INTRODUCTION

According to WHO, approximately 570,000 women are diagnosed with cervical cancer worldwide every year. It is the fourth most frequent cancer in women. Although in Switzerland it is the 17th cause of cancer death, it remains the first cause in 42 countries of the world, particularly in sub-Saharan African countries. Persistent infection with HPV is the necessary but not sufficient cause for cervical neoplasia. The association between chronic inflammation and carcinogenesis has been widely studied. The process of reactive oxygen and nitrogen species, cytokines, chemokines, and other growth factors produced during inflammation, causes damage in normal cells, which then proliferate and are more likely to accumulate DNA damage and/or gene mutations. It is not known if female...
genital mutilation/cutting (FGM/C), and particularly FGM/C type III (the narrowing of the vaginal orifice by apposition of the labia with or without excision of the labia and the clitoris), also called infibulation, could be a worsening or risk factor in the development of cervical dysplasia and cervical cancer. Different studies have shown that women and girls who have undergone FGM/C are at greater risk for genitourinary health problems. Not all types of FGM/C provoke the same consequences. WHO classifies FGM/C into four types (Table 1): about 15% of the worldwide cases of FGM/C are type III. FGM/C type III is the type of cutting mostly responsible for obstetric, urogynecologic, infectious, and sexual complications (e.g., dyspareunia and difficult penetration). Defibulation (or deinfibulation) is a surgical procedure that opens up the infibulation scar, treating most of the long-term complications.

There are currently only a few retrospective studies on FGM/C and HPV or cervical dysplasia and cancer. One study was conducted in 200 women between 15 and 60 years old in Nigeria. Despite potential confounding factors, 78.3% of HPV infections were found among the 98 women with FGM/C. Another study on 2398 women between 18 and 90 years old was conducted in Senegal. Among women with invasive cervical cancer, 37% had FGM/C and, in women with cervical abnormalities, 162 (27%) had FGM/C. After adjusting for factors such as age, children, HIV, being a commercial sex worker, smoking, marital status, ethnicity, visit year, education, sex partners, and age at first sexual intercourse, women with invasive cervical cancer were 2.50 times more likely to have had FGM/C (95% confidence interval [CI] 1.28–4.91). However, no significant associations between FGM/C and non-invasive cervical abnormalities were observed, except in commercial sex workers with FGM/C (odds ratio 2.01; 95% CI 1.19–3.40). Both studies concluded that further research is needed, particularly regarding the role of other risk factors for cervical dysplasia associated with FGM/C and of different types of cutting. They indeed acknowledged that not differentiating the four types of cutting was a limitation. A case–control study on risk factors of invasive cervical cancer from Mali, a country where FGM/C is highly prevalent, included 82 cases and 97 controls. Of these, 78 and 92 women, respectively, had been cut. The type of FGM/C was self-reported and largely unknown. However, more invasive types of FGM/C seemed less associated with cervical cancer. To our knowledge, there is no study focusing on FGM/C type III and cervical dysplasia and cancer.

Our aim is to assess the rate of cervical dysplasia in a population of migrant women with FGM/C type III who attended a specialized clinic for FGM/C. The secondary aim is to compare the rate of cervical dysplasia between women with FGM/C type III who underwent the procedure of defibulation and women who did not.

Our hypothesis is that due to the scarring of infibulation and the resulting more difficult and traumatic vaginal intercourse, FGM/C type III might increase the risk of chronic inflammation and sexually transmitted diseases including HPV, which can both lead to cervical dysplasia. No studies exist on the vaginal biome of women with FGM/C and in particular infibulation. It is only known that bacterial vaginosis and recurrent genitourinary infections are associated with FGM/C. Bacterial vaginosis is associated with increased risk of cervical cancer.

### TABLE 1 Classification of female genital mutilation/cutting according to the World Health Organization

| Classification | Description |
|----------------|-------------|
| 1. Partial or total removal of the clitoral glans, and/or the prepuc/ clitoral hood | a. removal of the prepuc/clitoral hood only  
b. removal of the clitoral glans with the prepuc/clitoral hood |
| 2. Partial or total removal of the clitoral glans and the labia minora, with or without removal of the labia majora | a. removal of labia minora only  
b. partial or total removal of the clitoral glans and the labia minora (prepuc/clitoral hood may be affected)  
c. partial or total removal of the clitoral glans, the labia minora and the labia majora (prepuc/clitoral hood may be affected) |
| 3. (Often referred to as infibulation). Narrowing of the vaginal opening with the creation of a covering seal. The seal is formed by cutting and repositioning the labia minora, or labia majora. The covering of the vaginal opening is done with or without removal of the clitoral prepuc/clitoral hood and glans. | a. removal and repositioning of labia minora  
b. removal and repositioning of labia majora |
| 4. All other harmful procedures to the female genitalia for non- medical purposes (e.g. pricking, piercing, incising, scraping, cauterizing) | |

*WHO (2018). “Types of female genital mutilation” from https://www.who.int/sexual-and-reproductive-health/types-of-female-genital-mutilation. Please note that when there is cutting of the clitoris, part of the clitoral body in addition to the glans might be involved.*

### 2 MATERIALS AND METHODS

We retrospectively reviewed the consecutive electronic medical records of all the infibulated migrant women who received follow-up at the outpatient clinic for women with FGM/C at the Geneva University Hospital between April 2010 and January 2016. This study was approved by the Institutional Review Board (13-133R). Informed consent was waived, as contacting all patients would have been difficult because of frequent changes in contact information. The FGM/C clinic opened in 2010 and currently receives women 2 days a month to be treated for health complications related to FGM/C. Women are screened according to current national guidelines, from 21 to 70 years old every 3 years after the first three annual normal cervical smears. HPV tests are performed using hybrid capture technology.

We first conducted a retrospective descriptive study on cervical dysplasia and its follow up in a sample of 338 consecutive women with any type of FGM/C. We then decided to focus on the sub-population of the above sample of 188 infibulated women (FGM/C type III), with or without a history of defibulation. The following inclusion criteria were applied: documented diagnosis of FGM/C type III after a gynecologic examination; presence of at least one cervical smear screening. The latter was considered as documented if stated in a patient’s file; or stated in cytologic report; or stated in referring physician’s letter.
Information was collected on available sociodemographic characteristics (age, original country, religion); parity; FGM/C (setting of the practice, defibulation and time of defibulation, re-infibulation after defibulation or delivery); cervical smear results, eventual colposcopy and treatments; blood, vaginal, and cervical laboratory results; and history of sexual violence. Any cervical smear showing atypical squamous cells of undetermined significance (ASCUS), dysplasia or cancer was identified as abnormal. We distinguished ASCUS with and without HPV infection, and low-grade (L-SIL) and high-grade (H-SIL) squamous intraepithelial lesions. We collected information on infections documented by blood tests, vaginal bacteriologic cultures or polymerase chain reaction for vaginal sexually transmitted infections. All the information was double checked by two of the authors (AA, AF) and compiled in an Excel file database.

A patient was considered positive for cervical dysplasia if at least one cervical smear result was abnormal: ASCUS with concurrent HPV infection, L-SIL, and/or H-SIL. Two groups were considered for cervical dysplasia: low-grade cervical dysplasia (L-SIL, ASCUS HPV-positive) and high-grade cervical dysplasia (atypical squamous cells, cannot rule out high-grade squamous intraepithelial lesion, H-SIL, squamous cell carcinoma).

We considered colposcopy follow up as regular when clinically relevant findings were followed by the indicated examinations and treatments, and as irregular, when clinically relevant findings were not followed by the indicated examinations and treatments. Follow up and treatment are proposed according to the current national guidelines.17

Some women underwent blood tests and vulvar, vaginal or cervical swabs for various reasons (e.g. pre-surgery, during a blood check, for sexually transmitted infection assessment, in case of symptoms or before an intrauterine device insertion). When such tests were performed, results were available for hepatitis B virus (HBV), hepatitis C virus, syphilis, and HIV; Candida, Escherichia coli, Gardnerella vaginalis, or “other” (e.g. Streptococcus agalactiae, Ureaplasma, Prevotella bivia), and Chlamydia trachomatis, Neisseria gonorrhoeae and herpes virus.

Descriptive statistics are provided. For continuous variables (age), we report mean ± standard deviation. For categorical variables, we report frequencies and relative proportions. We compared categorical variables between women with and without cervical dysplasia using either $\chi^2$ or Fisher’s exact tests, depending on test assumptions. We compared continuous variables between women with and without cervical dysplasia using Mann-Whitney non-parametric test, due to small numbers. We performed statistical analyses using STATA 16 IC (StataCorp., College Station, TX, USA). All P values less than 0.05 were considered as statistically significant.

3 | RESULTS

We reviewed 618 consecutive visits for a total of 360 women. We included 188 women with FGM/C type III, with a mean age of 37.7 (±5.2) years. More than half of the sample were originally from East Africa (particularly Somalia and Eritrea) (116, 61.7%), Muslim (113, 60.1%) and had one or two children (100, 53.2%) (Table 2).

A total of 113 (60%) had undergone defibulation, mostly (105, 92.9%) without undergoing re-infibulation. Most defibulated women reported that defibulation was performed during labor (78, 69.0%) or pregnancy (6, 5.3%) and in most cases during the first pregnancy (62, 73.8%) (Table 3). Re-infibulation had always been performed in Africa.

Eleven women of the total sample (5.8%) disclosed a history of sexual violence and 15 (7.9%) mentioned some other form of violence (physical or psychological or both).

Serologic results were available for 187 women and found to be positive for HBV or HIV in 39 of them (20.8%); 24 (12.8%) were naturally immune or vaccinated for HBV; nine (4.8%) had chronic HBV, and six (3.2%) were HIV-positive with undetectable viremia. Vaginal bacteriologoy was also available for 187 women and was abnormal in 40 (21.4%) of them: most of them for Candida albicans (25, 13.3%).

| TABLE 2 | Sociodemographic dataa |
|----------|------------------------|
| Characteristic (n = 188) |          |
| Age, y               | 37.7 ± 5.14 |
| Age category         |          |
| <25                  | 2 (1)     |
| 25–29                | 26 (14)   |
| 30–39                | 94 (50)   |
| 40–49                | 55 (29)   |
| >50                  | 11 (6)    |
| Country of origin    |          |
| Somalia              | 64 (34)   |
| Eritrea              | 52 (28)   |
| Burkina Faso         | 12 (6)    |
| Ethiopia             | 10 (5)    |
| Guinea               | 10 (5)    |
| Sudan                | 9 (5)     |
| Otherb               | 31 (16)   |
| Religion             |          |
| Muslim               | 113 (60)  |
| Christian            | 35 (19)   |
| Atheist              | 8 (4)     |
| Unknown              | 32 (17)   |
| Parity               |          |
| Nulliparous          | 23 (12)   |
| One or two children  | 100 (53)  |
| Three children       | 29 (16)   |
| More than three children | 36 (19) |

aValues are presented as mean ± standard deviation or as number (percentage).

bEgyp, Djibouti, Kenya, Liberia, Ivory Coast, Senegal, Cameroon, Yemen, Gambia, Mali, Sierra Leone.
Fourteen women presented with genital herpes and three with *Chlamydia trachomatis*.

Twenty women (10.6%) were found to have cervical dysplasia: 19 (10.1%) had L-SIL or ASCUS HPV-positive, four (2.1%) had H-SIL; one of the latter was a carcinoma in situ. The three women who were ASCUS HPV-positive became all negative within 2–5 years. There were also nine ASCUS HPV-negative women, which were not considered in the numbers for cervical dysplasia (Table 4).

Mean age of women with dysplasia was 36.9 (±7.0) years, their dominant origin (15, 75.0%) was East Africa.

We did not find any statistically significant differences regarding sociodemographic and clinical characteristics between women with and without dysplasia (Table 5).

Among women with dysplasia, two mentioned sexual violence (10.0%) and one some other form of violence (5.0%). The single case of H-SIL, which was a cervical cancer in situ, was diagnosed in an Ethiopian woman with FGM/C type III and a history of sexual violence. She underwent a total laparoscopic hysterectomy and attended all follow-up appointments. The two other women with dysplasia who suffered a form of violence were cases of L-SIL.

### Table 3 Data on defibulation

| Characteristic                        | Defibulation (n = 188) | Re-infibulation (n = 188) | Timing of defibulation (n = 113) | Defibulation during pregnancy or intrapartum (n = 84) |
|--------------------------------------|------------------------|---------------------------|---------------------------------|-----------------------------------------------------|
|                                      | Yes                    | No                        | Intrapartum                     | First pregnancy                                     |
|                                      | 113 (60.1)             | 73 (38.8)                 | 78 (69.0)                       | 62 (73.8)                                           |
|                                      | Unknown                |                           | During pregnancy                | Following pregnancy                                 |
|                                      | 2 (1.0)                |                           | 6 (5.3)                         | 22 (26.2)                                           |
|                                      | Yes, abroad            |                           | Outside of pregnancy            |                                                     |
|                                      | 6 (5.3)                |                           | 29 (25.7)                       |                                                     |
|                                      | No                     |                           |                                 |                                                     |
|                                      | 105 (92.9)             |                           |                                 |                                                     |
|                                      | Unknown                |                           |                                 |                                                     |
|                                      | 2 (1.8)                |                           |                                 |                                                     |

Values are presented as number (percentage).

*These women were of the following origins: Eritrea, Sudan, Ethiopia, Somalia, Senegal, and Egypt.

### Table 4 Cervical dysplasia

| Cervical dysplasia (n = 188) | ASCUS HPV-negative | ASCUS HPV-positive | L-SIL | H-SIL | Negative for intraepithelial lesion/malignancy |
|------------------------------|--------------------|--------------------|-------|-------|-----------------------------------------------|
|                              | 9 (4.8)            | 3 (1.6)            | 16 (8.5) | 4 (2.1) | 156 (83.0)                                    |

Abbreviations: ASCUS, atypical squamous cells of undetermined significance; H-SIL, high-grade squamous intraepithelial lesions; L-SIL, low-grade squamous intraepithelial lesions.

Values are presented as number (percentage).

### Table 5 Comparison between women with and without cervical dysplasia

|                                      | No cervical dysplasia (n = 168) | Cervical dysplasia (n = 20) | P value |
|--------------------------------------|---------------------------------|-----------------------------|---------|
| Age, y                               | 37.9 ± 7.7                      | 36.9 ± 7.0                  | 0.739<sup>a</sup> |
| Age category                         |                                  |                             | 0.858<sup>1</sup> |
| 20–30                                | 24 (14.3)                       | 4 (20.0)                    |         |
| 30–35                                | 32 (19.0)                       | 2 (10.0)                    |         |
| 35–40                                | 52 (31.0)                       | 7 (35.0)                    |         |
| 40–50                                | 50 (29.8)                       | 6 (30.0)                    |         |
| 50+                                  | 10 (5.9)                        | 1 (5.0)                     |         |
| Country                              |                                  |                             | 0.778   |
| East Africa                          | 121 (72.0)                      | 15 (75.0)                   |         |
| Other countries                      | 47 (28.0)                       | 5 (25.0)                    |         |
| Religion                             |                                  |                             | 0.329<sup>a</sup> |
| Muslim                               | 103 (61.3)                      | 10 (50.0)                   |         |
| Other religion                       | 65 (38.7)                       | 10 (50.0)                   |         |
| Parity                               |                                  |                             | 0.247<sup>c</sup> |
| 0                                    | 23 (13.7)                       | 0 (0)                       |         |
| 1                                    | 40 (23.8)                       | 7 (35.0)                    |         |
| 2                                    | 46 (27.4)                       | 7 (35.0)                    |         |
| 3 or more                            | 59 (35.1)                       | 6 (30.0)                    |         |
| Past violent events                  |                                  |                             | 0.584<sup>d</sup> |
| Sexual violence                      | 9 (5.4)                         | 2 (10.0)                    |         |
| Other forms of violence              | 14 (8.3)                        | 1 (5.0)                     |         |
| No                                   | 145 (86.3)                      | 17 (85.0)                   |         |
| Defibulation                         |                                  |                             | 0.999<sup>d</sup> |
| Yes                                  | 101 (60.1)                      | 12 (60.0)                   |         |
| No                                   | 65 (38.7)                       | 8 (40.0)                    |         |
| No information on eventual history of cervical dysplasia |                                  |                             |         |
| Timing of defibulation               |                                  |                             | 0.894<sup>d</sup> |
| Intra-partum                         | 70 (41.7)                       | 8 (40.0)                    |         |
| During pregnancy                     | 5 (3.0)                         | 1 (5.0)                     |         |
| Outside of pregnancy                 | 26 (15.5)                       | 3 (15.0)                    |         |
| No defibulation                      | 65 (38.7)                       | 8 (40.0)                    |         |
| Unknown                              | 2 (1.2)                         | 0 (0)                       |         |

Values are presented as mean ± standard deviation or as number (percentage).

<sup>a</sup>Mann-Whitney non-parametric test.
<sup>1</sup>χ<sup>2</sup> test.
<sup>d</sup>Fisher’s exact test.

<sup>Values are presented as number (percentage).<sup>
The rate and the timing of defibulation were not statistically different between women with and without dysplasia (Tables 5 and 6).

Seven women with dysplasia underwent colposcopies on a regular basis (35.0%), five underwent them irregularly (25.0%), and eight dropped out of the colposcopy follow up (40.0%). However, 11 out of the 13 women who did not or irregularly did go to the colposcopy follow up came back for a consultation at the outpatient FGM/C clinic. Only two of the women with irregular or no follow up never came back.

4 | DISCUSSION

Our study population of infibulated women followed up at a specialized clinic had a rate of cervical dysplasia of 10.6% and of high-grade cervical dysplasia of 1.6%. These findings are in line with those we found on the sample of 338 women with all types of FGM/C, including this subgroup with type III, who received follow up at the outpatient clinic for women and girls with FGM/C between April 2010 and January 2016. Forty-two (12.42%) had abnormal cervical smears: 32 (9.46%) were diagnosed with ASCUS with high-risk HPV or with L-SIL and 10 (2.95%) were diagnosed with H-SIL.18

Migrant women who are infibulated might be women at risk for cervical dysplasia as the result of several factors that deserve to be further investigated, such as being a migrant, mainly from sub-Saharan Africa, and having undergone FGM/C type III, which can be responsible for recurrent lesions during sexual intercourse and chronic inflammation.

In Switzerland, the real prevalence of cervical dysplasia is difficult to measure because 30% of all eligible women never take part in cervical cancer screening.21 A total of 230 women each year are diagnosed with cervical cancer with an incidence rate of 4.2 per 100 000.26 In sub-Saharan Africa, the same rate can be as high as 43.1 per 100 000 women, depending on the region.3,20 Considering that the majority of the women of our sample are originally from East Africa, we were expecting to find a high dysplasia rate. In addition, migrant women often have less access to regular cervical screening. Studies have shown that migrant women in Europe do not fully participate in cervical cancer screening, for reasons including language barrier, lack of information on cervical screening, lack of female healthcare providers, embarrassment, and distrust of the country’s healthcare system.21-24 A recent study in Italy found that migrant women were at a higher risk of cervical pathologic findings than women in the host country.25

We also found that women with FGM/C who had been diagnosed with dysplasia had the indicated examinations and treatments in only 35% of cases.

Many of the patients originating from the Horn of Africa are recognized refugees. They therefore benefit from Swiss health insurance coverage26 and have access to refunded Swiss health care. However, there could be language, social, economic, or cultural barriers that make follow up difficult. It is important to note that 11 out of the 13 women who did not comply with colposcopy follow up did later present for consultation at the outpatient FGM/C clinic. Only two of the women with irregular or no follow up never came back. Future studies might investigate if a dedicated clinic for women with FGM/C, staffed with medical and cultural experts and certified interpreters can improve patient access, information, and trust and optimize long-term follow up, including cervical screening, for women with FGM/C type III. Future involvement of stakeholders from the migrant and refugee communities, ethnic community-based organizations, and the Swiss Network against Female Genital Cutting might be useful to study and propose further strategies to tackle irregular attendance to cervical screening and follow up.

Our results reinforce the need for cervical cancer screening in migrant women with FGM/C type III. A speculum or gynecologic examination with cervical screening can be difficult in this population because of the narrowing of the vaginal orifice; patient’s resistance or pain; or fear/reluctance of both the patient and health professional.27,28 Half of our sample was Muslim and data have shown that Muslim women might consider cervical cancer screening as unnecessary due to the belief that religious norms prohibiting premarital sex ensure low HPV rates.29,30

Studies in countries such as Norway and Finland have shown that migrant women had a low cervical cancer screening participation rate: less than 50% of them had been screened within the last 5 years. This rate was particularly low among migrant women from sub-Saharan countries.31 Self-sampling could increase the participation rate by 6.5%.32 Women who tried this method found it to be less uncomfortable and less painful than a cervical smear test performed by a clinician.33 This could be an option to encourage women with FGM/C type III to obtain optimal cervical cancer prevention and follow ups. In case of infibulation, specific recommendations on how to perform a cervical smear are available in the

| TABLE 6 Information on cervical dysplasia among women with or without a history of defibulation |
|-----------------------------------------------|
| Defibulation | No cervical dysplasia (n = 168) | L-SIL (n = 16) | H-SIL (n = 4) | P value |
| Yes | 101 (60.1) | 10 (62.5) | 3 (75) | 0.941b |
| No | 65 (38.7) | 6 (37.5) | 1 (25) |
| No information available on history of defibulation | 2 (1.2) | 0 (1) | 0 (0) |

Abbreviations: H-SIL, high-grade squamous intraepithelial lesions; L-SIL, low-grade squamous intraepithelial lesions.

aValues are presented as number (percentage).
bFisher’s exact test.
WHO handbook for the care of women with FGM/C. It is suggested to always explain what you are about to do using appropriate language, discuss with the patient if she has had a cervical smear test before and if it was painful, why this was the case, use techniques to make the examination less painful (smallest available speculum, lubrication, breathing techniques), and most importantly reassure her that the procedure can be stopped at any time and never insist if the test is not possible. If this should be the case, it is important to take the time to explain to the patient why the examination was not possible. This would also be an appropriate time to discuss the option of defibulation or to propose an HPV test without use of the speculum.

We did not find any significant difference regarding dysplasia among women with FGM/C type III who had undergone defibulation and those who had not. However, the sample of the study was small. In addition, the majority of defibulated women with dysplasia had undergone defibulation late in their reproductive life: out of the 13 defibulated women with cervical dysplasia, 10 had been defibulated during labor or pregnancy (76.9%). One could hypothesize that if the period of exposure to micro-lesions during sex or eventual recurrent genitourinary infections due to the scarring of infibulation could be reduced, the risk of chronic inflammation and sexually transmitted infections due to the scarring of infibulation could be diminished.

There are no current recommendations concerning the optimal timing of defibulation. It would be interesting to study this subject diminished.

In conclusion, the present study shows that cervical dysplasia is frequent among women with FGM/C type III and highlights the importance of facilitating access, information, and adapted care and follow up for infibulated women, which includes cervical cancer screening. Further studies might investigate if defibulation can decrease the risk of chronic genitourinary inflammation and trauma as well as facilitate screening, follow up, and treatment.

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CONFLICTS OF INTEREST
The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS
JA conceived the work; AA and AF collected the data; the analysis and interpretation of the data were by AF and JA. AF and JA drafted the article and AF, AA and JA performed the critical revision of the article and final approval of the version to be published.

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