**INTRODUCTION**

Vesicovaginal fistula (VVF) is a devastating complication of obstructed labor. It is estimated that 90% of VVFs are caused by obstetric complications during labor in the underdeveloped world. The etiology is different in developed countries being 70% caused by pelvic surgeries. The World Health Organization (WHO) estimates that at least 2 million women currently live with fistula and that an additional 50,000–100,000 are affected each year in the developing world. They are often sub-classified into: Simple cases where the tissues are healthy and access is good; and complicated where there is tissue loss, scarring, impaired access, involvement of the ureteric orifices, and/or a coexistent rectovaginal fistula.

Treatment, in most of the cases, remains surgical. It is unlikely that VVFs close spontaneously after 4 weeks. In a series of 151 VVFs, only three cases closed spontaneously on 2–4 weeks catheter drainage. Simple fistulae can be repaired anatomically with reasonable success. The use of tissue interpositioning between the vaginal and bladder repairs is generally needed for more complex fistulae.

Despite the advances in the surgical management of VVFs in the recent decades, recurrence is still a distressing complication for both patients and surgeons. Recurrence further complicates the situation by decreasing the surgical success of following surgeries. Fibrin glue and sealants is an effective tool that achieved wide spread use for different surgical indications. They have been used as an adjunct to hemostasis, wound healing, tissue adhesion, and drug delivery. They have been shown to increase tissue healing and having sealing effect when used with different types of urological anastomosis such as pyelo-plasty, ureteral anastomosis, vasovasostomy, and vasopexy.

Treatment of a urinary fistula with fibrin glue has been described only in case reports and small series. Among those that have been successfully sealed include a vesicovaginal fistula, ureterovaginal fistula, colo-vaginal fistula, vesico perineal fistula, colovesical fistula, fistula between an ileal conduit and the skin, and refractory transplant kidney-ureter fistula.

It is our aim in this study to investigate the ability of fibrin glue to improve the results of complicated VVF repair. Anatomical repair with fibrin glue interpositioning will be compared to anatomical repair with Martius flap interpositioning. We will use home-made fibrin glue in this study to decrease the expenses and prevent blood borne diseases that can be transmitted via the commercially available fibrin glue.

**MATERIALS AND METHODS**

This study was conducted in different African areas, mostly in university hospitals: Abdou Moumouni University, Niamey, Niger, West Africa; The National hospital of Djibouti, East Africa; Addis Ababa fistula hospital, Ethiopia; etc. This study was conducted in 3 African institutions. Forty female patients with complicated VVF were randomized into 2 groups. Group A were repaired anatomically using PG as an interpositioning layer. Group B were repaired anatomically using MF as an interpositioning layer. FG used in this study was prepared from patients own blood. Complicating factors were recurrence, local moderate to severe fibrosis, fistula location involving the bladder neck, and or size of the fistula being more than 1.5 cm in its largest diameter. Patients were evaluated after 2 weeks, one month and 3 months postoperatively.

**Results:** Thirty eight patients were evaluable as 2 patients, one from each group, lost to follow-up. Patient demographics were not different between the two study groups. The frequency of occurrence of complicating factors was not different between the 2 groups. Thirteen of group A and eleven from group B were rendered dry and that was maintained for as long as they were followed-up. The difference in the outcome was not statistically significant.

**Conclusion:** The use of FG as an interpositioning layer during the vaginal anatomical repair of complicated VVF appears to be of great value as an alternative to the use of MF interpositioning. Decreasing the operative time and adding simplicity to the already complicated procedure are additional values of using this procedure.

**Key words:** fibrin glue; multicenter; prospective; randomized; vesicovaginal fistula
Student’s variables were expressed as numbers and percentage.

Preparation of the Biological Glue (Fibrin Glue)

Two different components of the fibrin glue were prepared and kept separate until the time of usage. First component was prepared as follows: 100 ml of patients’ blood were drawn on 10% sodium citrate. This blood was centrifuged for 8 min at 3,200 rpm. The plasma was then removed. One hundred percent ethanol was added to part of the plasma in a ratio of 1:7. This mixture is then refrigerated at –18 for 20 min and then centrifuged for 8 min at 3,200 rpm. The supernatant was discarded leaving the fibrinogen pellets. The rest of the plasma was used to dissolve the fibrinogen pellets by incubating them at 37°C for 15 min.

Component II of the adhesive was prepared by adding 9.2 ml calcium chloride solution (40 mmol/L) to thrombin. This was kept at 37°C and ready to be used. At the time of surgery, the two components were mixed together to yield a gelatinous substance, which is positioned between the vaginal and bladder repair.

Statistical Methodology

Statistical analysis of data was done using SPSS (statistical program for social science version 16). All quantitative variables were expressed in the text as mean ± SD. Qualitative variables were expressed as numbers and percentage. Student’s t-test was used to compare quantitative variables. $\chi^2$-test was used to compare qualitative variables. Fisher exact probability test was used instead of $\chi^2$ when one expected cell or more are less than 5.

<table>
<thead>
<tr>
<th>TABLE I. Patients Demographics</th>
<th>Fibrin glue group</th>
<th>Martius flap group</th>
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<tbody>
<tr>
<td>Age at presentation</td>
<td>23.11 ± 5.16</td>
<td>27.21 ± 7.2 years</td>
</tr>
<tr>
<td>Age at marriage</td>
<td>15.63 ± 4.65</td>
<td>16.79 ± 2.44 years</td>
</tr>
<tr>
<td>Age at first labor</td>
<td>17.68 ± 4.83</td>
<td>18.84 ± 3 years</td>
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<tr>
<td>Parity</td>
<td>2.37 ± 2.57</td>
<td>3.26 ± 3.07</td>
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<tr>
<td>Duration of labor</td>
<td>2.63 ± 1.5 days</td>
<td>2.26 ± 1.33 days</td>
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The difference between means was considered significant if $P$-value is <0.05 and highly significant if $P$<0.001.

RESULTS

Thirty-eight patients were evaluable as two patients, one from each group, lost to follow-up. Patient demographics were not different between the two study groups including age, age at marriage, and age at first labor. Furthermore, parity and number of days in labor was not different statistically (Table I).

In group A, 69.2% were subjected to previous surgical interventions for fistula repair, compared to 63.2% of group B. This difference was not statistically significant.

The fibrosis detected by physical examination in group A: 57.89% of patients had mild to moderate fibrosis, while 42.11% had severe fibrosis. In group B: 36.84% had mild to moderate fibrosis and 63.16% had severe fibrosis. There was statistical difference between the two groups using $\chi^2$-test.

Regarding the site of the fistula, the two groups were very comparable. This was as follows: Group A: 52.63% were urethrovaginal (involving bladder neck), and 47.37% were trigonal or supratriagonal. Group B: 57.89% were urethrovaginal (involving bladder neck) and 42.11% were trigonal or supratriagonal. There was no statistically significant difference between the studied groups regarding the site of the VVF using $\chi^2$-test.

Fistula size was 2.05 ± 0.88 cm in the 1st group and 2.53 ± 1.51 cm in the 2nd group which was not statistically different. Patients were further stratified based on fistula size (Table II). Statistically, there was no difference in the outcome between patients sub-categories globally ($P = 0.688$) and between the two treatment groups ($P = 0.516$).

The outcome of these two groups was not statistically different. After 3 months of follow-up, 13 out of 19 patients of group A were rendered dry, while 11 out of 19 of group B were dry. It is worth mentioning that all failures were wet since the 14th day postoperative even while the urethral catheter still in place. None of these wet patients healed favorably later on.

We tried to evaluate different factors affecting the outcome of the repairs. Parity, patient age, attempts of previous repairs, fistula size, and fistula location have no significant impact on the outcome of any of the two repairs.

DISCUSSION

Fibrin glue is a mixture of coagulation factors. It has been used in surgery for almost a century.\(^6\) It is used for three major reasons in Urological surgery: as a urinary tract sealant, hemostatic agent, and as a tissue adhesive. It has been used in many urological applications as hemostatic in partial nephrectomy, as sealant after percutaneous nephrolithotomy, after urethral anastomosis, and radical prostatectomy.\(^10\)–\(^15\) It has been, as well, used as a sealant to prevent lymphocele after lymphadenectomy.\(^15\)
Fibrin sealant seems to promote successful transcervical management of iatrogenic cystotomy sustained during transvaginal hysterectomy. It has been observed that direct transvaginal fibrin sealant injection functions well as a bolster interposition over the cystotomy repair thus preventing the additional time and morbidity required for abdominal bladder repair or tissue interposition with a Martius or omental flap.6

In addition to sealing tissue planes, fibrin sealant promotes closure of urinary fistulae by promoting the local proliferation of fibroblasts and subsequent replacement by connective tissue. The fibrin polymer promotes the in-growth of fibroblasts during wound healing. The complex interaction of neutrophils, macrophages, and fibroblasts provides the basis of wound contraction and remodeling necessary for healthy wound healing.16

Morita and Tokue reported successful closure of a radiation induced vesicovaginal fistula with the endoscopic injection of fibrin sealant.17 Evans et al.6 reported the definitive treatment of six cases of vesicocutaneous and urethrocutaneous fistulae by sealing the tract with the direct injection of 5 ml commercial fibrin sealant after endoscopic fulguration with 100% success.

Vesicovaginal fistulae were described since the beginning of the written record. Numerous methods for the treatment of vesicovaginal fistulae have been described. The techniques of the vaginal approach involve tension-free closure of the fistula with or without excision of the tract, creation of an anterior vaginal wall flap, and appropriate use of vascularized interposition grafts.18

Martius flap interpositioning has a definitive advantage when compared to anatomical repair alone not only in the straightforward uncomplicated cases but also in patients with multiple fistulae or recurrence.18

To our knowledge this is the first study to include fibrin glue as interpositioning material between suture lines during anatomical repair of complicated VVF. Our aim was to try to improve the results of the standard technique by using such easy technique that apparently does not add much to the operative time or to the complications.

Our study has shown the outstanding outcome of the fibrin glue as compared to Martius flap for repair of fistulae with complicating factors. This demonstrates the superb features of this concept, as it does not only act by separating suture lines but also as hemostatic and healing promoter.

Experts always state that fistula size is a detrimental factor in vesicovaginal fistula repair. Apparently, the larger the fistula, the higher the chance that the repair will be under tension. It is not clear from the literature whether there is some sort of correlation, linear or not, or if there is a cut-off size above which repair results get worse.20 We examined this hypothesis in our study and found no correlation between fistula size and outcome of surgery. Other factors were also examined in this work and found not to affect the outcome of different repairs. The small number of patients in each group may have obscured any impact of such factors on the outcome of each of the repairs.

Fibrin glue has several other advantages over Martius flaps in complicated cases. Fibrin was easy in application in addition to being safe (as the patient blood was used to avoid transmission of infectious diseases). Furthermore, it was also not time consuming and no extra incisions were needed that may cause disfigurement of external genitalia. Additionally, the use of fibrin glue does not negate the use of Matius flaps simultaneously in exceedingly complicated cases. Whether this would create an additional benefit, was not studied in this work and may form the basis for a future study.

In conclusion, fibrin glue is a valuable tool that can improve the outcome of the repair of VVFs and decreases the time and complexity of the procedure. To our knowledge, this is the first study to report such advantage in such indication. The success of this material may encourage us and others in the future to use it in conjunction with Martius flap in very complicated fistulae. It may also serve the base to use it in procedures of restoring continuity of the urinary tract.

REFERENCES