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Original Article

Prevalence of inguinoscrotal pathologies and risk factors in a cohort of 388 children with spina bifida

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ABSTRACT

Background. There is limited information about the prevalence and risk factors of inguinal hernia and undescended testis in patients with spina bifida (SB). The aim of this study was to identify the properties and prevalence of inguinoscrotal diseases in these patients.

Methods. A questionnaire was completed by parents of patients with the diagnosis of SB in our center. Together with demographic data, presence an of inguinal hernia, side, operation history, presence of ventriculoperitoneal (VP) shunt, type of SB aperta or occulta, recurrence and presence of undescended testis were questioned. Patients were grouped into 2 as SB aperta and occulta. The prevalence of these pathologies and their clinical properties were evaluated.

Results. In this study, 388 patients were evaluated. Of these, 238 patients had SB aperta and 150, SB occulta. There was no significance in comparison of gender. The prevalence of inguinal hernia was 12.6% in general. A hernia was noted in 37 SB aperta patients (15.6%) whereas this was seen in 12 of the SB occulta patients (8%) (p=0.029). When there was a VP shunt, hernia prevalence was 21.5% and when there was no shunt, this ratio was 7.1% (p=0.0001). Prevalence of inguinal hernia was 21.8% in males and 3.2% in females (p=0.0001). When there was a VP shunt with SB aperta the prevalence was 21.9% and when a VP shunt was present with SB occulta, this number was found to be 13.3% (p=0.006). The prevalence of undescended testis was 17.7% and there was no difference between SB aperta and occulta patients.

Conclusions. Inguinal hernia and undescended testis are more frequent in SB patients when compared to the normal population. VP shunts and male gender may be risk factors for inguinal hernia in these children. These findings may imply neurological factors in the etiology of inguinal hernia and undescended testis.

Key words: inguinal hernia, undescended testis, spina bifida, children.

Spina bifida (SB) is a developmental anomaly of the neural tube when there is incomplete closure of this fetal structure. This maldevelopment results in neural injury and various neurological deficits related to the level of the lesions. Two major forms of the disease have been named as SB aperta (SBA) and SB occulta (SBO) according to the closure of the skin over the vertebral defect. In a wide study in the United States, the overall prevalence of this anomaly has been found to be 3.1 in 10000 live births.[1] In a recent meta-analysis, the pooled prevalence of SB has been shown to be 4.76 cases in 10000 births including live births, stillbirths and termination of pregnancies.[2]

Inguinoscrotal pathologies, including inguinal hernia (IH) and undescended testis (UDT) are the most commonly encountered group of diseases in pediatric surgical practice.

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IH and UDT are linked together in their etiopathogenesis. The processus vaginalis is expected to obliterate after the testes complete their descent and failure of obliteration causes IH. The incidence of IH is quite high, as much as 1-4%, equivalent to 10-20 cases per 1000 live births.[3] The incidence of UDT varies according to the gestational age of the newborn and is accepted to be 1-4.6% in full-term and 1.1-45% in preterm male babies.[4] There are various theories about how UDT develops in children.[5,6]

The association of UDT and SB had not been understood until 1981.[7] Various studies have reported an incidence of UDT with SB to be between 1-25.6%, afterward.[8-10] In general, the incidence of UDT has been accepted to be higher in patients with SB in comparison to the general population. On the other hand, the association of IH and SB has not been delineated, yet and the factors affecting the occurrence of IH in these patients have not been fully demonstrated.

The aim of this present study was to identify the prevalence of IH and UDT in a large patient cohort with SB as well as the factors that might affect its coexistence. To the best of our knowledge, the present study is the largest cohort in the literature on this subject and the only study that questions the risk factors for IH in this patient group.

Material and Methods

Patients who were admitted to our SB center with the diagnosis of SBA and SBO were included in the study. Ethical approval was obtained from the institutional review board for the study (İstanbul Medeniyet University Göztepe Prof. Dr. Süleyman Yalçın City Hospital Ethical Review Board, IRB No:2020/0618). Clinical data for SBA and SBO were collected retrospectively. The clinical information regarding the type of spinal anomaly and past medical history were also collected from the patient files. All parents of the patients were interviewed prospectively to note the information for IH and UDT. Together with demographic data, presence of an inguinal hernia, laterality, presence of ventriculoperitoneal (VP) shunt, type of SB (aperta or occulta), recurrence of IH and presence of UDT were questioned. Patients with noncommunicating hydrocele were not included in the study and communicating hydrocele was accepted in the spectrum of IH due to the persistence of the processus vaginalis.

Patients were grouped as SBA and SBO. Clinical data as well as the prevalence of IH were questioned as per the diagnosis, presence or absence of VP shunt and combined prevalence according to the diagnosis and VP shunt, together. Thus, the factors that affect the generation of IH were sought.

Statistical Analysis

The statistical analyses were done with the statistical program SPSS 22.0 (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA). Numeric values were given as mean ± standard deviation (SD) and categorical values in percentage. Firstly, all relations between numeric and categorical variables in the groups were investigated by using univariate tests (i.e. Pearson chi-square test and Student's t-test). After univariate evaluations, statistically significant p values lower than 0,05 were selected for multivariate binary logistic regression analysis to evaluate the major factors influencing IH and UDT formation. Results of multivariate binary logistic regression were given with a p-value, odds ratio (OR) and 95% confidence interval (CI) for Exp B. One sample t test for proportions was used to analyze the prevalence of IH in this study with an estimated prevalence of 3% in the general population. A p-value below 0.05 was considered to be statistically significant.

Results

A total of 388 patients who were admitted to our SB center were evaluated. Of these, 238 patients had SBA and 150 patients had SBO. The mean age of the patients was 5.56±4.29 years (between 2 months and 18 years of age) and 207 of them

were males and 181 females. In the SBA group, there were 123 males and 115 females and in the SBO group there were 80 males and 70 females. The comparison of gender distribution was not significant (p=0.613). The mean age in SBA group was 5.09±3.89 years whereas the mean age in SBO group was 6.33±4.71 years (p=0.008).

Prevalence of IH was 12.6% in general including all the SB patients. This ratio was statistically significant when compared to the estimated prevalence in the population (p<0.001). Hernia was noted in 37 SBA patients (15.6%) whereas this was seen in 12 of SBO patients (8%) (p=0.029). Hernia was bilateral in 22 patients (44.9%), right sided in 14 (28.6%), left sided in 12 (24.4%) and undefined in one patient. Recurrence was noted in 9 patients (18.4%). When there was a VP shunt, hernia prevalence was 21.3% (35 patients among 164 patients with VP shunt) and when there was no shunt, this ratio was 7.1% (15 patients among 211) (p=0.0001). The prevalence of IH was 21.8% in males and 3.2% in females (p=0.0001). When there was a VP shunt with SBA the prevalence was 21.9% and when a VP shunt was present with SBO, this number was found to be 13.3% (p=0.006) (Table I). The prevalence of UDT was 17.7% and there was no difference between SBA and SBO patients.

Table I. Summary of major clinical factors affecting inguinal hernia development.

	Presence of IH (%)	*p**
Gender		
Male	21.8	0.0001
Female	3.2	
SBA+VP	21.9	0.006
SBO+VP	13.3	
VP(+)	21.3	<0.0001
VP(-)	7.1	
SBA	15.6	0.029
SBO	8	

IH: inguinal hernia, SBA: spina bifida aperta, SBO: spina bifida occulta, VP: ventriculoperitoneal shunt
*The *p* values give the comparison of each parameter with the data one line under.
Pearson chi-square test.

Cross comparisons were done to evaluate the risk factors for IH. Of the 165 patients with a VP shunt, 140 (84.8%) were males in this cohort whereas this figure was 15.2% (n:25) for females (p<0.0001). Male SBA patients with IH were compared with male SBO patients with IH in terms of VP shunt presence. Of the 31 male SBA patients with IH 27 (87%) had a VP shunt while only 16.7% of male SBO patients with IH (n:2 among 12 patients) had this intervention for hydrocephalus (p<0.0001).

Multivariate binary logistic regression analysis was done to identify the risk factors in the development of IH and UDT in this patient group. Male gender (p<0.0001, OR=0.107, 95%CI for ExpB 0.045-0.254) and presence of a VP shunt (p<0.0001, OR=0.185, 95%CI for ExpB 0.083-0.408) were found to be significant risk factors in the formation of IH in patients with SB. Then, we analyzed the prevalence of SB patients with IH but without a VP shunt. There was a total of 15 patients (7.1%) with IH but without a VP shunt. When we compared this ratio with an estimated prevalence of 3% in the general population with one sample t test for proportions, the difference was statistically significant (p=0.017). No significant risk factor

Table II. Clinical data of the patients according to the type of the spinal dysraphism.

	SBA	SBO	*p**
Patients, n	238	150	
Age (years)	5.09±3.89	6.33±4.71	**0.008**
Gender, n			
Male	123	80	0.613
Female	115	70	
VP(+), n (%)	148(62.2%)	17(11.3%)	**<0.0001**
IH(+), n (%)	37(15.6%)	12(8%)	**0.029**
UDT(+), n (%)	24(19.7%)	12(14.8%)	0.375

SBA: spina bifida aperta, SBO: spina bifida occulta, VP: venriculoperitoneal shunt, IH: inguinal hernia, UDT: undescended testis
‡122 patients in SBA group had data for testicular position and 81 patients in SBO group. 24 patients in SBA group (19.7%) had UDT and 12 patients (14.8%) in SBO group had UDT.
*Age comparison with Student's t test, other comparisons with Pearson chi-square test.

was found in the development of UDT in SB. The comparisons between groups are summarized in Table II.

Discussion

The development of inguinoscrotal pathologies can be better explained with the descent of the testis. After the migration of primitive germ cells to the gonadal ridge at about the 6th week of gestation, the differentiation of the gonad, either as a male or a female, takes place. During the elongation of the fetus, the testes are attached to the internal ring. Later, the gubernaculum is formed at the caudal portion of the testes and the peritoneum bulges towards the inguinal canal to form the processus vaginalis. After the 7th month of gestation, the testicular descent happens and the processus vaginalis obliterates. Failure of the obliteration of the processus vaginalis causes an IH and hydrocele in about 1-3% of children with a male predilection of 6:1.[3,11,12] This value of a maximum 3% was used as an estimated ratio of IH in the general population in this study. Many risk factors have been defined in the generation of IH but SB as a risk factor has not been delineated, yet.[11,12] In females, ovaries descend similarly but this descent stops in the pelvis. The cranial portion of the gubernaculum forms the ovarian ligament and the distal portion, the round ligament. The gubernaculum seems to be important in the descent of ovaries as well and the rudimentary development of the processus vaginalis forms the canal of Nuck, with its persistence, causing the inguinal hernia.[12]

SB is a neurodevelopmental anomaly of the neural plate closure during fetal life. Due to spinal cord injury in the course of the disease, it causes various clinical problems like hydrocephalus after Arnold Chiari Type 2 malformation, lower urinary tract and gastrointestinal dysfunction, motor and sensorial problems of lower extremities and erectile dysfunction.[13] The prevalence of this condition has dropped from 1/1000 live births to 3.1-4.6/10000 in the United States after food fortification with folic acid and early termination of pregnancy.[1,2,13] However, the prevalence is still high in other regions of the world.[2]

The true prevalence of IH in patients with SB has not been clearly defined in the English literature. In a large, nationwide study on the co-occuring malformations seen with SB, the patients were defined as isolated and non-isolated, the non-isolated cases were those with associating anomalies involving other organ systems. In this study, 1170 patients were included between 1976 and 2011. Only UDT was mentioned in this study among genital defects but IH has not been evaluated.[8]

In the current study, we observed an increased prevalence of IH in patients with SBA. VP shunt was also an associating risk factor with male gender. When we compared SBA patients with VP shunts and SBO patients with VP shunts, the prevalence was 21.9% in SBA vs. 13.3% in SBO. Whereas, when we evaluated the prevalence of IH patients without a VP shunt among all SB patients (7.1%), this ratio was still high in comparison with the estimated IH ratio in the general population. To the best of our knowledge, SB itself has not been previously reported as a potential risk factor for IH in children.

VP shunting is a classically known etiological factor for IH in children.[11,12] Increased intraabdominal pressure and high patency rates of the processus vaginalis in children have been accepted to be the main reason for this finding.[14,15] In a large cross-sectional study in Taiwan, medical records of 675 children with a VP shunt and 6704 children without this intervention had been followed up for 8 years. After 8 years, IH had been observed in 4.1% of control patients whereas 13.3% of patients with a VP shunt developed IH ($p<0.001$).[16] In other studies, the same prevalence was observed to be between 15 to 23.8% after VP shunting.[14,15,17,18]

The coexistence of IH with VP shunting has a direct relationship with the patency of the processus vaginalis. This patency is believed to be present in 70-80 % of babies at birth, dropping to 30-40% by 3 to 4 years of age.[15,19,20] Weaver et al.[21] followed 1548 children after laparoscopy was done for various surgical indications. They detected 308 patients with asymptomatic patent processus vaginalis. After a median of 8.1 years, 13% of the patients were seen to develop IH.[21] In this current study, 29.7% of the SB patients with a VP shunt were found to have an associating IH giving a slightly higher prevalence than the general information in the literature.

IH is 5-10 times more common in males than females. The nuck canal, equivalent to the processus vaginalis, obliterates earlier at 7 months of gestation in females than in males and this factor is believed to be the cause of this gender predilection.[22] Similarly, the prevalence of IH was 21.8% in males with SB and 3.2% in females with statistical significance, in this study.

Until the observation of Kropp and Voeller[7] in 1981, UDT had been evaluated as a coincidence rather than an association with SB. Several studies have demonstrated this relationship with a prevalence of 1-25.6% among children with SB significantly higher than the general population.[7-10,22] This figure was 17.7% in this study with no difference between SBA and SBO patients. Neurological functional impairment in nerve fibers of the genitofemoral nerve in SB is believed to be the cause of this high prevalence.[9] The genitofemoral nerve originates from L1-L2 nerve roots and the level of the vertebral defect in SB has been shown to affect the prevalence of UDT, being about 19% in low lesions and about 36% in high lesions.[9] The genital branch of the genitofemoral nerve innervates the gubernaculum with the cremasteric muscle and the gubernaculum is an important factor in testicular descent. Beasley et al.[23] in their experimental study, had divided the genitofemoral nerve of newborn rats below two days of age and had demonstrated that denervation of the gubernaculum results in UDT. This explanation has merit to describe the association between UDT and SB but no information for IH has been found in English literature describing how IH associates with SB other than patients with VP shunts. This current study demonstrated that IH prevalence in our SB patient group is significantly higher than the estimated prevalence of IH in the general population.

Tanyel has a different explanation for the spectrum of inguinoscrotal pathologies including IH, hydroceles and UDT. According to his theory, a transient decrease in sympathetic tonus coupling with increased parasympathetic tonus initiates apoptosis of the smooth muscles surrounding the processus vaginalis after testicular descent. The smooth muscles of the processus vaginalis are necessary to propel the testis to the scrotum. After the completion of descent, this programmed cell death causes obliteration of the processus vaginalis. Aberrations in timing, intensity or sustainance of this activity cause hernia, hydrocele and UDT. If no necessary autonomic activity happens after the descent of the testis, no obliteration of the processus vaginalis occurs and this ends up with IH. If this activity happens earlier than expected, early apoptosis of the smooth muscle of the processus vaginalis causes an inability of testes to be propelled to the scrotum. This autonomic activity which is called central catecholaminergic activity is mediated by the central nervous system and spinal cord towards autonomic ganglions.[6] When we consider the high prevalence of IH and UDT in patients with SB, Tanyel's theory may explain why we observed an increased prevalence of these inguinoscrotal pathologies when compared to the general population and this theory covers both the explanation for IH and UDT. However, this explanation should be thoroughly investigated in this patient group to increase knowledge.

An age difference was found between the SBA and SBO patients in this study. This may be attributed to the late presentation of SBO patients for surgery. IH was found to be

bilateral in nearly half of the patients and thus, contralateral exploration should be considered in these patients.

There are certain limitations of the current study. This study was an observational, descriptive study without any data of neurological examination and the etiological explanations are only hypothetical. The data derived from the questionnaire relies on the declaration of the parents and patients. A detailed neurological examination with the information of spinal defect level might support the etiological explanations and should be planned for prospective studies. The processus vaginalis samples taken from the children with SB and IH should be investigated to question Tanyel's theory and if possible together with magnetic resonance tractography for the tracts of central catecholaminergic activity.

In conclusion, IH hernia and UDT are seen more frequently in children with SB when compared to the general population. VP shunting and male gender seem to be independent risk factors for IH in these children. The findings of the current study may support the impaired neurological activity as an etiological explanation for the generation of IH and UDT in the normal population, as well. Further clinical studies are necessary to test this hypothesis.

Ethical approval

This study was conducted in compliance with the ethical principles according to the Declaration of Helsinki, and it was approved by the Institutional Review Board of İstanbul Medeniyet University Göztepe Prof. Dr. Süleyman Yalçın City Hospital (IRB No: 2020/0618).

Author contribution

The authors confirm contribution to the paper as follows: ŞKÖ, study design, analysis, interpretation of results and draft manuscript preparation, MAK, DÖÖ, VÖ, data collection, HC, İA, interpretation of results. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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