

CLASSIC BLADDER EXSTROPHY MANAGEMENT AND OUTCOME AMONG SUDANESE PEDIATRIC PATIENTS: MULTICENTER STUDY (2012-2015)

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ABSTRACT

Background: Bladder Exstrophy (BE) is a rare congenital malformation carrying functional and psychosocial impact on patient's life. In Sudan we do not have any registry for patients with bladder exstrophy, some record in the Hospitals are lost and difficult contact patients from remote region in the country. **The aim of this study:** To identify the pattern and outcome of classic bladder exstrophy management in Sudan pediatric surgery centers.

Patients and methods: This is a retro-prospective study conducted from 2012 to 2015. The data was collected via structured questioner and telephone interview with parents and patients from Alrebat University Hospital, Soba University Hospital and Algizera National Pediatric Surgery Center. We included all patients with CBE who were operated on during the study period and those who had surgery earlier and they came for follow up. We used SPSS computer program version 19 for data analysis. **Result:** 49 patients with complete medical data records were reviewed and managed during study period. 32 patients were males and 17 were females. The mean age of patients was 2.6 years range between 3days to 18 years. Two patients were twins, one patient was the product of invetro-fertilization (IVF) and two patients have family history of CBE. Inguinal hernia was observed in 9 (18.3%) patients, undescended testis seen in 5 (10%) patients and renal anomalies in 5 (10%) patients. Six (18.3%) patients underwent CPRE, Twenty eight (57.1%) patients underwent MSRE, and 13(26.5%) patients underwent ureterosegmoidostomy. Postoperative complications include pyelonephritis 11 patients, vesical stone 10 patients, urethral stricture 5 patients and renal and electrolyte disturbance in one patients. Regarding the continence rate in those finished their operation as follow: 2/6 patients 33.3% underwent CPRE were continents. While 6/13 of the patients 46.1% underwent MSRE were continent, and 12/13 of patients 92.6% who had diversion were continent. Two patients died one patient due to sever sepsis and other one due to electrolyte and renal impairment.

In conclusion: Late presentation is still a major factor that affects the choice of surgical procedure and may affect the outcome. Long-term follow-up still problem in Sudan pediatric surgery centers attributed to incomplete medical records and loss of contact with some patients.

KEYWORDS: Bladder Exstrophy (BE), bladder exstrophy management in Sudan pediatric surgery centers.

INTRODUCTION

Bladder Exstrophy (BE) is rare congenital malformations that carry long term functional and psychosocial impact on patients' life. The earliest account for bladder exstrophy found on Assyrian tablets, dating back to 2000 BC. Von grafenberg first described the medical condition in 1597, and Mowat is providing a complete description of bladder exstrophy in 1748. Chaussier first gave the term "exstrophie" since then various papers have been published with an increasing rate. now a days successful management of be attributed to a better health facilities as well as better understanding of the

anatomy, embryology and histology of urinary bladder.^[1,2,3,4,5]

Data from the international clearing house of birth defects monitoring systems and the healthcare cost estimate the incidence of bladder exstrophy to be 3.3 in 100,000 live births.^[6]

Goals of surgery are preservation of kidney function, urinary continence, low pressure urine storage reservoir, functionally and cosmetically acceptable external genitalia. Since identification of different types of

operations used in the treatment of CBE may lead to improvement of the postoperative outcome; so we select 3 main pediatric surgery centers in Sudan trying to describe the outcome of different surgical operations used in short and long term in Sudanese pediatric patients.

PATIENTS AND METHOD

It's a retro-prospective multicenter study between 2012 to 2015 in

- Alrebat University Hospital pediatric surgery
- Soba University Hospital pediatric surgery center
- Algezira National Pediatric Surgery

We include all Patients with CBE who were operated on during the study period in the three mentioned centers and those who had surgery earlier and came for follow up.

Exclusion criteria

- Cloacal exstrophy
- Pure Epispadias
- Patients treated outside these specific centers
- Patients with incomplete records or no contact

Procedure of data collection

The data was collected using structured questionnaire which consist of demographic data, antenatal history of maternal exposure to drug, chemical, medical radiation, associated abnormality, surgical procedures and post-operative outcome during study period as variables. Telephone interview for patients and parents was used for regular followup.

Data analysis

The data was collected and analyzed after excluding all patients with incomplete records and those who lost contact during study period. We are using computer program SPSS version 19 for analysis. Descriptive analysis and tests of significance as chi-square Test & T-test were used and the P value will be considered significant if ≤ 0.05 .

Ethical consideration

Ethical clearances from the different authorities were ruled out (SMSB ethical committee, pediatric surgery centers). An Informed verbal and written consent was taken from the parents and older patients.

RESULT

72 patients were operated on during the study period "Dec 2012 to Dec 2015" in three main pediatric surgery centers in Sudan. 49 patients have complete medical records and they were contactable, remain 23 patients were excluded from this study due to their deficient medical records or loss contact during the follow-up.

49 patients included in this study, 19 of them from Alrebat University Hospital, 15 from Algezira National Pediatric Surgery Center and 15 from Soba University Hospital.[Table-1].

32 patients were males and 17 were females, the ratio between male: female was 1.9:1 [Figure -1].

The age of patients at time of operation ranged from 3days to 18years, over all the mean age was 2.6years old. Seven (14.2%) of the patients were neonates mean age was 7.1days, 10(20.4%) of the patients were infants their mean age was 5.2month and thirty two (66.4%) patients were older than 1 year, mean age was 6.6years. [Table-2].

No patient was diagnosed during antenatal period. Regarding the etiological factors that associated with BE; 2 patients are twins and their twins are normal, one patient was the product of invetro-fertilization (IVF) and 2 patients have family history of bladder exstrophy recurrent in their brothers, all mothers (100%) neither alcoholic nor smoker. Associated other anomalies include bilateral inguinal hernia observed in 9 (18.3%) patients, bilateral undescended testes seen in 5(10%) patients and renal anomalies in 5(10%) patients. [Table-3] [Table-4].

Regarding the operative modalities used in our centers as follows, six (18.3%) patients underwent CPRE (5 neonates and one infant). Twenty eight (57.1%) patients underwent MSRE (2 neonates, 9 infants and 17 above 1year). 15(30.61%) patients underwent urinary diversion (13 patients underwent Uretrosegmoidostomy and 2 patients underwent appendiceovesicostomy and bladder neck closure) all of them above 1year. [Table.5].

Early postoperative complications include wound infection and dehiscence 22.4 % (n=11) of cases, two patients developed intestinal obstruction due to small bowel intussusceptions and Vesico- cutaneous fistula in two patients. [Figure -2].

Late postoperative complications according to the type of surgical operation are; In MSRE; six patients developed Pyelonephritis, eight patients had vesical stones and 3 patients had urethral stricture. In CPRE two patients developed pyelonephritis, two patients had vesical stone and two had urethral stricture. Regarding patients with urinary diversion three patients developed pyelonephritis, one patient suffered from electrolyte and acid base disturbance and one patients developed renal failure. [Table-6].

Regarding continence outcome assessed in those who finished their operation; in CPRE; 6 patients finished their operation; two of them were continent so the continent rate was 33.3% ($P \geq .005$). In MSRE thirteen of them finished their operations, 6 patients were continent so the continent rate was 46.1% ($P \geq .05$). 13 patient

underwent diversion 12 of them were continent and the continent rate was 92.6% ($P \geq .005$). [Table -7].

Two patients died; one neonate developed wound dehiscence and severe sepsis following CPRE and second one 5years old female who died because of electrolyte and acid base disturbance and renal failure 3years after ureterosegmoidostomy (diversion).

Table 1: Number and percentage of patients with CBE in three pediatric surgery centers in Sudan (n=49).

Pediatric surgery Centers	Count	Percent
Alrebat University Hospital	19	38.8%
Al Gezira National Pediatric Surgery Center	15	30.6%
Soba University Hospital	15	30.6%

Table 2: Age distribution of patients with BE in Sudan.

Age	Count	Percent
Neonates (below 1 month)	7	14.2%
1-12moth	10	20.4%
≥ 1 year	32	66.4%

Table 3: Congenital abnormalities associated with CBE (n=49).

Congenital Abnormalities	Count	Percent
Bilateral inguinal hernia	9	18.3%
Bilateral UDT	5	10%
Renal anomalies*	5	10%

Table 4: Renal anomaly associated with CBE in Sudan (N=5).

Congenital renal anomaly	Male	Female
Bilateral congenital hydronephrosis	1	-
Bilateral polycystic kidneys	1	-
Duplex left ureter	-	1
Left PUJ obstruction	1	1

Table 5: surgical procedures in relation to age done for patients with CBE in three centers (n=49).

Operative modality	Neonates	Infants	≥ 1 year	Count	Percent
CPRE	5	1	0	6	18.3%
MSRE	2	9	17	28	57.1%
Uretrosegmoidostomy	0	0	13	15	30.61%
Total	7	10	32	49	100%

Table 6: Late postoperative complications in relation to surgical operation in patients with CBE in Sudan (n=49).

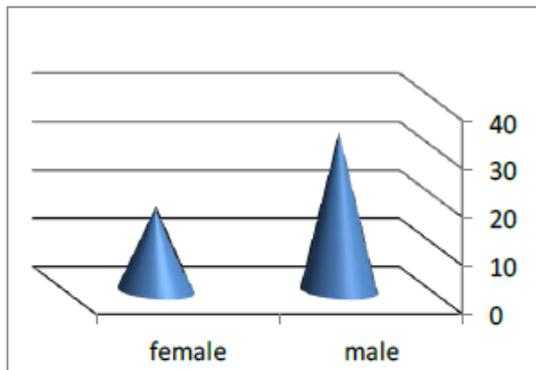
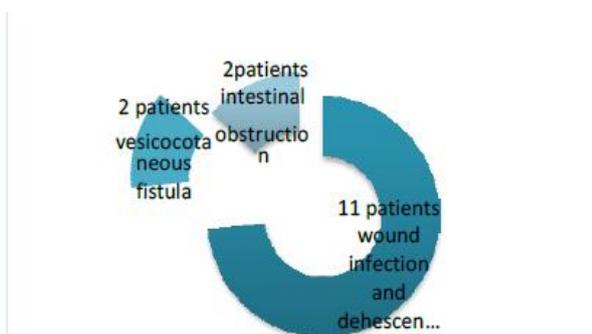
Complications	MSRE N=28	CPRE N=6	UN
Pyelonephritis	6	2	3
Electrolyte and acid base disturbance	0	0	1
Vesical stone formation	8	2	0
Urethral stricture	3	2	0
Renal function impairment	0	0	1

Table 7: Continent outcome of different operative modalities.

Operative modality	CPRE N=6	MSRE N=28	Ureterosegmoidostomy N=13	Total N=49
Patients finish their operation	6	13	13	32
Continent patients	2	6	12	20
Continent rate	33.3% $P \geq .005$	46.1% $P \geq .05$	92.6% $P \geq .005$	62.5% $P \geq .905$

Table 8: Compare the types of operations and their outcome among different pediatric surgery centers in Sudan.

The centers	MSR	CPRE	Diversion	Operative outcome			Continent outcome
				Wound dehiscence	Pyelonephritis	Vesical stone	
Alrebat University Hospital	9	2	8	6	6	5	9
Soba University Hospital	10	3	2	3	4	3	7
Algizera pediatric surgery Center	9	1	5	5	1	2	4

**Figure 1: Gender distribution in patient with BE in Sudan.****Figure 2: Showing early postoperative complication in patients with BE in Sudan n=49.**

DISCUSSION

Bladder Exstrophy Epispadias complex (BEEC) is a serious congenital urological abnormality which greatly impairs both bladder function and the quality of patient life.^[1-5]

Total numbers of patients included in this study are 49 patients including those who were operated on and those who were operated earlier and came for follow-up during the study period from Dec 2012 to Dec 2015; in the three pediatric surgery centers in Sudan.

BE is common in males more than female as evident in many studies including Gambhir *et al.*,^[10] Bhavnagar *et al.*,^[11] and Patricio G *et al.*,^[21] the ratio between males and females was 1.4:1, 2:1 and 2:1 respectively. In this

study we have 32 males and 17 females, the ratio between male: female was 1.9:1 respectively which is the same as found in the literature. [Figure-1]

25% of BE infants are diagnosed antenatally, BE is suggested on antenatal scan by absence of bladder, low insertion of umbilical cord and bony pelvis anomaly.^[14] Antenatal diagnosis is important in parent counseling and delivery plan.^[15] No patient in this study have antenatal diagnosis because lack of scan facilities and expert personnel in most maternal antenatal care.

The age of patients at time of operation one of factors that have been implicated in successful management.^[21] Early neonatal BE reconstruction offers the advantage of early bladder cycling, which theoretically might lead to the best possible bladder development in subsequent years.^[52]

In our review 14.1% were repaired in neonatal period and 66.4% were repaired after 1 year of age similar to study from South Africa 58% of the patients presented late.^[6] [Table-2]

in our study 2 patients are twins and their twins are normal, one patient was the product of in vitro fertilization (IVF), and 2 patients have family history of bladder exstrophy recurrent in their brothers so in one study so the risk of recurrence of bladder exstrophy in a given family has been estimated to be approximately 1 in 100.^[10]

Congenital anomalies associated with BE are extremely rare in comparison with CE.^[15] Andrew *et al* from The Johns Hopkins Medical Institute reported 1.8% GIT anomalies associated with CBE (congenital rectal prolapse) and 69% incidence of inguinal hernia.^[16] The main associated congenital anomalies in Sudanese BE include bilateral inguinal hernias observed in 9 (18.3%) patients, bilateral undescended testis seen in 5(10%) patients and renal anomalies in 5(10%) patients. [Table-3]

Operative modalities used in three pediatric surgery centers in Sudan depend on Surgeon preference and experience, as well as the timing of reconstruction.

These are CPRE, MSRE and diversion.^[18] In Sudan BE repaired without pelvic osteotomy.

Considering CPRE is the least operative modality used in the management of BE by all centers in Sudan because it's not preferred associated with risk of wound dehiscence.

Among the 6 patients who underwent CPRE three patients developed wound dehiscence, two patients developed pyelonephritis, two patients had vesical stone. No one had renal impairment and 2(33.3%) ($P \geq .005$) patients were continent. So CPRE were done in female neonates and in males patients with adequate bladder capacity as well as adequate length epispadiac phallus.^[44]

John P. Gearhart et al reported 30 patients underwent CPRE in neonatal period 28 patients required bladder neck reconstruction later in their life and they reported only 3 patients were continent and 19 patients developed wound dehiscence because were repaired without pelvic osteotomy.^[20] Shoukry et al reported 51 patients underwent CPRE, 8 patients failed repair, 8 developed fistula, and 16 patients lost follow-up and the remaining were continent only after augmentation cystoplasty.^[27] So in this study the outcome of CPRE similar to regional and international studies.

Regarding MSRE; the preferred operative option in Sudan pediatric surgery centers, in this study Twenty eight (57.1%) patients underwent MSRE in three centers; 6 (21.4%) of them developed pyelonephritis, 8 (28.57%) patients developed vesical stone and 3 patients developed urethral stricture.

13 patients underwent BNR. The high rate of febrile UTI postoperatively observed in this study most probably due to postoperative reflux evident by study conducted by Pippi Salle et al compare postoperative complications in two group those underwent bilateral ureteral reimplantation (A) and those (B) not they observe their finding was: Two patients in group (A) had hydronephrosis postoperatively Compared to 10 in group (B), again One patient in group (A) had a febrile urinary tract infection vs.^[11] in group (B). No patients in group (A) had postoperative vesicoureteral reflux.^[37]

Continent outcome in MSRE is determined after BNR. Ultrasound, cystogram (VCUG) and urodynamic study (UDS) were performed to assess bladder capacity before bladder neck repair.^[35,38] About 11% of patients undergoing MSRE develop VUR will require UR before BNR. Closure without osteotomy and patients who develop outlet obstruction after closure are at increased risk for developing high-grade VUR. We don't have data recorded or observed during follow-up of patients regarding VUR complication.^[34] In this study the continent rate was 46.1% observed In 6 patients ($P \geq .005$). Most literature shows the rate range between 94% in highly advanced centers to 46% in developing

country so our data similar to many regional countries review.

Urinary diversion is indicated if the primary reconstruction failed or patients presented late with small bladder plate.^[39] Regarding diversion technique 15 patients underwent Uretrosegmoidostomy. [Table -4] Diversion techniques can provide urinary continence with less surgical operations.^[39] In this study 15 patients underwent diversion 14 of them were continent. This data similar to previous study done in Alrebat University Hospital conducted in 2006 by Islam et al, It was 6years Retrospective study the continence rate was 100% after diversion.^[39] Another study from Soba University Hospital conducted in 2000 by Suleiman et al they found 91% continence rate.^[40] Diversion as operative modality seem to be simple, no complex anatomical reconstruction with good early and short term outcome,^[42] but we don't have data to assess long term outcome of diversion due to some difficulties like absences of complete medical records and loss of contact with patients from far areas.

In this study There was no retrospective records to assess renal function in long term follow up also absent data about pre and post-operative vesicouretral reflux as part of long term outcome of BE surgery.

Regarding the operative modalities and their outcome between our pediatric surgery centers; there was no significant deference between them [Table-8]. Most patients underwent MSRE in all centers again all redo cases or failed primary repair underwent diversion.

No pelvic osteotomy in all centers: in Alrebat and Algizera they repair with pubic bone approximation using non absorbable suture while in Soba center the repair without pubic bone approximation in spite of that we observed no difference in postoperative outcome. The diversion observed mainly in Alrebat and Algizera in cases of failure primary repair or late presentation while in soba in case of primary repair failure they do redo repair plus augmentation and appendiceovesicostomy (mitrofanoff operation) for continence.

CONCLUSION

- Lack of antenatal diagnosis of bladder exstrophy affect early patient management.
- Late presentation affect successful primary repair and increase the rate of redo and diversion modality.
- The outcome of management of BE in Sudan is similar to outcome of regional and some international studies.
- High rate of postoperative wound dehiscence attributed to repair without pelvic osteotomy.
- Postoperative bladder stone associated with suture material used in pubic bone approximation.

- No retro or prospective data reporting the rate of uretral reflux and it implication on renal infection and function.
- In Sudan incomplete or loss of medical record and loss of contact with patients still problem affect over all outcome and follow-up.

RECOMMENDATIONS

Improvement of medical record system in all pediatric surgery centers; By encourage young doctors (registrars and medical officers) to complete medical data and follow-up records.

Multidisciplinary approach is needed in management of this malformation; especially orthopedic surgeons regarding pelvic osteotomy operation.

Initiation highly specialized center for management and follow-up regarding this malformation and other complex congenital malformations.

Further study is needed in Sudan regarding long term follow-up of these patients.

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