

**THE RELATIONSHIP BETWEEN NOCTURNAL ENURESIS AND SPINA BIFIDA OCCULTA. A PROSPECTIVE STUDY AT THE DEPARTMENT OF UROLOGY AND KIDNEY TRANSPLANTATION, FOUNDATION UNIVERSITY MEDICAL COLLEGE/FAUJI FOUNDATION HOSPITAL, RAWALPINDI**

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**Abstract:** Nocturnal enuresis (NE) and spina bifida occulta (SBO) are common problems in childhood. SBO is more prevalent in patients with NE than in the asymptomatic general population. SBO in patients with NE may be associated with worse symptoms and affect the response to treatment. The present study was carried out to document the frequency of SBO in patients with NE and to determine its effect on the response to treatment. This prospective study was conducted at the Department of Urology and Kidney Transplantation, Foundation University Medical College/Fauji Foundation Hospital, Rawalpindi, from 24 August 2022 to 23 March 2023. Pediatric patients aged 6-15 years with NE were included in the study. A plain X-ray KUB, among other investigations, was performed to look for SBO. Patients were divided into two groups based on SBO. The severity of symptoms, treatment response, and other variables were recorded on proforma. All patients were treated with behavioral therapy and Imipramine 25mg. The response was assessed by a reduction in the number of wet nights at 3 months of treatment. Data were analyzed using SPSS version 21. Percentages and frequencies were given; mean  $\pm$  SD was used for quantitative data. For the comparison of two categorical variables, the Chi-Square test was used. A total of 78 patients (51 boys and 27 girls), aged 6-15 years, and a mean age of  $10.7 \pm 2.8$  years with nocturnal enuresis were included in the study. SBO was detected in 28.2% of children. SBO was most commonly seen at L5-S1 and S1 levels (31.8%). Patients with SBO had more severe symptoms and responded poorly to treatment. A complete response to treatment was observed in 66% of patients in the non-SBO group and only 22.7% in the SBO group. No response was seen in 8.9% of children in the SBO group and 27.2% in the SBO group. The difference in response to treatment in both groups was statistically significant ( $P=0.001$ ) SBO is a frequent finding in patients with NE. It may be associated with more severe symptoms and adversely affect the treatment response.

**Keywords:** Nocturnal, Urinary Enuresis, Spina Bifida Occulta, Pediatric Incontinence.

## Introduction

Nocturnal enuresis (NE), or nighttime bed wetting during sleep, is a common pediatric problem. It adversely affects the self-esteem, social and psychological development of the child. The etiology of NE is complex and often multifactorial (Bahnasy et al., 2018; Gong et al., 2021; Tai et al., 2021). Enuresis may be a symptom of many disorders, including spinal dysraphism. Spina bifida occulta (SBO) is a subtle form of dysraphism with failure of fusion of the posterior arch of the lumbosacral spines (Elkashlan et al., 2020). SBO has a wide range of prevalence between 1.2-21% (Shin et al., 2013; Zaganjor et al., 2016). Literature suggests that enuretic children have a higher incidence of SBO, which may affect their treatment response (Elkashlan et al., 2020). The data concerning the effect of SBO on treatment response among patients with NE is controversial. Kumar et al. and Ritchey et al. did not report any significant effect of SBO on the response to treatment in NE patients, while Shin et al. and Elkashlana et al. reported that the presence of SBO significantly affected the response to treatment and suggested that SBO should be verified in such cases to predict the response to treatment (Elkashlan et al., 2020; Kumar et al., 2005; Ritchey et al., 1994; Shin et al., 2013). The present study was conducted to record the

frequency of SBO in patients with NE, determine their response to treatment, and compare it to those without SBO.

## Methodology

The prospective study was conducted at the Department of Urology and Kidney Transplantation Foundation University Medical College/Fauji Foundation Hospital, Rawalpindi, from 24<sup>th</sup> August 22 to 23<sup>rd</sup> March 23. Prior ethical approval was sought from the hospital's ethical committee. Patients between 6-15 years of age presenting with NE with a minimum 1 episode of nighttime bed wetting per week for 3 consecutive months were included in the study by nonprobability consecutive sampling and evaluated for the presence of SBO by a digital X-Ray Lumbosacral spine. The sample size was calculated using Raosoft, margin of error of 5%, a confidence level of 95%, a population size of 100, and an anticipated population proportion of 33%, and it was found to be 78. Patients were divided into two groups. Group I included patients with NE without SBO, and Group II included patients with NE with SBO. Patients were evaluated for symptom severity and response to treatment. Patients with daytime urinary incontinence, neurogenic bladder, diabetes mellitus, diabetes insipidus, history of

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spinal surgery, spina bifida with skin findings, and active urinary tract infection were excluded from the study. All the patients were evaluated with a detailed history and a physical examination, including a focused neurological exam. Urine RE, serum creatinine, complete blood count, an ultrasound KUB with pre and post-void residual urine volume. A digital X-Ray lumbosacral spine was obtained in all patients and was reported by a consultant radiologist for the presence of SBO and its level. Patients with one-bed wetting per week were labeled as mildly symptomatic, those with 2 or 3 episodes per week were labeled moderately symptomatic, and those with 4 or more nighttime bedwetting per week were labeled severely symptomatic. All patients were treated with behavioral therapy and imipramine 25mg at bedtime, followed after 4 weeks for 3 months, and assessed for response to treatment (reduced bedwetting episodes per week). Patients whose symptoms persisted with the same severity after 3 months were labeled as non-responders, Patients with decreased severity of symptoms were labeled as partial responders, and patients who became dry were labeled as complete responders. Patient data of multiple variables, including age, gender, symptom severity, presence of SBO, its level, and response to treatment, was recorded on a predesigned proforma. The data was analyzed using SPSS version 21. Percentages and

frequencies were given; mean ± SD was used for quantitative data. For categorical variables, the Chi-Square test was used. Pearson correlation was used to see the relationship between the two groups in terms of severity of symptoms and response to treatment. P value ≤0.05 was taken as statistically significant.

**Results**

A total of 78 patients (51 boys and 27 girls), aged 6-15 years, mean age 10.7 ± 2.8 years with nocturnal enuresis, were included in the study. SBO was detected in 28.2% of children (Figure 1). SBO was most commonly seen at L5-S1 and S1 levels (31.8%), S1-2 at 13.6%, L5 at 9 %, and L4 and L4-5 at 4.5% (Table 1, Figures 2 and 3). The severity of symptoms was more in group II, as summarized in Table 2 but was statistically insignificant (P=0.289). Patients with SBO responded poorly to treatment (Table 3). A complete response to treatment was observed in 66% of patients in the non-SBO group and only 22.7% in the SBO group. No response was seen in 8.9% of children in non SBO group and 27.2% in SBO group. The difference in response to treatment in both groups was statistically significant (P=0.001).

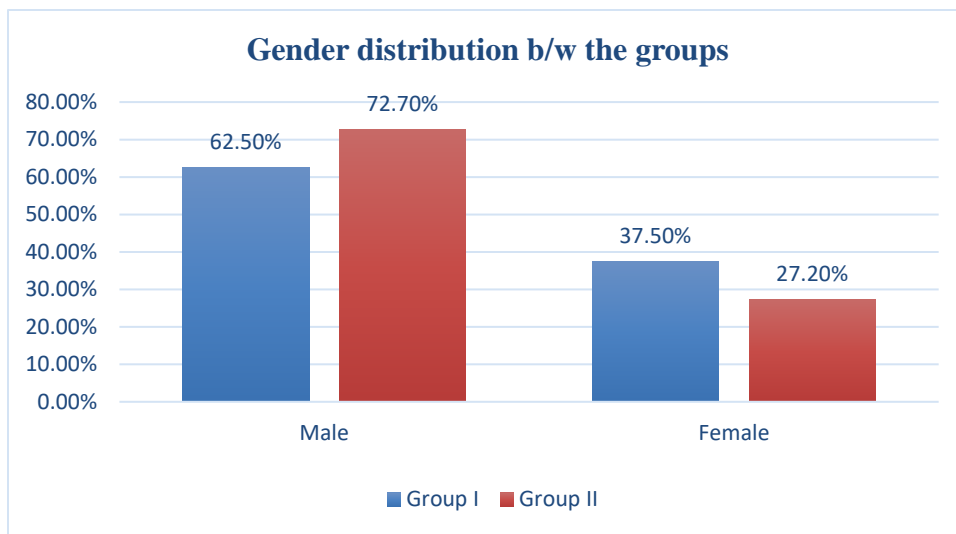


Figure 1: Distribution of gender

Table 1: Level of Spina bifida occulta

SBO Level	Number of Patients (N=22) 28.2%
L4	1 (4.5%)
L5	2 (9%)
L4-5	2 (9%)
L5-S1	7 (31.8%)
S1	7 (31.8%)
S2	-
S1-S2	3 (13.6%)

Table 2: Severity of Symptoms

Symptom Severity	Group I (N=56)	Group II (N=22)	Chi-square = 1.124 and P value = 0.289
Mild	19 (33.9%)	4 (18.1%)	
Moderate	26 (46.4%)	13 (59%)	
Severe	11 (19.6%)	5 (22.7%)	

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Figure 1: L5-S1 Spina bifida occulta



Figure 2: S1 Spina bifida occulta

Table 3: Response to treatment

Outcome	Group I (N=56) %	Group II (N=22) %	Chi-square = 11.377 and P value = 0.001
Complete response	37 (66%)	5 (22.7%)	
Partial response	14 (25%)	11 (50%)	
No response	5 (8.9%)	6 (27.2%)	

**Discussion**

In 1875 Virchow coined the term spina bifida occulta. Even though they were based on anatomical dissections, early findings suggested that SBO was not common in the general population. Once the X-Ray of the spine became available, it revealed that the most frequent congenital malformations of the spine were nonfusion of the spinous processes of the lumbar and sacral vertebrae. Initially believed to be a typical anatomical variety, SBO was linked to several illnesses in the early 20th century. SBO was found to be more common in patients with back pain, lower urinary tract and bowel problems, stress incontinence, and enuresis (Kajbafzadeh et al., 2004). Enuresis may be the only symptom of SBO (Cakiroglu et al., 2014).

The frequency of SBO in the present study was 28.2%. This is comparable to other series in the literature. In their series of 163 patients with NE, Kurt et al. reported SBO in 28.8% (Kurt et al., 2015). Shin et al. reported SBO in 26.9% of patients with NE. (Shin et al., 2013) Their series of 184 patients with NE, Yavuz et al. reported SBO in 19.5%.

Literature suggests that SBO is more prevalent in patients with NE than in the general asymptomatic population, and its presence may affect the response to treatment. In a recent study conducted by Elkashlana et al., similar results were observed, where children with SBO had a poor response to treatment with behavioral therapy and imipramine compared to those without SBO. They proposed that SBO impairs the neural control of urination by impairing sacral nerve excitement due to insufficient bladder filling, which lowers cerebral cortex stimulation intensity below the waking threshold and produces an arousal disorder. Therefore, the intensity of nocturnal enuresis symptoms may worsen due to SBO, making therapy more challenging (Elkashlan et al., 2020). Shin et al., in their series of 160 patients with NE, documented higher response rates to

treatment with desmopressin in patients without SBO than those with it.<sup>5</sup> Similarly, Cakiroglu et al. divided 223 children with NE into 2 treatment groups, one group received Desmopressin, and the second group received a combination of Desmopressin and Tolterodine. They concluded that the presence of SBO adversely affected the success of medical treatment (Cakiroglu et al., 2014). Kurt et al. studied the effect of SBO on the success of behavioral therapy in patients with NE and concluded that the presence of SBO was significantly related to the success of behavioral therapy (Kurt et al., 2015). Similarly, Yavuz et al. studied the effect of SBO in their 183 patients with monosymptomatic and non-monosymptomatic NE. They treated Monosymptomatic NE patients with desmopressin and non-monosymptomatic NE patients with a combination of desmopressin and oxybutynin. They reported a significantly lower success rate in their patient with NE with SBO to treatment (Yavuz et al., 2018). Similarly, Chaikaew et al., in their series, reported a lower response to desmopressin to melts therapy in patients with non-monosymptomatic nocturnal enuresis with spina bifida (Chaikaew et al., 2021). In another series, Miyazato et al. studied the effect of the location of SBO and bladder abnormalities on ultrasonography to predict the outcome of treatment to treatment in children with NE and concluded that children with lumbar and lumbosacral SBO showed a higher rate of concomitant ultrasonographic bladder abnormalities and had a poorer response to treatment compared with the children who had sacral SBO (Miyazato et al., 2007).

On the other hand, an earlier study on 48 patients with NE treated with behavioral therapy by Kumar et al. concluded that the treatment outcome was not different in patients with SBO than those without SBO. However, their sample size was small, and only 18 patients had SBO (Kumar et al., 2005). In contrast to our study, Ritchew et al. compared the

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treatment success rates among 127 children with diurnal enuresis. The patients were initially treated with timed voiding, and an anticholinergic agent was added to those with persistent enuresis. Their series included 48 SBO patients. At three years of mean follow-up, the authors concluded that the outcome for enuretic children with SBO was comparable to those with normal spine X-rays (Ritchey et al., 1994).

Despite the disparity in results, it should be noted that SBO is more frequent in patients with NE as compared to asymptomatic patients (Elkashlan et al., 2020). Although earlier literature on this subject is equivocal, most recent studies strongly suggest that the presence of SBO should not be overlooked in patients with NE. We suggest that SBO should be sought in every patient with NE by at least performing a Plain X-Ray lumbosacral spine as its presence may affect the severity of symptoms and response to treatment.

Our study had a few limitations. We did not have a control arm to determine the frequency of SBO in asymptomatic patients. NE can be treated with behavioral therapy alone or with different medications, including desmopressin, anticholinergics, and antidepressants. We managed all the patients with a combination of behavioral therapy and imipramine.

## Conclusion

SBO is a frequent finding in patients with NE. If present, it may be associated with more severe symptoms and adversely affect the treatment response.

## Declarations

### Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

### Ethics approval and consent to participate

Ethical approval was obtained from Hospital's ethical committee on 23.8.2022 (598/RC/FFH/RWP)

### Consent for publication

Not applicable

### Funding

Not applicable

## Conflict of interest

The authors declared an absence of conflict of interest.

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