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Research Paper

The Role of Antidiuretic Hormone (ADH) in Involuntary Urination among Children in the Sharqat District

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Abstract:

Nocturnal Enuresis (NE), or the condition of involuntary urination, is observed in children aged between five and sixteen worldwide, spanning all cultures, social, and economic classes. This study was conducted on 119 children in some regions within the district of Al-Shirqat in Salah al-Din province from the beginning of October 2022 to the end of January 2023, to estimate the concentration of the antidiuretic hormone (ADH). Samples were tested in the laboratory, and information pertaining to each case was recorded based on a pre-prepared form which included relevant information like name, age, and gender. The concentration of ADH in blood serum was measured using the ELISA technique.

Results indicate that the frequency of involuntary urination in boys is significantly higher than in girls, with respective proportions of 54 (60%) and 36 (40%). Also, the study's outcomes confirm an elevated rate of involuntary urination in children within the age range of 1-5 years at 65.55% (59), and 25.55% (23) in the 5-10 years age group. Regarding the level of ADH hormone, results demonstrate a significant decrease ($P \leq 0.05$) in the level of antidiuretic hormone (ADH) in patients with involuntary urination, 2.04 ± 0.14 pg/ml, compared to the healthy control group, 5.17 ± 0.35 pg/ml.

The aim of this study is to evaluate the frequency of involuntary urination among children aged between 5 and 10 years in the Al-Shirqat district in Salah al-Din province, understand the relationship of nocturnal enuresis with age and gender in the child cohorts under study, and examine hormonal variables such as the Antidiuretic hormone (ADH) and its association with the condition of involuntary urination.

Keywords: Nocturnal Enuresis (NE), Involuntary urination, Antidiuretic hormone (ADH), Children, Age and gender, Frequency, Hormonal variables, Salah al-Din province.

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Introduction:

Nocturnal enuresis, also known as bedwetting, is described as an unintentional discharge of urine during sleep among children aged five or older, with no demonstrable abnormalities in the central nervous system or urinary tract. It is estimated that around 6 million children experience this condition annually in the United States. This condition presents in 15% of 5-year-old children, 5% of 10-year-old children, and 1% of 13-year-old children. Without intervention, about 15% of children outgrow bedwetting each year[1].

Worldwide, Nocturnal Enuresis (NE) is present in children aged between five and sixteen, transcending cultural, social, and economic boundaries[2]. A distinct correlation between parental enuresis and childhood enuresis has been observed[3,4]. Several definitions and symptom descriptions of involuntary urination in children and adolescents have been proposed in past studies[2]. The reported prevalence rates of these symptoms can differ based on the selected definition and the age of the children included in the study. This variance complicates the comparison of NE's different facets across age groups, cultures, and regions[5]. Furthermore, the actual occurrence of NE might be underreported due to the embarrassment or cultural factors[6].

According to the International Children's Continence Society (ICCS), NE is equivalent to intermittent nocturnal incontinence, meaning episodic urinary incontinence during sleep. It is labeled "primary" if the child has been dry during sleep for less than six months previously and "secondary" if the child starts to wet the bed after at least six consecutive dry months[2]. The Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V), describes it as "a continuance of involuntary urination for three months at a frequency of at least two nights a week for a child who has attained the age and/or mental development of five years"[7].

The prevalence rate of NE declines as the child progresses from school age to adolescence, a phenomenon attributed to the spontaneous resolution accompanying the child's maturation. This process occurs at an approximate rate of 15-20% annually, reducing to 1-2% by the age of fifteen and further into adulthood[8]. The ICCS further categorizes it as "monosymptomatic nocturnal enuresis" (MSNE), and NE is labeled non-monosymptomatic nocturnal enuresis if it is accompanied by symptoms of lower urinary tract syndrome (NE-LUTS), such as dysuria, suprapubic pain, and daytime incontinence. Additionally, it elucidates common associated conditions that are considered relevant to NE, including constipation, urinary tract infection (UTI), abdominal pain, asymptomatic bacteriuria, vesicoureteral reflux, psychological and learning disorders, sleep disorders, and diabetes[2].

A potential cause of involuntary urination is the diminished concentration of the antidiuretic hormone (ADH) in the blood, an inhibitory hormone for urine formation that is located in a region of the brain known as the hypothalamus and stored in the posterior pituitary gland[9]. This hormone is secreted in both males and females and helps regulate water concentration in the blood and control the amount of water filtered and excreted through the kidneys[10]. It also helps in maintaining the body's internal temperature and is secreted in stressful or painful situations[11].

Predictive relationships have been observed between factors like race, age, sex, birth order, education level, parental employment status, family size, income, socioeconomic status, and sleeping habits, and the incidence of NE and involuntary urination[5]. In most instances, the underlying cause of bed

wetting remains unidentified. The first step should always involve a medical examination to rule out any covert diseases or conditions such as diabetes, urinary tract

infections, urethral valve abnormalities in boys, ureteral abnormalities in girls, and spinal cord deformities[12].

The objective of this study is to assess the frequency of involuntary urination among children aged 5 to 10 years in the Sharqat district of Salah al-Din province, to understand the relationship of nocturnal enuresis with age and sex in the studied child groups, and to investigate hormonal variables like the Antidiuretic Hormone (ADH) and their connection to nocturnal enuresis.

****Methods****

****Study Population:****

This study was conducted on 119 children in select areas within the Sharqat district of Salah al-Din province from the beginning of October 2022 until the end of January 2023. The goal was to determine the concentration of the Antidiuretic Hormone (ADH). Samples were analyzed in the laboratory and the corresponding data for each case was recorded based on a previously prepared form that included relevant information to the study such as: name, age, and gender.

****Sample Collection:****

***Blood Sample:** Blood samples were collected from the children, drawing 5 ml of venous blood using medical syringes. The blood was placed in tubes containing an anticoagulant and stored in an icebox to preserve the samples until the desired quantity was gathered. Thereafter, the samples were placed in gel-containing tubes and centrifuged using a centrifuge at a speed of 3000 revolutions per minute for 15 minutes to separate the blood serum. The serum was then extracted using a micropipette and placed in a small test tube and stored in a freezer at -20°C until biochemical and hormonal parameters, which were the focus of our current study, could be evaluated.

Estimation of the Concentration of Antidiuretic Hormone (ADH) in the Blood Serum:

The examination kit from Sunlong Biotech, China, which utilizes the Enzyme-Linked ImmunoSorbent Assay (ELISA) technique was used. The ELISA kit used the Sandwich ELISA method and came equipped with a microelisa strip plate coated with antibodies specific to ADH. Standards or samples were added to the microelisa plate wells and combined with a designated antibody. Then, Horseradish Peroxidase (HRP), conjugated with an antibody specific to ADH, was added to each well and incubated. Unbound compounds were washed away.

A Tetramethyl benzidine (TMP) solution was added to each well containing ADH and HRP conjugated with ADH antibodies, which initially appeared blue and turned yellow after adding a stop solution. The optical density (OD) was spectrophotometrically measured at a wavelength of 450 nm. The OD value is proportional to the concentrations of ADH, and the concentration of ADH in the samples can be calculated by comparing the optical density of the samples with the standard curve.

****Statistical Analysis:****

Statistical analysis of the current study data was performed using the Chi-square test with the assistance of SPSS software. The current study data were displayed using tables and graphs.

Results

The results in Table 1 show the distribution of study groups where the control group consisted of 29 individuals (24.4%) and the patient group included 90 individuals (75.6%), with a total of 119 individuals (100%). In Table 2, the group of individuals with enuresis is displayed according to gender, with male representation in the control group being 14 (48.3%) and female representation being 15 (51.7%). In the patient group,

male representation was higher, being 54 (60%), while female representation was 36 (40%). Table 3 is not provided, but it seems to discuss the distribution of enuresis in the control group by age.

Table 1: Distribution of Study Groups by Disease Incidence

Study Groups	Count (%)
Control	29 (24.4%)
Patients	90 (75.6%)
Total	119 (100%)

p-value: 0.0021**

The results in Table 2 show that the frequency of enuresis occurrence in boys is significantly higher than in girls, at 54 (60%) and 36 (40%) respectively.

Table 2: Distribution of Enuresis Group by Gender

Study Groups	Males	Females
Control (n=29)	14 (48.3%)	15 (51.7%)
Patients (n=90)	54 (60%)	36 (40%)

p-value: Males 0.021*, Females 0.001*

*, **: Statistically Significant

The current study results indicated a high incidence of enuresis in children in the age group of 1-5 years, at a rate of 65.55% (59), and a rate of 25.55% (23) in the age group of 5-10 years.

Table 3: Distribution of Enuresis Group by Age

Study Groups	0-5 Years (%)	5-10 Years (%)	10-15 Years (%)
Control (n=29)	0 (0%)	0 (0%)	0 (0%)
Patients (n=90)	59 (65.55%)	23 (25.55%)	8 (8.88%)

p-value: 0-5 years 0.021*, 5-10 years 0.001*, 10-15 years 0.020*

*, **: Statistically Significant

As for the level of the antidiuretic hormone (ADH), the results demonstrated a significant decrease ($P \geq 0.05$) in the ADH hormone level in patients suffering from enuresis (2.04 ± 0.14 pg/ml), compared to the healthy control group (5.17 ± 0.35 pg/ml) (Figure 1).

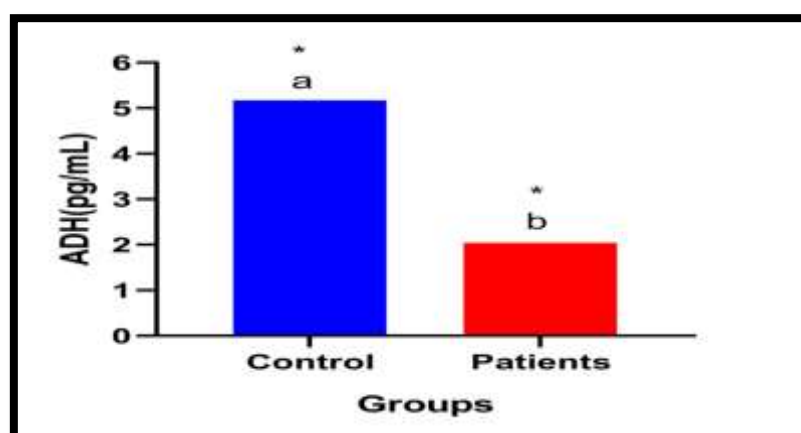


Figure 1: Level of the antidiuretic hormone in both the patient group and control group.

Discussion:

The attainment of nocturnal bladder control is typically expected between the ages of 4 and 6. Nevertheless, an increased likelihood of nocturnal enuresis, or involuntary urination, between 4 and 9 years is reported in children who have faced early childhood stressors. It is postulated that this condition arises due to three interrelated factors within the central nervous system (CNS), characterized as a delay in maturation rather than a disorder. As children mature, those affected with late-onset enuresis are predicted to progressively acquire better bladder control, enhanced CNS recognition of bladder fullness, and a capacity to suppress untimely bladder contractions. Therefore, despite achieving control at an older age compared to their peers, these children are expected to eventually attain full control [13].

In terms of gender distribution, the prevalence of involuntary urination is higher among boys (60%) compared to girls (40%), aligning with several preceding local and international studies [14]. These findings are in concordance with a Turkish study by a researcher [12], which revealed a male to female ratio of 60% to 40%. Similar results were replicated in another study that reported a male to female ratio of 52.2% to 47.8% respectively. However, the gender disparity may be influenced by societal and cultural factors which may cause reluctance in reporting involuntary urination [15].

There's an observed increased incidence and duration of enuresis in boys as compared to girls [16]. The gender differential could be attributed to the quicker maturation in females as compared to males. Although the condition affects diverse age, gender, and ethnic groups, research limitations and sample diversity may cause apparent differences in study outcomes.

The frequency of involuntary urination among children aged 5-7 years in this study aligns with findings of previous studies [18]. The multifactorial etiology of nocturnal enuresis is not fully understood but may result from a combination of factors [19]. Spontaneous recovery is observed at a rate of around 14% annually [20].

A strong correlation between enuresis and family history has been observed in various studies. Children with a positive family history of enuresis are significantly more likely to experience involuntary urination compared to those with a negative family history [21,22].

Enuresis has multifaceted origins involving biological, behavioral, psychological, and social factors. The period between 2-4 years is crucial for achieving bladder control. High parental stress during this period can negatively impact toilet training [23], leading to an increased risk of bladder dysfunction [24].

Stress hormone cortisol, known to negatively impact pituitary gland function, may interfere with the production and/or secretion of the antidiuretic hormone (ADH). Reduced ADH levels can cause overproduction of urine, thus increasing the risk of nocturnal enuresis [25,26].

Night-time urine overproduction may fill the bladder rapidly causing either nocturnal arousal for urination or involuntary urination in deep sleepers [27]. Decreased secretion of ADH, observed in about two-thirds of children with nocturnal enuresis, leads to increased urine production [28].

Desmopressin, a synthetic analogue of ADH, is often used in treating conditions like diabetes insipidus due to its ability to reduce urination. Involuntary urination in some children may be an indication of diabetes insipidus, which results from a deficiency in ADH [29]. This aligns with our study outcomes, further emphasizing the role of hormonal factors in nocturnal enuresis.

Conclusions

1. There's a significant genetic or familial factor involved in enuresis. If one of the parents has suffered from the condition, the risk for their children to develop it increases significantly.
2. Enuresis is not merely a behavioral issue; it's a complex condition with multiple contributing factors, including biological, behavioral, psychological, and social aspects.
3. The period between ages 2-4 is a critical time for developing bladder control, and parents' stress levels or lack of time for toilet training can impact a child's progress during this period.
4. Inadequate or late toilet training could contribute to various bladder issues, including urgency, urinary incontinence, and voiding difficulties. Bladder weakness is associated not only with daytime urination but also with involuntary nighttime urination.
5. Physiological factors, particularly stress hormones like cortisol and their influence on the antidiuretic hormone (ADH), play significant roles in bladder function. The dysregulation of these hormones can lead to a higher volume of urine produced than the bladder can store, leading to involuntary urination.
6. Nocturnal enuresis can occur due to a discrepancy between nighttime urine production and bladder capacity, often resulting from physiological factors such as insufficient nocturnal vasopressin secretion or low levels of ADH.
7. Diabetes insipidus, characterized by decreased reabsorption of water from the kidneys leading to polyuria and polydipsia, may manifest in some children showing symptoms of diabetes. This could be due to decreased levels of the antidiuretic hormone (ADH), underlining the importance of ADH and its synthetic analogue, Desmopressin, in the regulation of urination and in the treatment of conditions like diabetes insipidus.

Recommendations

1. **Toilet Training Onset:** Initiation of toilet training during the key developmental window of 2-4 years of age is recommended for fostering optimal bladder control.
2. **Parental Stress Mitigation:** Active stress management strategies should be adopted by parents to prevent a potential adverse impact on their child's toilet training and bladder control processes.
3. **Healthcare Consultation:** Should the problem of enuresis continue despite adequate toilet training and stress management, it is advised to seek medical consultation from a pediatrician or urologist.
4. **Hereditary Considerations:** Given the high likelihood of enuresis being inherited, families with a history of this condition should monitor their children's bladder control development closely.
5. **Hormonal Evaluation:** In view of the role hormones such as ADH and cortisol play in bladder control, hormonal imbalances or disorders like diabetes insipidus in children exhibiting persistent enuresis should be considered.
6. **Therapeutic Alternatives:** In case a child is diagnosed with a condition like diabetes insipidus, the exploration of treatment options, such as Desmopressin - a synthetic analogue of ADH, can be beneficial.
7. **Continual Medical Monitoring:** Regular medical follow-up is advised for children with diagnosed bladder control conditions to keep track of progress and modify treatments as required.
8. **Comprehensive Management Approach:** The approach to managing enuresis should encompass not just physiological, but also psychological and social aspects that can influence the condition.

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