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Title Page for Journal of Pediatric Urology

Prevalence of nocturia, fecal and urinary incontinence and the association to childhood obesity: a study of 6803 Danish schoolchildren

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Ethical approval:

The study was approved by the Legal Office of the North Denmark Region prior to initiation, in accordance with the Danish Law on Personal Data §3no1.

Prevalence of nocturia, fecal and urinary incontinence and the association to childhood obesity: a study of 6803 Danish schoolchildren

Short title: Nocturia, incontinence and childhood obesity.

Key Words: Incontinence, Enuresis, Nocturia, Obesity, Child, Adolescent.

Abbreviations:

FI: Fecal Incontinence
DUI: Daytime Urinary Incontinence
NE: Nocturnal Enuresis
BMI: Body Mass Index
BMI-SDS: Body Mass Index Standard Deviation Score

Summary

Introduction

Fecal and urinary incontinence are common disorders in children. Obesity and its associated comorbidities have become increasingly common and a relation between obesity, nocturia, incontinence and nocturnal enuresis has been suggested.

Objective

This large scale population study aim to determine the prevalence of fecal incontinence (FI), daytime urinary incontinence (DUI), nocturnal enuresis (NE) and nocturia in children at school entry and in adolescence and to clarify whether obesity is associated to any of the above.

Study design

First grade children and their parents and adolescents in the seventh to ninth grades were interviewed in relation to school-nurse visits in eight municipalities in the North Jutland Region of Denmark. The interview included questions on whether incontinence or nocturia were experienced at least once per month. The participants´ age was recorded and weight and height were measured. Body Mass Index (BMI) was calculated and age-standardized by use of BMI-SDS, with reference to WHO normative BMI data. Obesity was defined as BMI-SDS >2. Associations between obesity and incontinence and nocturia were quantified by odds ratio.

Results

Completed interview questionnaires and measurements were obtained from 4002 (95.1%) in the child population and 2801(84.4%) in the adolescent population.

Mean age of children was 6.45±0.39 years, and 4.4% were obese. Overall 11.2% reported FI, 21.8% DUI, 16.8% NE, and 31.4% experienced nocturia. Obesity was associated with FI in first grade boys (OR 1.86 compared to normal weight).

Mean age of adolescents was 13.9±0.85 years and 7.6% of adolescent boys and 5.5% of the girls were obese. FI was reported by 2.1% of the adolescents, 4.5% had DUI, 1.0% stated to have NE and 32.3% reported nocturia. Obesity was significantly associated with nocturia in adolescents (OR 1.74-2.01).

Discussion

The prevalence of nocturia seems constant throughout childhood and adolescent life, this has not previously been documented. Incontinence is very common at school entry, with DUI reported more frequently than enuresis by both children and adolescents. Obesity is associated with nocturia in adolescents and FI in first grade boys, but no significant association between obesity and NE or DUI is found. A strength of this study is the very high participation rates but the study does not reveal information on previous treatment, subtype or severity of symptoms.

Conclusions

Incontinence is very common in children. One-third of both children and adolescents experience nocturia. Obesity is associated with FI in 6- to 7-year-old boys and nocturia in adolescents.

Associations between symptoms and BMI		**Girls**					**Boys**				
		Normal weight	Overweight		Heavily overweight		Normal weight	Overweight		Heavily overweight	
		OR	OR	95% CI	OR	95% CI	OR	OR	95% CI	OR	95% CI
Children	Fecal incontinence	1	1.42	0.94-2.15	1.22	0.57-2.58	1	1.47	1.06-2.03	1.86	1.10-3.15
	Daytime urinary incontinence	1	1.16	0.85-1.58	1.27	0.76-2.13	1	1.17	0.89-1.55	1.03	0.62-1.70
	Enuresis	1	1.13	0.78-1.66	1.26	0.67-2.37	1	0.90	0.67-1.21	1.18	0.72-1.93
	Nocturia	1	1.24	0.94-1.62	1.56	0.99-2.46	1	1.18	0.92-1.51	0.91	0.58-1.44
Adolescents	Fecal incontinence	1	2.98	1.27-6.96	-		1	1.20	0.51-2.81	1-57	0.54-4.60
	Daytime urinary incontinence	1	1.32	0.76-2.31	1.44	0.60-3.45	1	0.68	0.27-1.78	1.92	0.78-4.72
	Enuresis	1	0.56	0.07-4.51	1.74	0.21-14.08	1	-		1.84	0.53-6.41
	Nocturia	1	1.17	0.86-1.60	2.01	1.25-3.23	1	0.78	0.58-1.06	1.74	1.17-2.60

Introduction

Obesity is considered to be one of the world's biggest threats to public health and is empirically believed to be associated with incontinence in children[1–4]. In 1975, 0.8% of children were classified as obese, yet this number had, by 2016 grown steeply to 8% in boys and 6% in girls[5]. Childhood obesity is a precursor to adult obesity and many of the related disorders in adulthood[6]. However, the immediate somatic consequences of obesity for the affected children are less well explored.

Incontinence comprises urinary and fecal types as well as a combination of these. Around 10% of 7-year-old children suffer from nocturnal enuresis (NE)[7] and 2-12% from daytime urinary incontinence (DUI)[8–10]. Functional fecal incontinence (FI) is reported as ranging from 0.8-7.8%[11]. However, reports on the prevalence of childhood nocturia are remarkably few in number and based on small populations, proposing a prevalence of 4.0-35.2%[12,13]. Urinary incontinence is thought to decrease with age, giving resolution rates of around 15-20% per year[8,10], but large-scale studies including adolescent populations in particular are currently limited[14].

Specific pathophysiological mechanisms behind a possible relation between obesity, nocturia and NE are poorly elucidated. A number of comorbidities such as hypertension, sleep disturbances and hormonal abnormalities seen in obese children are also known to be related to polyuria and incontinence[6]. Indeed, circadian rhythm abnormalities are assumed to play an important role in both obesity and NE[15,16]. Obesity has similarly been linked to constipation[4,17]. Plausible biological explanations for the obesity/constipation association include: dietary concerns (high in calories, low in fiber diet), physical inactivity, impaired hormonal production such as motilin and pancreatic polypeptide, as well as autonomic dysfunction with increased sympathetic tone[3,17]. With FI being a result of constipation in most children[18], an association between FI and Obesity seems reasonable. Moreover, a relation to urinary incontinence could be suspected, since

constipation and urinary incontinence are proven to be assosiated[19,20]. However, the prevalence of urinary incontinence among children suffering from obesity has only been investigated in a few studies. These report a possible association[3,21,22], including up to a six fold higher risk of NE in obese children[2].

In adults, the obesity/DUI association is well documented, especially concerning stress-incontinence in women[1]. Besides the direct influence of obesity on intraabdominal and intravesical pressure[23], features of metabolic syndrome, hormonal changes, higher sympathetic activity and low-grade inflammatory activity, are believed to contribute to lower urinary tract symptoms in obese adults[24].

Nonetheless, the hypothesized associations between childhood obesity and urinary and fecal incontinence as well as nocturia, currently lack investigation in comprehensive population studies. The aim of this study was to determine the prevalence of FI, DUI, NE and nocturia, and to investigate a possible association between these symptoms and obesity in a large unselected population of children and adolescents.

Materials and Methods

All Danish children are offered regular health examinations by the municipality school nurses including visits in the first grade and between the seventh and ninth grades. Data on age, gender, incontinence, nocturia and body composition were obtained for this study at these visits. Eight out of 11 municipalities in the North Jutland Region of Denmark agreed to participate in collecting data from August 2015 to June 2016 for a population of first-grade children. Six of the municipalities further agreed to participate in the second round from August 2016 to June 2017, collecting data from sixth to eight-grade adolescents. All nurses were instructed to complete interviews of whole

classes, without selection of children and were trained in the interviewing technique. They also received training concerning treatment and referral options for childhood obesity and incontinence. First-grade children were accompanied by their parents at the nurse visit, while the adolescents attended the nurses alone. The test instrument used was an anonymous one-page questionnaire filled out during the interview by the nurse. A simple format with the following four questions and possible answers of either “yes” or “no” was applied: 1) Have you had accidents with feces/soiling your pants within the last month? 2) **Have you had accidents with daytime urine leakage /wetting your pants within the last month?** 3) Have you wet your bed within the last month? 4) Do you wake up at night with the urge to go to the toilet to pee, once or more per month? In addition, all children were measured for height and weight on altimeters and calibrated weights respectively. The school nurse noted weight, height, sex and age in the questionnaire.

All questionnaires were tabulated into Microsoft Excel 2013 (Microsoft, Washington, USA). Quality assurance of data entry of 5% of all forms was undertaken by an external reviewer. Only minor typing errors of 1.9% without significance to results were found. Subjects with incomplete questionnaires were excluded from the data analysis. Body Mass Index (BMI) was calculated as (weight in kg /(height in m)^2) and age-standardized by use of BMI-z-scores (BMI-SDS), with reference to WHO normative BMI data[25]. Overweight and obesity were defined by the WHO criteria for children[25]. Thus, Obesity was defined as BMI-SDS >2, Overweight as BMI-SDS>1, Normal weight as 1≤ BMI-SDS ≥-2, and Underweight as BMI-SDS <-2.

Statistical Analysis

All statistics were conducted using STATA 14.0 (StataCorp LP, College Station, TX), with installation of the who2007.ado file (http://www.who.int/growthref/tools/en/) for calculating BMI-z-scores. Descriptive information on demographic information and prevalence of overweight and associated symptoms were estimated and compared using t-test for ratio-interval measures,

Mann-Whitney U test for ordinal variables and Pearson chi-square test for categorical variables. Logistic regression analysis was used to estimate the association between variables, Odds Ratio (OR) with 95% confidence intervals was used as a measure of associations. A p-value of <0.05 was considered statistically significant.

Results:

A total of 7.087 children and adolescents were examined and interviewed (Figure 1). Of the first-grade children at the included schools, 99% attended the school nurse visit, **leading** to the return of 4,165 questionnaires. Of these, 163 were incompletely filled out, leaving the child population sample at 4.002 (95.1%), 2.063 boys and 1.939 girls. Mean age was 6.45±0.39 years (demographics are presented in Table 1A and 1B). There were significant gender differences within the child group regarding age, height and weight, with boys being older, taller and heavier. However, BMI was equal between genders. According to WHO criteria, 4.4% were categorized as obese, 15.1% were overweight, 79.5% were normal weight, and 1.0% were categorized as underweight. The distribution of overweight and obesity was equal for genders.

Of the adolescents, 88% attended the nurse visit and were included in the study, corresponding to the return of 2.922 questionnaires. Of these, 121 were incomplete, leaving 2.801 (84.4%) for the final analysis (Figure 1). Boys accounted for 50.5% and 49.5% were girls. The adolescents´ mean age was 13.9±0.85 years. There were gender differences regarding age, height, weight, and BMI, with the boys being older, taller and heavier than the girls. Girls had a slightly higher BMI (Table 1B). Of the adolescents, 6.5% were obese, 17.0% were overweight, 74.5% normal weight, and 2.0% underweight. Significantly more adolescent boys than girls were obese (7.56% vs 5.48% (p<0.05)).

Prevalence of incontinence and nocturia:

Incontinence and nocturia were highly prevalent in the child population. FI was found in 11.2% (Table 1A and Figure 2), and was statistically more common in boys than girls (13.7% vs. 8.6%) with OR of 1.70 (95% CI 1.38-2.09). A high prevalence of DUI at 21.8% was seen. DUI was more frequent in boys (23.1%) than girls (20.5%), OR 1.16 (95% CI 1.00-1.36). NE was reported by 16.8% and was most common in boys (21.0% boys vs 12.1% girls) OR 1.95 (95% CI 1.63-2.32). Nocturia was reported by 31.4%, of boys, more frequently than girls (33.2% vs 29.6%), OR 1.18 (95% CI 1.03-1.35) (Table 1A).

Incontinence was markedly less common in the adolescent population. FI was reported by 2.1%, 4.5% had DUI, and only 1.0% reported NE (Table 1B, Figure 2). In contrast to the findings of the child population, DUI was significantly more frequent in adolescent girls than boys (6.0% vs 3.0%, $p<0.0001$). Interestingly, nocturia was just as frequent in adolescents (32.2%) as in first grade children (31.4%). As with the child population, significantly more adolescent boys than girls experienced nocturia (35.2% vs. 29.3% (OR 1.31 (95% CI 1.11-1.54)) (Table 1B).

In the child population, 51.2% presented at least one symptom. Two or more concomitant symptoms were seen in 22.2%.

In the adolescent population more than one-third (36.5%) reported at least one of the symptoms . The majority of these had solely nocturia (92.0%). A few adolescents (3.1%) had two or three concomitant symptoms, while none reported having all four.

The association between obesity and incontinence and nocturia:

In the child population an association between obesity and FI was seen for the male participants with an OR of 1.86 (CI: 1.10-3.15) for FI in obese boys when compared to normal weight boys (Table 2). Nocturia was associated with obesity in girls but not significantly in boys. Moreover, an association between DUI and nocturia and BMI was observed, as girls with one of these symptoms had significantly higher average BMI than girls with no symptoms (BMI-SDS 0.18 vs. 0.30

($p<0.05$) and 0.17 vs 0.29 ($p<0.01$) respectively). We also found that, in girls, obesity was associated with having one symptom, OR 1.83 (CI: 1.12-2.99).

In the adolescents studied, obesity led to a significant increased risk of nocturia in both boys and girls (OR 1.74 (CI: 1.17-2.60) and OR 2.01 (CI: 1.25-3.23) respectively). As in the child population, adolescent obese girls had one of the symptoms significantly more often, OR 1.88 (CI: 1.16-3.04). Similarly in boys, obesity led to an increased risk of one, and two or three symptoms, OR 1.85 (CI: 1.23-2.60), and OR 2.92 (CI: 1.15-7.42).

Discussion:

An association between bladder and bowel symptoms and obesity in children, has been suggested by a few previous studies[3,21]. **Also, childhood and adolescent nocturia has only been sparsely addressed**[12,13]. This large population-based study seeks to shed light on the prevalence of, and association between, obesity and nocturia and incontinence in children and adolescents.

We found that obesity is associated with nocturia in adolescents and that the obese share a nearly two-fold risk of nocturia. Interestingly, however, we did not find a significant association between obesity and NE. Thus, even though obesity leads to nocturnal urine accommodation inability (nocturia) but it does not influence the ability to wake up to a full bladder. **We cannot clarify by the present study, whether obesity gives rise to nocturnal bladder overactivity. However, the nocturia may result** from obesity-induced entities such as hypertension, obstructive sleep apnea, and endocrinological circadian rhythm changes that are known to be able to induce nocturnal polyuria[15,16,26–28]. It could be speculated that the findings reflect the existence of general disturbances in circadian rhythms in relation to obesity, but future studies are needed in order to elucidate this.

Regarding DUI, we did not find a significant association with childhood obesity. This association is well established with regard to stress incontinence in adult women[1,7]. However, stress incontinence is uncommon in children and adolescents and a hypothesis could be that pelvic floor

insufficiency arises after a longer period of obesity. In obese men, incontinence is also overrepresented, but primarily due to prostate problems[7,24]. Whether childhood obesity makes one more susceptible to developing incontinence and nocturia than later onset obesity is unknown but is also a subject for future studies.

In addition, we found obesity and FI associated in boys at school entry, but not in adolescents. This may reflect that obesity does not influence FI in adolescents. However, since FI is frequently a consequence of constipation[18], the disappearance of a FI-Obesity association in adolescent age could also reflect, that any obesity-related constipation in childhood has either been handled successfully or spontaneously resolved.

In the child population we found that 21.8% and 16.8% suffer from DUI and NE respectively. These figures are somewhat higher than those of previous reports[7–10]. This could be due to an actual increase in the frequency of symptoms. Moreover, the method of this study was an interview, which may implicate/support social acceptance and thus lead to less underreporting. Finally, changing definitions over time including the fact that we used the low threshold of “once per month” as a minimum criterion for the significance of symptoms could have resulted in higher figures than previously reported.

To the best of our knowledge, no previous large-scale population-based studies have dealt with childhood and adolescent nocturia. It has been assumed that the prevalence among children and adolescents is low in general, but increases through adulthood. Our study and studies in young adults support a high prevalence of nocturia. A recent meta-analysis by Bosch and Weiss covering young adults aged 18-30, found prevalence rates of nocturia to be higher in women (ranging from 20.4-43.9%) than in men (range 11- 35.2%)[29]. In young adults who have previously been treated for NE, a prevalence of nocturia of 35% was found[13] and it has been suggested that children treated for NE later develop or pass on to nocturia[30]. Our study, in contrast, suggests that the

prevalence may, in fact, be constant throughout childhood and adolescent life. However, it should be emphasized that it is not possible in this study to distinguish **children successfully treated for enuresis** from the other adolescents. What seems clear from this study is that, despite the FI, DUI and NE rates decreases markedly with age, nocturia frequency remains unchanged, with a prevalence of around 30%.

A low participation rate is a common limitation of population studies. By conducting the interviews by the school nurse, a safe and professional environment was entered, believed to give high quality and valid responses. We also obtained very high participation rates, which strengthen the study. Nonetheless, 15.5% of the adolescents invited did not participate and one could speculate that they may have represented a specific group.

A weakness of the study is that, since the questions were designed in a simplified manner, the study does not reveal information on previous treatment, subtype or severity of symptoms.

Conclusions:

In this study of 6.803 children and adolescents, we find a high and persisting prevalence of nocturia of around one-third. Obesity is prevalent in 4.4% and 6.5% of children and adolescents respectively. Obesity is associated with nocturia and leads to a nearly two-fold risk. We cannot confirm that obesity is directly associated with a specific incontinence type among this population, but being obese makes it more likely to have one or more of the symptoms of FI, DUI, NE or nocturia.

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Legends for figures and tables:

Table 1: Description of two Danish cross-sectional samples, consisting of A) 4.002 pupils, aged 5-7 years, and B) 2.801 pupils, aged 11-15 years, divided by gender. Numbers are mean±SD or numbers (percentage) unless otherwise stated.

Table 2: Associations between symptoms and BMI, odds ratio and 95% confidence interval, among 4.002 pupils in the child population and 2.801 pupils in the adolescents, divided by gender. Normal weight, Overweight and Heavily overweight according to WHO BMI-SDS.

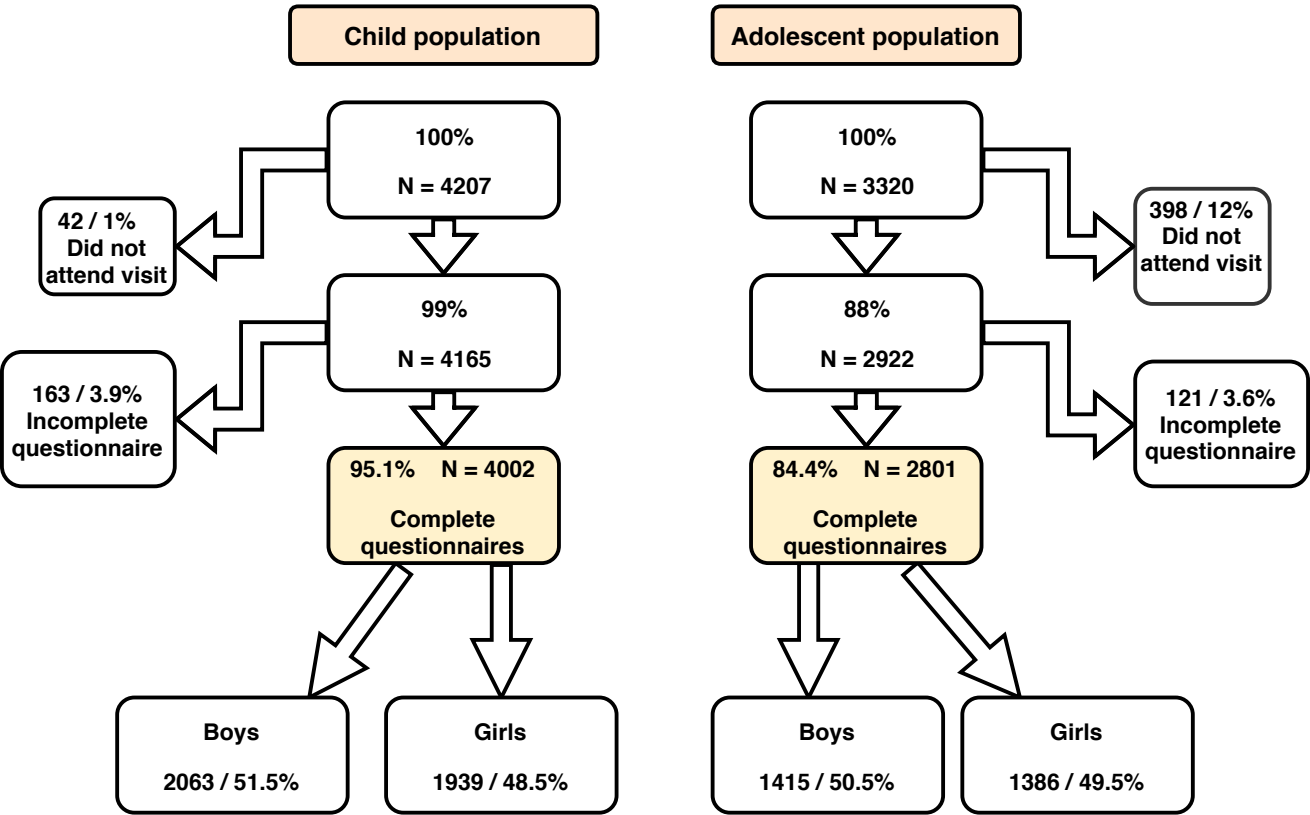
Figure 1: Flowchart of participants in two populations, consisting of children from first school year and adolescents examined at seventh, eighth or ninth school year, Denmark 2015/16 and 2016/17.

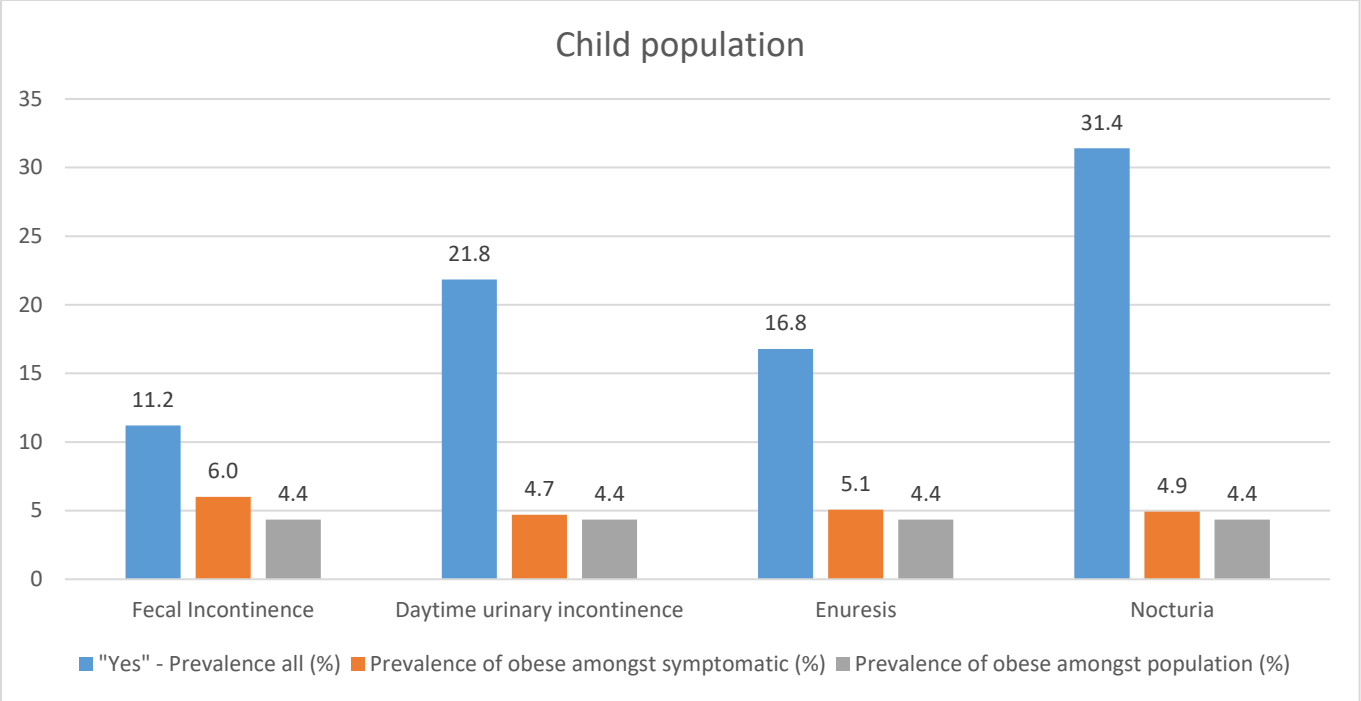
Figure 2: Bar charts illustrating prevalence (%) of fecal incontinence, daytime urinary incontinence, enuresis and nocturia and prevalence of obesity when answering “yes” against overall prevalence of obesity.

A) Child population		All	Boys	Girls	p-value, boys vs girls
N		4002	2063 (51.5)	1939 (48.5)	
Age (years)		6.45±0.39	6.49±0.41	6.40±0.37	<0.0001
Weight (kg)		23.46±3.74	23.73±3.71	23.18±3.75	<0.0001
Height (cm)		121.4 ±5.3	122.0±5.2	120.6±5.2	<0.0001
BMI (kg/m^2)		15.87±1.74	15.87±1.67	15.86±1.81	0.8270
BMI-SDS WHO		0.22±1.01	0.23±1.04	0.21±0.97	0.5055
	<-2 -2-1 1-2 >2	43 (1.07) 3180 (79.46) 605 (15.12) 174 (4.35)	30 (1.45) 1617 (78.38) 325 (15.75) 91 (4.41)	13 (0.67) 1563 (80.61) 280 (14.44) 83 (4.28)	0.057
Fecal incontinence (yes)		449 (11.2)	283 (13.7)	166 (8.6)	<0.0001
Daytime urinary incontinence (yes)		874 (21.8)	477 (23.12)	397 (20.5)	0.043
Enuresis (yes)		672 (16.8)	437 (21.2)	235 (12.1)	<0.0001
Nocturia(yes)		1257 (31.4)	684 (33.2)	573 (29.6)	0.014
Number of symptoms	0 1 2 or more	1954 (48.83) 1160 (28.99) 888 (22.19)	936 (45.37) 581 (28.16) 546 (26.47)	1018 (52.50) 579 (29.86) 342 (17.64)	<0.0001

B) Adolescent population		All	Boys	Girls	p-value, boys vs girls
N		2801	1415 (50.5)	1386 (49.5)	
Age (years)		13.90±0.85	14.00±0.85	13.83±0.84	<0.0001
Weight (kg)		56.27±12.39	57.38±13.21	55.14±11.39	<0.0001
Height (cm)		165.71 ±8.83	167.96±9.84	163.42±6.94	<0.0001
BMI (kg/m^2)		20.37±3.52	20.17±3.45	20.56±3.59	0.0034
BMI-SDS WHO		0.23±1.10	0.24±1.13	0.21±1.08	0.5205
	<-2 -2-<1 1-2	57 (2.03) 2086 (74.47) 475 (16.96)	31 (2.19) 1035 (73.14) 242 (17.10)	26 (1.88) 1051 (75.83) 233 (16.81)	0.128
	>2	183 (6.53)	107(7.56)	76 (5.48)	0.026
Fecal incontinence (yes)		60 (2.14)	37 (2.61)	23 (1.66)	0.081
Daytime urinary incontinence (yes)		126 (4.50)	43 (3.04)	83 (5.99)	<0.0001
Enuresis (yes)		29 (1.04)	19 (1.34)	10 (0.72)	0.104
Nocturia (yes)		904 (32.27)	498 (35.19)	406 (29.29)	0.001
Number of symptoms	0 1 2 or more	1780 (63.55) 935 (33.38) 86 (3.07)	861 (60.85) 517 (36.54) 37 (2.61)	919 (66.31) 418 (30.16) 49 (3.54)	0.001

Associations between symptoms and BMI		**Girls**					**Boys**				
		Normal weight	Overweight		Obesity		Normal weight	Overweight		Obesity	
		OR	OR	95% CI	OR	95% CI	OR	OR	95% CI	OR	95% CI
Children	Fecal incontinence	1	1.42	0.94-2.15	1.22	0.57-2.58	1	1.47	1.06-2.03	1.86	1.10-3.15
	Daytime urinary incontinence	1	1.16	0.85-1.58	1.27	0.76-2.13	1	1.17	0.89-1.55	1.03	0.62-1.70
	Enuresis	1	1.13	0.78-1.66	1.26	0.67-2.37	1	0.90	0.67-1.21	1.18	0.72-1.93
	Nocturia	1	1.24	0.94-1.62	1.56	0.99-2.46	1	1.18	0.92-1.51	0.91	0.58-1.44
Adolescents	Fecal incontinence	1	2.98	1.27-6.96	-		1	1.20	0.51-2.81	1-57	0.54-4.60
	Daytime urinary incontinence	1	1.32	0.76-2.31	1.44	0.60-3.45	1	0.68	0.27-1.78	1.92	0.78-4.72
	Enuresis	1	0.56	0.07-4.51	1.74	0.21-14.08	1	-		1.84	0.53-6.41
	Nocturia	1	1.17	0.86-1.60	2.01	1.25-3.23	1	0.78	0.58-1.06	1.74	1.17-2.60


Child population
100%
N = 4207
42 / 1%
Did not
attend visit
99%
N = 4165
163 / 3.9%
Incomplete
questionnaire
95.1% N = 4002
Complete
questionnaires
Boys
2063 / 51.5%
Girls
1939 / 48.5%
Adolescent population
100%
N = 3320
398 / 12%
Did not
attend visit
88%
N = 2922
121 / 3.6%
Incomplete
questionnaire
84.4% N = 2801
Complete
questionnaires
Boys
1415 / 50.5%
Girls
1386 / 49.5%



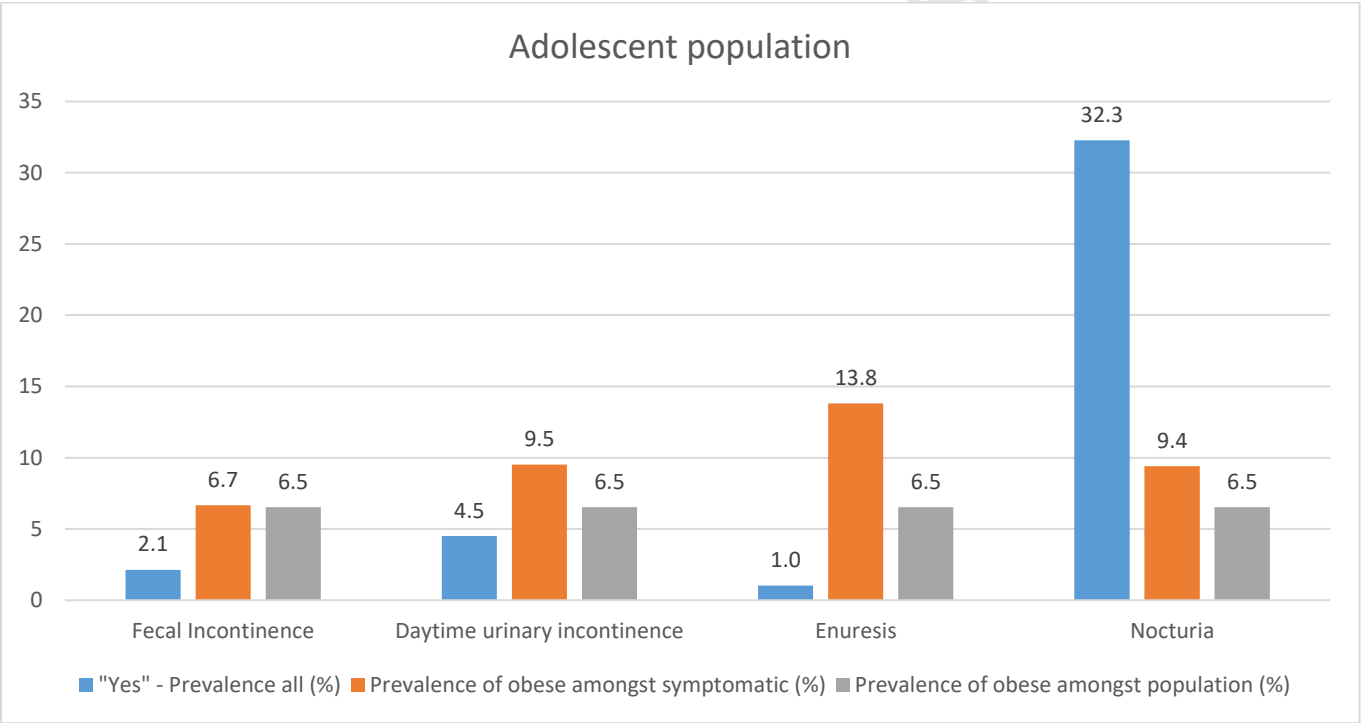


Figure 2: Bar charts illustrating prevalence (%) of fecal incontinence, daytime urinary incontinence, enuresis and nocturia and prevalence of obesity when answering “yes” against overall prevalence of obesity.