least once per month [28]. In accordance with DSM-5, FI was diagnosed from the age of 4.0 years when soiling occurs at least once per month. In addition to these diagnoses, incontinence was also considered to be present if any subtype of incontinence is present and if the frequency was lower (i.e. once a month or less) [29]. The questionnaire was translated into Polish followed by a back translation to English.

Thereafter, diagnoses and missing information for individuals with FASD (e.g. date of births) belonging to the unique ID numbers were obtained from the center's database. Additional descriptive data for the included subjects (e.g. head circumference, intelligence quotient (measured with Wechsler Intelligence Scale for Children® Fourth Edition (WISC-IV); Wechsler, 2004) were also considered and, when available, included [30].

Analyses

Subsequently, data were entered by one researcher in SPSS software package, version 22.0. Then, a second researcher randomly checked data entries of the questionnaires. Data from the parental questionnaire were further processed

Table 2 Sample characteristics FASD.

Variable	Total sample FASD, N = 71	N	Children aged 4–12 years, N = 50	N	Adolescents aged 13–17 years, N = 17	N	Adults aged >17 years, N = 4	N
Sample characteristics								
Male n (%)	46 (64.8)	71	34 (68)	50	10 (58.8)	17	2 (50.0)	4
Mean age of completion questionnaire in years (SD)	10.14 (3.52)	71	8.34 (2.13)	50	13.46 (1.23)	17	18.38 (0.87)	4
Current use of medication n (%)	28 (41.8)	67	15 (32.6)	46	10 (58.8)	17	3 (75.0)	4
Mean gestational age or HBD[a] in weeks (SD)	39.06 (3.35)	47	39.21 (3.38)	34	39.7 (1.16)	10	35.33 (6.35)	3
Mean birth weight in g (SD)	2636.04 (598.88)	53	2736.25 (566.51)	40	2413 (485.69)	10	2043.33 (1014.22)	3
Mean head circumference or OFC[b] in cm (SD)	49.95 (3.84)	52	49.27 (4.41)	35	51 (1.54)	15	53.25 (0.35)	2
Mean Apgar scale on birth (SD)	9.85 (1.96)	40	9.88 (2.18)	32	9.71 (0.49)	7	10	1
Mean weight for age in kg (SD)	30.69 (11.57)	60	25.85 (7.17)	43	40.13 (8.18)	15	64 (15.56)	2
Mean height for age in cm (SD)	131.91 (17.07)	58	124.35 (13.36)	41	149.41 (10)	15	155.5 (3.54)	2
Mean BMI for age (SD)	16.86 (3.11)	57	16.03 (2.32)	40	17.82 (2.42)	15	26.34 (5.23)	2
Mean BMI percentile (SD)	38.67 (29.64)	57	38.86 (28.55)	40	31.74 (28.95)	15	87 (16.97)	2
Mean IQ (SD)	89.21 (18.15)	42	90.65 (17.72)	31	88.13 (21.04)	8	77.33 (15.57)	3
Incontinence characteristics								
Any type of incontinence, n (%)	17 (23.9)	71	14 (28)	50	3 (17.6)	17	0	4
NE > 5 yr, n (%)	7 (9.9)	71	7 (14)	50	0	17	0	4
DUI > 5 yr, n (%)	8 (11.3)	71	7 (14)	50	1 (5.9)	17	0	4
FI > 4 yr, n (%)	9 (12.7)	71	7 (14)	50	2 (11.8)	17	0	4
Any type of incontinence less frequent n (%)	9 (12.7)	71	7 (14)	50	1 (5.9)	17	1 (25)	4
Mean LUTS score (SD)	5.44 (3.3)	71	5.92 (3.24)	50	4 (2.78)	17	5.5 (5)	4
Straining, n (%)	1 (1.7)	60	0	45	0	13	1 (50.0)	2
Urgency, n (%)	34 (52.3)	65	27 (57.4)	47	4 (28.6)	14	3 (75.0)	4
Voiding postponement, n (%)	6 (10)	60	4 (8.5)	47	2 (18.2)	11	0	2

FASD, fetal alcohol syndrome disorder; BMI, body mass index; SD, standard deviation; LUTS, lower urinary tract symptoms; IQ, intelligence quotient; NE, nocturnal enuresis; DUI, daytime urinary incontinence; FI, fecal incontinence.
Note: Abbreviations in this table are as follows [a]HBD = Hebdoma, [b]OFC = occipitofrontal circumference.

using SPSS software package, version 22.0, and R, version 3.2.3 [31]. Some variables were categorized: Age groups were formed for children (aged 4–12 years), adolescents (aged 13–17 years), and young adults (older than 17 years); reported LUTS scores were calculated and considered indicative for LUTS if a score was 13 or higher; ID was defined as intelligence quotient (IQ) scores equal to or lower than 70; body mass index (BMI) was calculated using the following formula: weight in kilograms/(height in meters * height in meters). Body mass index percentiles were calculated based on Polish norm data [32]. Percentiles less than five were defined as underweight; percentiles between the 5th and 85th as normal weight; percentiles between 85th and less than the 95th as overweight; and percentiles equal to or greater than 95 as obese.

Statistical analyses were then carried out using SPSS software package, version 22.0, and R, version 3.2.3. For each outcome, primarily 95% confidence intervals (CIs) were reported, followed by sample point estimates. Fisher's exact test was used for categorical data and univariate analyses of variance (ANOVA) for parametric data. To keep the probability of making a type 1 error at 5%, all p-values were adjusted for multiple testing using the false discovery rate approach. All statistical analyses are made publicly available at the Open Science Framework (OSF; https://osf.io/huz2c/). Because of the relatively low sample sizes, to avoid implying high accuracy and urge cautious interpretation, Blackstone's recommendation will be followed for rounding numbers [33] (note that the raw output is available in the OSF repository).

Results

Of the initial 198 questionnaires to the FASD cohort, 66 were returned (33% response rate), of which 13 were excluded from further analysis: 10 questionnaires were returned unopened or empty, and there were three refusals to participate. Given the low response rate (e.g. foster caregivers or institutional care facilities are often associated with a change of address), active follow-up (a physician asked patients under study who visited the outpatient and inpatient center between 2016 and 2017 to complete the questionnaire) resulted in 18 additional questionnaires. This yielded in total 71 completed questionnaires (36% response rate). From the initial 60 questionnaires sent to the two clinical control groups (GKA: $n = 44$, and GKG: $n = 16$), a total of 50 questionnaires returned (GKA = 87% response rate, GKG = 88% response rate). No reasons were given for non-participation.

The total number of questionnaires eligible for further analyses was 125 (FASD: $n = 73$, GKA: $n = 37$, and GKG: $n = 15$). However, six patients were excluded because they were younger than 4 years; therefore, the remaining sample contains data from 119 questionnaires: FAS ($n = 24$), pFAS ($n = 19$), ARND ($n = 28$), GKA ($n = 34$), and GKG ($n = 14$).

Sample characteristics and data regarding incontinence are described in the following piece of the article. An overview of incontinence data for each diagnosis can be observed in Table 1, an overview per age group is shown in Table 2, and a complete overview of the prevalence estimates is available in Table 3. Further descriptions for incontinence data regarding FASD and the two clinical control groups are provided in the following and can be inspected at the OSF repository https://osf.io/huz2c/.

Sample characteristics

In the FASD cohort, a total of 71 questionnaires were analyzed. The mean age was 10 years (standard deviation [SD] = 3.5; range = 4–19 years), and 46 participants were male (64.8%). Parental questionnaires were completed by mothers ($n = 35$), fathers ($n = 1$), others (e.g. caregivers; $n = 32$), and people with an unspecified relationship with the individuals ($n = 3$). Questions related to where the participants were living showed that the majority of participants lived with their parents ($n = 36$), followed by other cohabitation situations (e.g. foster family; $n = 22$) and an institutional care center ($n = 8$); five participants did not specify living arrangements. The majority of

Table 3 Sample point estimates and 95% CI for incontinence.

Incontinence	FASD	FAS	pFAS	ARND	GKA	GKG
Overall incontinence	$23.94_{n/N=17/71}$ (14.61–35.54)	$16.67_{n/N=4/24}$ (4.74–37.38)	$26.32_{n/N=5/19}$ (9.15–51.2)	$28.57_{n/N=8/28}$ (13.22–48.67)	$11.76_{n/N=4/34}$ (3.3–27.45)	$14.29_{n/N=2/14}$ (1.78–42.81)
NE	$9.86_{n/N=7/71}$ (4.06–19.26)	$8.33_{n/N=2/24}$ (1.03–27)	$21.05_{n/N=4/19}$ (6.05–45.57)	$3.57_{n/N=1/28}$ (0.09–18.35)	$2.94_{n/N=1/34}$ (0.07–15.33)	$14.29_{n/N=2/14}$ (1.78–42.81)
DUI	$11.27_{n/N=8/71}$ (4.99–21)	$16.67_{n/N=4/24}$ (4.74–37.38)	$5.26_{n/N=1/19}$ (0.13–26.03)	$10.71_{n/N=3/28}$ (2.27–28.23)	$6.06_{n/N=2/33}$ (0.74–20.23)	$0_{n/N=0/14}$ (0–23.16)
FI	$12.68_{n/N=9/71}$ (5.96–22.7)	$8.33_{n/N=2/24}$ (1.03–27)	$5.26_{n/N=1/19}$ (0.13–26.03)	$21.43_{n/N=6/28}$ (8.3–40.95)	$5.88_{n/N=2/34}$ (0.72–19.68)	$0_{n/N=0/14}$ (0–23.16)
Occasional incontinence	$12.68_{n/N=9/71}$ (5.96–22.7)	$4.17_{n/N=1/24}$ (0.11–21.12)	$15.79_{n/N=3/19}$ (3.38–39.58)	$17.86_{n/N=5/28}$ (6.06–36.89)	$0_{n/N=0/34}$ (0–10.28)	$0_{n/N=0/14}$ (0–23.16)

FASD, fetal alcohol syndrome disorder; FAS, fetal alcohol syndrome; pFAS, partial fetal alcohol syndrome; ARND, alcohol-related neurodevelopmental disorder; NE, nocturnal enuresis; DUI, daytime urinary incontinence; FI, fecal incontinence.
Note: This table represents percentages of incontinence sample point estimates including the associated confidence intervals per FASD diagnosis whereby *n* represents the number of cases. Overall incontinence was measured when criteria met for: NE, 'every night,''2x/week or more,' or '2x/month or more'; DUI, 'Every day,' '2x/week or more,' or '1x/month or more'; or FI 'Every day,' '2x/week or more,' or '1x/month or more.' For more details, see https://osf.io/huz2c/.
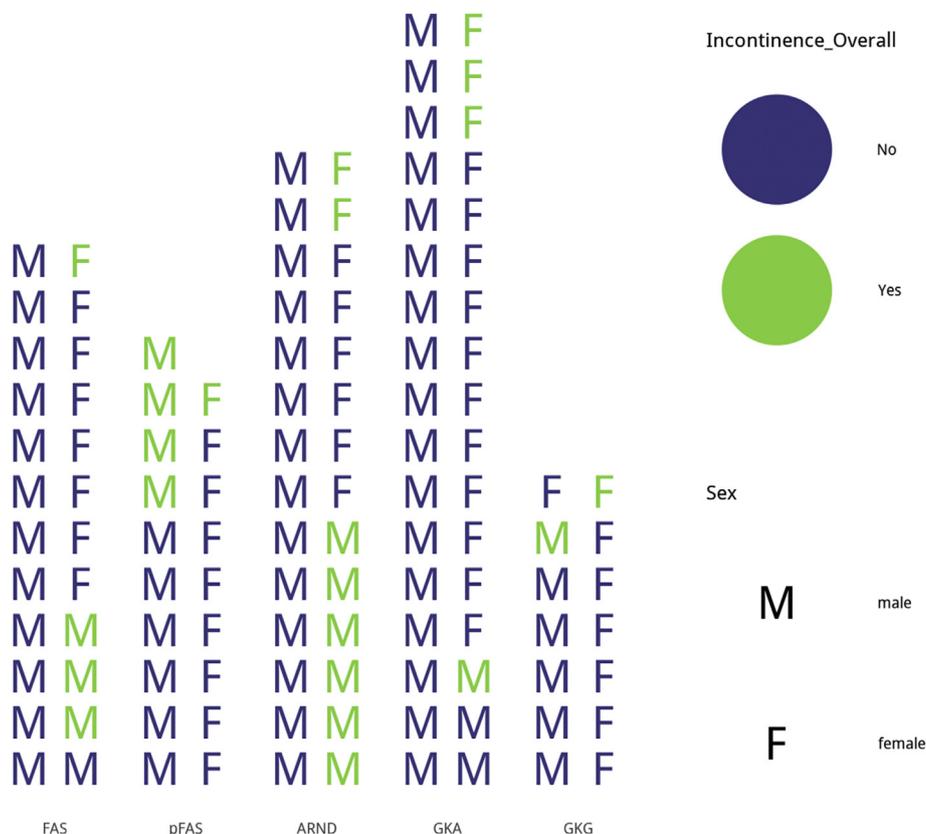
Fig. 1 Prevalence frequencies.

participants followed regular education (e.g. preschool, mainstream school), and ten participants received special education or additional developmental support (FAS: $n = 2$, pFAS: $n = 3$, ARND: $n = 3$).

Questions on maternal information showed that 20 (28.2%) mothers completed university, 16 (22.5%) completed college, 12 (16.9%) attained qualified training, and 12 (16.9%) graduated from high school; specifics

regarding education were not specified for 11 (15.5%) mothers. Questions on paternal information showed that 15 (21.1%) fathers completed university, 20 (28.2%) completed college, 11 (15.5%) attained qualified training, and 10 (14.1%) graduated from high school; specifics regarding education were not specified for 15 (21.1%) fathers.

For gestational data (see also Table 1), the mean birth weight was 2636.04 g ($SD = 598.88$), gestational age (or
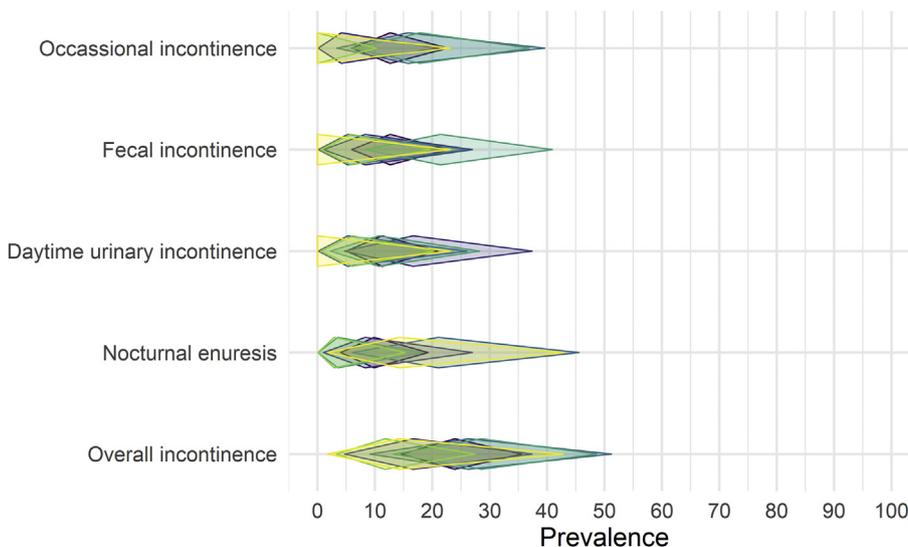

Fig. 2 Prevalence intervals.

Hebdomas or gestation) 39.0 weeks (*SD* = 3.35), and an average Apgar score (or AG) 9.9 (*SD* = 1.96). Other data included the mean head circumference (or occipitofrontal circumference) of 49.95 cm (*SD* = 3.8), mean weight of 30.7 kg (*SD* = 11.6), mean height of 131.9 cm (*SD* = 17.1), mean IQ of 89.2 (*SD* = 18.2), and mean age-corrected BMI of 16.9 (*SD* = 3.1). From the BMI percentile data, the majority of participants (*n* = 51; 86.4%) had a normal weight, 6.8% were underweight, 5.1% overweight, and 1.7% obese. Intellectual disability (IQ score < 70) was present in six participants (8.5%). Physical disability or chronic illness (e.g. congenital heart defect, seizures) affected 17 participants (30.36%). In addition, 28 participants (41.8%) were currently using medication; however, none of the reported medication was used for treatment of incontinence (e.g. risperidone, valproic acid).

For the two clinical control groups, a total of 48 questionnaires were analyzed (GKA = 34; GKG = 14). The mean age for GKA was 8.3 (*SD* = 2.7; range 4−14 years) and 9.9 for GKG (*SD* = 3.7; range 5−19 years); for GKA, 20 participants were male (58.8%), and for GKG, eight participants were female (57.1%). The majority of questionnaires were completed by mothers (*n* = 40, 83%). All participants live with their parents and follow mainstream education. A majority of fathers and mothers completed university (*n* = 23, 51%, and *n* = 30, 68%, respectively). Current average height was 130.8 cm (*SD* = 17.7) for GKA and 138.6 cm (*SD* = 20.6) for GKG. The mean weight was 30.7 kg (*SD* = 15.2) for GKA and 38.3 kg (*SD* = 19.4) for GKG. The average BMI was 17.1 (*SD* = 3.5) for GKA and 18.7 (*SD* = 4.5) for GKG. The BMI percentile data revealed a majority of GKA (*n* = 25, 73.5%) and GKG (*n* = 11, 78.6%) had a normal weight, one GKA patient was underweight (2.1%), five GKA patients (14.7%) and one GKG patient (7.1%) were overweight, and three GKA patients (8.8%) and two GKG patients (14.3%) were obese. Furthermore, three patients reported to have congenital heart defects (GKA: *n* = 1, GKG: *n* = 2), one patient reported to have seizure (GKG), and two reported to have another disability and/or illness, namely scoliosis and allergy (GKG *n* = 2). Finally, seven patients (GKA: *n* = 5, GKG: *n* = 2) currently use medication but not for treatment of incontinence (e.g. cetirizine, omeprazole). Data regarding gestation, head circumference, or IQ were unavailable for these two clinical groups.

Incontinence

Incontinence as established based on ICCS guidelines is illustrated in Fig. 1. Note that this figure shows the entire sample. The 95% CIs for the prevalence estimates are shown in Fig. 2. Overall incontinence among individuals with FASD was present in FAS = 4 patients with FAS, pFAS = 5 with pFAS, and ARND = 8 with ARND (23.9%, CI ranges from 14.61 to 35.54); NE was present in FAS = 2 patients with FAS and pFAS = 4 with pFAS (9.9%, CI ranges from 4.06 to 19.26); DUI was present in FAS = 4 patients with FAS, pFAS = 1 with pFAS, and ARND = 3 with ARND (11.3%, CI ranges from 4.99 to 21); and FI in FAS = 2 patients with FAS, pFAS = 1 with pFAS, and ARND = 6 with ARND (12.7%, CI ranges from 5.96 to 22.7). Less frequently or occasionally (<1/

month) reported problems of incontinence were present in FAS = 1 patient with FAS, pFAS = 3 patients with pFAS, and ARND = 5 with ARND (12.7%, CI ranges from 5.96 to 22.7). For two individuals with pFAS (male aged 11 years and female aged 19 years), anomalies of the urogenital tract (undescended testicle, urinary incontinence) were reported without problems of NE, DUI, or FI. For the females (aged 19 years), LUTS were observed in the clinical range (score of 13) and symptoms of straining were reported. Lower urinary tract symptoms were also observed for another individual with FAS (aged 8 years) which had a score of 18 and all three types of incontinence (NE, DUI, and FI). For all other individuals, no LUTS in the clinical range were observed with a mean average score of 5.4 (*SD* = 3.3). Specific symptoms of urgency were reported for FAS = 14 patients with FAS, pFAS = 8 with pFAS, ARND = and 12 with ARND (52.3%); postponement was reported for FAS = 1 patient with FAS, pFAS = 2 with pFAS, and ARND = 3 with ARND (10%); and straining was reported for pFAS = 1 patient with pFAS (1.7%).

For the two clinical control groups, overall incontinence was present for four GKA participants (11.8%, CI ranges from 3.3 to 27.45) and two GKG participants (14.3%, CI ranges from 1.78 to 42.81); NE was present in one GKA participant (94%, CI ranges from 0.07 to 15.33) and in two GKG participants (14.3%, CI ranges from 1.78 to 42.81); DUI was present in two GKA participants (6.1%, CI ranges from 0.74 to 20.23) and in no GKG participant (0%, CI ranges from 0 to 23.16); FI was present in two GKA participants (5.9%, CI ranges from 0.72 to 19.68) and in no GKG participant (0%, CI ranges from 0 to 23.16). No incontinence less frequent than once a month was reported for these groups. Lower urinary tract symptom scores were in the normal range, with average scores of 3.2 (*SD* = 2.75) for GKA and 3.4 (*SD* = 1.95) for GKG. Symptoms of urgency were reported for four GKA participants (15.4%) and one GKG participant (7.1%); straining was reported in four GKA participants (15.4%); and voiding postponement was reported in three GKA participants (11.5%) and one GKG participant (7.1%).

Between-group analyses

Between-group analysis did not reveal significant differences in sample or incontinence characteristics (the CIs in Fig. 2 clearly illustrate this). For further inspection of the data and intermediate analyses, refer to the OSF repository https://osf.io/huz2c/.

Discussion

Only one previous study reported incontinence problems among persons diagnosed within the spectrum of FASD [24]. This study among Polish children and adolescents is the second study to assess incontinence in relation to FASD. Overall rates in this Polish cohort were higher than in typically developing individuals. Incontinence was reported in 17 participants (23.9%), present in both children and adolescents. Fecal incontinence was the most common subtype (*n* = 9, 12.7%), followed by DUI (*n* = 8, 11.3%) and NE (*n* = 7, 9.9%). Moreover, specific symptoms were frequently reported for urgency in 34 participants (52.3%),

followed by voiding postponement in six participants (10%) and straining in one participant (1.7%). Except for two participants, the overall LUTS scores were below the clinical range. Subsequent analysis did not reveal significant relations between incontinence and sample characteristics (e.g. BMI, IQ, medication use). For all participants, with one exception (undescended testicle), there were no structural urogenital anomalies in those participants with incontinence. In participants with FASD, higher rates of non-organic (i.e. functional) incontinence were observed. Moreover, the types of incontinence and LUTS are observed to be heterogeneous. Persons diagnosed within the spectrum of FASD show a range of comorbid conditions, mediated by abnormal functioning of the central nervous system (CNS) [10,34]. The present rates of incontinence could be attributed to possible neurocognitive and maturational deficits in this sample. Further research is needed to understand the underlying mechanisms responsible for incontinence, especially regarding the effects of CNS dysfunction in these individuals.

The only data on the incontinence prevalence in general pediatric population in Poland are unpublished and come from Czajka et al. [35]. On the basis of data from the parents of 954 schoolchildren, the researchers established that NE occurred in 5.2% of children, while daytime incontinence was present in 9.4% of children. The prevalence of incontinence among individuals with FASD seems to be only moderately higher than the data reported by Czajka et al. [35]. However, the majority of individuals with FASD in Poland attend public schools; so in fact, patients with FASD may significantly contribute to general prevalence of incontinence.

In a previous South African study, overall incontinence was present in 20% of children with an FASD [24], mainly NE. Most of these had full FAS, which means they were more severely affected than the Polish individuals with FASD. In comparison, the rates are slightly lower. One explanation could be that the previous study was based on interviews only and possible under-reporting of the problem. In the Polish cohort, children were affected by DUI, FI, and NE with comparable rates. In the present study, no gender differences were observed.

The present study has several limitations. The participation rate was low (e.g. adoptive population often associated with a change of address), so the data should be interpreted with caution. In addition, only one Polish center was included, which could also be responsible for selection effects. Incontinence was assessed only through questionnaires. Objective clinical examinations such as uroflowmetry, ultrasound, and voiding diaries were not performed. Moreover, there were missing data due to incomplete questionnaires. In addition, owing to the small sample size, differentiated between-group analyses were not possible. Therefore, the current findings should be replicated in future studies with a larger sample size of persons with FASD.

Despite these limitations, the present study also has strengths. Most of the questionnaires are validated and include standardized questions. In addition, international guidelines (ICCS and DSM-5) were used for the diagnosis of incontinence.

In conclusion, incontinence was reported to be present in children and adolescents with FAS, pFAS, and ARND. Incontinence rates were observed lower than in individuals with special needs (38% NE, 39% DUI, and 30.5% FI) and higher than in typically developing persons (9.1–18.2% NE, 4.4–16.9% DUI, and 1.4–5.4% FI) [23]. These differences in incontinence rates could be associated with the low rates of intellectual disability among this Polish sample.

This study shows that children and adolescents with FAS, pFAS, and ARND may be affected by incontinence. It is therefore recommended that incontinence should be routinely assessed and treatment provided, as effective guideline-based therapy options are available for treatment of incontinence [36].

Author statements

Author contributions

S.R., K.A.D., J.N., A.v.G., G.K., and L.C. designed the study and directed its implementation, including quality assurance and control. K.A.D., K.P., and S.R. helped supervising the field activities. S.R. and G-.J.Y.P. conducted the analyses, and S.R., K.A.D., and J.N. prepared the Materials and Methods and the Discussion sections of the text. All other co-authors contributed to successive drafts. All authors gave significant input in the preparation of the article and approved the manuscript and submission.

References

[1] Hoyme HE, Kalberg WO, Elliott AJ, Blankenship J, Buckley D, Marais AS, et al. Updated clinical guidelines for diagnosing fetal alcohol spectrum disorders. Pediatrics 2016;138. https://doi.org/10.1542/peds.2015-4256. e20154256—e20154256.

[2] Chudley AE, Conry J, Cook JL, Loock C, Rosales T, Leblanc N. Fetal alcohol spectrum disorder: Canadian guidelines for diagnosis. Can Med Assoc J 2005;172:S1–21.

[3] Astley S. Diagnostic guide for fetal alcohol spectrum disorders: the 4-digit diagnostic code. 3rd ed. 2004.

[4] Abel EL, Sokol RJ. Incidence of fetal alcohol syndrome and economic impact of FAS-related anomalies. Drug Alcohol Depend 1987;19:51–70.

[5] Centers for Disease Control and Prevention (CDC). Fetal alcohol syndrome-Alaska, Arizona, Colorado, and New York, 1995-1997. MMWR Morb Mortal Wkly Rep 2002;51:433.

[6] Roozen S, Peters G-JY, Kok G, Townend D, Nijhuis J, Curfs L. Worldwide prevalence of fetal alcohol spectrum disorders: a systematic literature review including meta-analysis. Alcohol Clin Exp Res 2016;40:18–32. https://doi.org/10.1111/acer.12939.

[7] Okulicz-kozaryn K, Borkowska M, Brzózka K. FASD prevalence among schoolchildren in Poland. J Appl Res Intellect Disabil 2017;30(1):61–70.

[8] Okulicz-Kozaryn K, Terlikowska J, Brzózka K, Borkowska M. Prevention and intervention for FASD in Poland. J Pediatr Neuropsychol 2017. https://doi.org/10.1007/s40817-016-0025-9.

[9] Jones KL, Smith DW. Recognition of the fetal alcohol syndrome in early infancy. Lancet 1973;302:999–1001.

[10] Tsang TW, Lucas BR, Carmichael Olson H, Pinto RZ, Elliott EJ. Prenatal alcohol exposure, FASD, and Child behavior: a meta-analysis. Pediatrics 2016;137:e20152542. https://doi.org/10.1542/peds.2015-2542.

[11] Moore EM, Migliorini R, Infante MA, Riley EP. Fetal alcohol spectrum disorders: recent neuroimaging findings. Curr Dev Disord Reports 2014;1:161–72. https://doi.org/10.1007/s40474-014-0020-8.

[12] Riley EP, Infante MA, Warren KR. Fetal alcohol spectrum disorders: an overview. Neuropsychol Rev 2011;21:73–80. https://doi.org/10.1007/s11065-011-9166-x.

[13] Streissguth AP. A Long - term Perspective of FAS Few people in their adolescent or adult years are diagnosed. Alcohol Health Res World 1994;18:74–81.

[14] Joinson C, Heron J, von Gontard A. Psychological problems in children with daytime wetting. Pediatrics 2006;118:1985–93. https://doi.org/10.1542/peds.2006-0894.

[15] Joinson C, Heron J, Emond A, Butler R. Psychological problems in children with bedwetting and combined (day and night) wetting: a UK population-based study. J Pediatr Psychol 2007; 32:605–16. https://doi.org/10.1093/jpepsy/jsl039.

[16] Joinson C, Heron J, Butler U, Team CS. Psychological differences between children with and without soiling problems. Pediatrics 2006;117. https://doi.org/10.1542/peds.2005-1773.

[17] von Gontard A. Enuresis. In: Rey JM, editor. IACAPAP E-Textb. Child Adolesc. Ment. Heal. Geneva: International Association for Child and Adolescent Psychiatry and Allied Professions; 2012.

[18] von Gontard A, Neveus T. Management of disorders of bladder and bowel control in childhood. London: MacKeith Press; 2006.

[19] Järvelin MR, Vikeväinen-Tervonen L, Moilanen I, Huttunen NP. Enuresis in seven year old children. Acta Paediatr 1988;77: 148–53.

[20] Fergusson DM, Horwood LJ, Shannon F. Factors related to the age of attainment of nocturnal bladder control: an 8-year longitudinal study. Pediatrics 1986;78:884–90.

[21] Hellström AL, Hanson E, Hansson S, Hjälmås K, Jodal U. Micturition habits and incontinence in 7-year-old Swedish school entrants. Eur J Pediatr 1990;149:434–7.

[22] Largo RH, Gianciaruso M, Prader A. Die Entwicklung der Darm- und Blasenkontrolle von der Geburt bis zum 18. Lebensjahr Longitudinale Studie Schweiz Med Wochenschr 1978;108: 155–60.

[23] von Wendt L, Similä S, Niskanen P, Järvelin MR. Development of bowel and bladder control in the mentally retarded. Dev Med Child Neurol 1990;32:515–8.

[24] Roozen S, Olivier L, Niemczyk J, von Gontard A, Peters G-JY, Kok G, et al. Nocturnal incontinence in children with fetal alcohol spectrum disorders (FASD) in a South African cohort. J Pediatr Urol 2017;13. https://doi.org/10.1016/j.jpurol.2017.02.009.

[25] von Gontard A. Encopresis. In: Rey JM, editor. IACAPAP E-Textb. Child Adolesc. Ment. Heal. Geneva: International Association for Child and Adolescent Psychiatry and Allied Professions; 2012.

[26] Niemczyk J, Schäfer S, Becker N, Equit M, von Gontard A. Psychometric properties of the "parental questionnaire: enuresis/urinary incontinence" (PQ-EnU). Neurourol Urodyn 2018. https://doi.org/10.1002/nau.23564.

[27] De Gennaro M, Niero M, Capitanucci ML, von Gontard A, Woodward M, Tubaro A, et al. Validity of the international consultation on incontinence questionnaire-pediatric lower urinary tract symptoms: a screening questionnaire for children. J Urol 2010;184:1662–7. https://doi.org/10.1016/j.juro.2010.03.075.

[28] Austin PF, Bauer SB, Bower W, Chase J, Franco I, Hoebeke P, et al. The standardization of terminology of lower urinary tract function in children and adolescents: update report from the standardization committee of the International Children's Continence Society. Neurourol Urodyn 2014;35:471–81. https://doi.org/10.1002/nau.22751.

[29] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Washington DC: DSM-5; 2013.

[30] Wechsler D. Wechsler intelligence scale for children—. 4th ed. San Antonio: WISC-IV; 2003.

[31] R Development Core Team, Language R:A. And environment for statistical computing. 2014.

[32] Gurzkowska B, Napieralska E, Litwin M, Olaf B. Siatki centylowe wysokości , masy ciała i wskaźnika masy ciała dzieci i młodzieży w Polsce — wyniki badania OLAF. Stand Med 2010;7: 690–700.

[33] Blackstone EH. Rounding numbers. J Thorac Cardiovasc Surg 2016;152:1481–3. https://doi.org/10.1016/j.jtcvs.2016.09.003.

[34] Popova S, Lange S, Shield K, Mihic A, Chudley AE, Mukherjee RAS, et al. Comorbidity of fetal alcohol spectrum disorder: a systematic review and meta-analysis. Lancet (Lond, Engl) 2016;387:978–87. https://doi.org/10.1016/S0140-6736(15)01345-8.

[35] Czajka Sz KA, Grabowski A, Malek P, Wyciszczok A. How often does urinary incontinence really affect primary school children. 2017.

[36] Equit M, Sambach H, Niemczyk J, von Gontard A. Urinary and fecal incontinence a training program for children and adolescents. Hogrefe Publishing; 2014.

Abbreviations

ARBD	Alcohol-Related Birth Defects
ARND	Alcohol-Related Neurodevelopmental Disorders
BMI	Body Mass Index
CI	Confidence Interval
CNS	Central nervous system
DUI	Daytime urinary incontinence
FAS	Fetal Alcohol Syndrome
FASD	Fetal Alcohol Spectrum Disorders
FI	Fecal incontinence
HBD	Hebdomas or gestation
ICCS	International Children's Continence Society
ICIQ-CLUTS	International-Consultation-on-Incontinence-Questionnaire — Pediatric Lower Urinary Tract Symptom
ID	Intellectual Disabilities
LUTS	Lower urinary tract symptoms
ND-PAE	Neurobehavioral Disorder with Prenatal Alcohol Exposure
NE	Nocturnal enuresis
OFC	Occipitofrontal Circumference
PFAS	Partial Fetal Alcohol Syndrome