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Research article

Effect of type III female genital mutilation on obstetric outcomes: A systematic review and meta-analysis

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ABSTRACT

Background: Controversial evidence suggests a potential association between female genital mutilation (FGM/C) and adverse obstetric outcomes, with type III FGM/C (infibulation) carrying the greatest risk. The aim of this systematic review and meta-analysis was to assess current rate of adverse obstetric outcomes in women with type III female genital mutilation and cutting (FGM/C; infibulation) delivering across different settings worldwide.

Methods: **We searched** PubMed, Scopus, Embase, and ClinicalTrials.gov databases from inception to Jan 1, 2023. **Studies were selected if they included the main outcome of postpartum haemorrhage (PPH) or secondary outcomes, which included** major conditions affecting maternal-neonatal health during labour and delivery. DerSimonian-Laird random effects meta-analysis including pooled effect estimates with corresponding 95 % confidence intervals was performed. Heterogeneity was assessed using the I^2 statistic. Meta regression for relevant covariates was performed when data on relevant confounders were available. The Newcastle-Ottawa scale (NOS) was used to assess quality of observational studies. The level of evidence was assessed with the GRADE method.

Results: 14 observational studies including 15,320 type III FGM/C women and 59,347 controls were eligible. The risk for postpartum haemorrhage was significantly increased in type III FGM/C, in the main analysis (OR 1.83, 95 % CI 1.03 to 3.24, $I^2 = 93$ %), in pooling of data adjusted for confounders (aOR 1.76, CI 1.42 to 2.17, $I^2 = 0$ %), and in sensitivity analysis of higher quality studies with NOS≥7 (OR 2.76, CI 1.38 to 5.51, $I^2 = 95$ %). Meta-regression showed that nulliparity was significantly and positively associated with postpartum haemorrhage. Similarly, analysis of data adjusted for confounders showed an increased risk of episiotomy in type III FGM/C (aOR 1.56, CI 1.03 to 2.35, $I^2 = 52$ %). Sensitivity analysis of studies with NOS≥7 revealed a significant increase for episiotomy (OR 7.53, CI 1.19 to 47.54, $I^2 = 96$ %), perineal tears (OR 4.24, CI 1.09 to 16.46, $I^2 = 66$ %), prolonged second stage of labour (OR 5.19, 95 % CI 1.00 to 26.85, $I^2 = 66$ %), and Apgar score less than 7 (OR 4.19, CI 1.64 to 10.70, $I^2 = 0$ %). No difference was found regarding obstetric anal sphincter injuries and mode of delivery in these women.

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Deinfibulation achieved similar obstetric and neonatal outcomes to women who never had type III FGM. The overall quality of the studies was adequate (median NOS score: 7; IQR: 6–8), the level of evidence, according to the GRADE assessment, was low.
Conclusions: These results consistently show an increased risk of adverse obstetric outcomes in women with FGM/C type III. Infibulation substantially increases the risk for PPH, particularly in nulliparae. **Systematic Review registration**: PROSPERO CRD42023421993.

1. Introduction

Female genital mutilation/cutting (FGM/C) includes all non-medical procedures that involve partial or total removal of the external female genitalia, or any other injury to the female genital organs [1]. This practice represents a violation of the human rights principles and an extreme form of discrimination against women, threatening a person's right to health, security, and physical integrity. FGM/C are highly prevalent in several regions of Africa, as well as, Asia and the Middle East [1]. Efforts to end FGM/C are included in the 2008 World Health Assembly resolution WHA61.16[2] as well as in the 2020 Sustainable Development Goals of the United Nations (UN) [2], as part of Goal 5, to achieve gender equality and for women's empowerment, a necessary foundation for a peaceful, prosperous, and sustainable world.

Although the exact burden of FGM worldwide is unknown, the United Nations International Children's Emergency Fund (UNICEF) estimates that there are more than 200 millions of women alive today who underwent FGM, and 3 million girls are at risk each year worldwide [3].

The practice of FGM/C often results in well documented short- and long-term sequelae that can negatively impact on women's reproductive health and quality of life [4–11]. Moreover, it is not possible to fully recover from the associated psychological trauma and health-related complications [12].

Recently, two studies have pointed out the significant lack of evidence regarding obstetric outcomes and postpartum care in women living with genital mutilation [13,14]. Systematic reviews and meta-analyses [15–19] including heterogeneous and low-quality studies suggested that women with some type of FGM/C face serious obstetric risks, but these results were controversial and varied by study design, settings, and FGM/C subgroup.

Type III FGM/C (infibulation) represents the most severe form of genital mutilation and is a cause of scarring and vaginal obstruction in the long-term The formation of scars could hinder the progression of regular labor restricting the birth canal, thereby putting both the mother and fetus at risk of morbidity and mortality. The largest cohort study [20] was conducted by WHO in 2006 at 28 obstetric centres in six different African countries, confirming that FGM type III carried the highest risk of experiencing adverse obstetric and neonatal outcomes. Recently, two meta-analyses [21,22], with very low-quality evidence, suggested that deinfibulation, (the surgical procedure aiming to re-open the vaginal introitus of women with type III FGM/C), can significantly improve outcomes, regardless of timing of the procedure (antepartum or intrapartum). Today there is still no consensus regarding the optimal timing of deinfibulation, although international guidelines [23,24] recommend that it be performed intrapartum.

In view of the evidence above, we conducted a systematic review and meta-analysis with the aim to collect all available knowledge evaluating maternal and neonatal outcomes of women with type III FGM/C across different settings worldwide.

2. Matherials and methods

The study protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42023421993).

2.1. Search strategy

We searched PubMed, Scopus, Embase, and ClinicalTrials.gov databases from inception to January 2023 using the following key words alone or in different combinations: "female circumcision", "female genital mutilation", "female genital cutting", "infibulation", "obstetric outcome", "reproductive health", and "delivery". Search strategies are listed in Appendix S1. The current study is following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines [25].

Original studies reporting on obstetric outcomes in women with type III FGM/C with no language restriction were considered eligible. Case series, case reports, review articles, abstracts, commentaries or letters to the editor were excluded. Studies reporting other types of FGM/C were also included in the review, but only patients with FGM/C type III were selected for qualitative and quantitative analysis. The literature search was performed by two authors (GB and SLS). Articles were initially screened on the basis of the titles and abstracts, and then carefully evaluated by each author independently. References of relevant articles were hand-searched for additional reports.

2.2. Data collection

Data extracted from all articles were tabulated, including study design, obstetric outcomes and potential confounders (Table 1).

The FGM/C subtype was defined according to the WHO [1] classification system that divides FGM/C into three types: type I, including partial or total removal of clitoris; type II characterized by partial or total removal of clitoris and labia minora, with or without excision of labia majora, and type III (infibulation) associated with excision of part or all of external genitalia and stitching of the two sides together. Missing data were clearly identified and addressed. No automated tools were used for data extraction. Disagreements were resolved by reaching consensus or by discussion with a third senior author (PIC).

2.3. Variables and outcomes

The primary outcome of the study was post-partum haemorrhage (PPH), defined as a blood loss greater than 500 mL for vaginal deliveries and greater than 1000 mL for caesarean deliveries, representing the major outcome affecting maternal health perinatally. Secondary outcomes were all major outcomes affecting maternal and neonatal health during labour and delivery. For the maternal

Table 1
Summary of studies included in the meta-analysis.

Author	Country	Study design	Exposure	Obstetric and neonatal outcomes (assessment)	Adjustment/Matching for confounding variables*
Rouzi [26] (2001)	Saudi Arabia	Case-control	FGM III 158 No FGM 116	A,E,F (medical records)	NO
Banks [22] (2006)	Sudan, Burkina Faso, Ghana, Kenya, Nigeria, Senegal	Cohort	FGM III 6595 No FGM 7171	A,C,E,F (medical records)	Study center, age, parity, number of children (in multiparous), education, socioeconomic status, residence (urban/rural), time taken to get to hospital, antenatal care
Andro [27] (2014)	France	Cross-sectional	FGM III 16 No FGM 1706	A, B, C, E, F (self-reported)	Age, parity, experience of miscarriage or stillbirth, qualifications, command of French language, employment status, and years since migration.
Minsart [28] (2015)	Republic of Djibouti	Cohort	FGM III 238 No FGM 29	A, B, C, G, H (medical records)	NO
Rodriguez [29] (2016)	Burkina Faso, Ghana, Kenya, Nigeria, Senegal, Sudan	Cross-sectional	FGM III 6187 No FGM 6696	A, C, H (medical records)	NO
Varol [30] (2016)	Australia	Cross-sectional	FGM III 65 No FGM 8558	A, B, C, E, H (medical records)	NO
Gebremicheal [31] (2018)	Ethiopia	Cohort	FGM III 59 No FGM 139	A, C, D, F, G (medical records)	NO
Anikwe [32] (2019)	Nigeria	Cross-sectional	FGM III 6 No FGM 248	A, B, C, D, E, F, G (medical records)	NO
Davis [33] (2019)	Australia	Cohort	FGM III 58 No FGM 8421	E, H (medical records)	NO
Taraldsen [34] (2021)	Norway	Cross-sectional	FGM III 886 No FGM 74	A, B, G (medical records)	Age, education, comorbidity, delivery year (A)
Suleiman [35] (2021)	Tanzania	Cross-sectional	FGM III 90 No FGM 25,611	A, C, E, G (medical records)	Age, GA, parity, BMI, APH, Anaemia (A, E, C); Age, GA, parity, APH, Preeclampsia, GSM, DM type II, Anemia, birth weight (G)
Bonavina [36] (2022)	Sudan	Cohort	FGM III 174 No FGM 171	A, B, C, D, E, F, H (medical records)	Maternal age, parity
Taraldsen [37] (2022)	Norway	Cross-sectional	FGM III 662 No FGM 46	B, C, D, E, G, H (medical records)	Age, education, delivery year (I)
Idoko [38] (2023)	Gambia	Cohort	FGM III 126 No FGM 361	A,C (medical records)	NO

Table Legend: *FGM* female genital mutilation, *GA* gestational age: *A(eC-delivery), B (Instrumental delivery), C (Post-partum haemorrhage), D (Prolongued 2nd stage of labour), E (Episiotomy), F (Perineal laceration), G (5 min Apgar score <7), H (3/4° tear).

side, secondary outcomes were: caesarean delivery due to any urgent or emergent indication, episiotomy including all types and techniques, perineal lacerations (defined as any perineal trauma occurring either spontaneously with vaginal delivery or secondarily as an extension to an episiotomy [39]), obstetric anal sphincter injury (OASI) defined as a third or fourth degree perineal tears occurring either spontaneously with vaginal delivery or secondarily as an extension to an episiotomy [39], prolonged second stage of labour (>2 h for nulliparous and >1 h for multiparous women), instrumental delivery with vacuum or forceps extraction, preterm or late term delivery, meconium-stained amniotic fluid, premature rupture of membranes (PROM), induction of labour and, maternal death. For the neonatal side secondary outcomes were: Apgar score less than 7 at 1 and/or 5 min, perinatal death, neonatal intensive care unit admission, infant resuscitation, birth asphyxia and, neonatal acidosis (defined as umbilical cord arterial pH < 7.1). Outcomes related with pregnancy but not related with labour and delivery such as low birth weight (EWF <2500gr) and neonatal malformation, were not considered for the analysis.

2.4. Risk of bias, study quality and level of evidence

Potential sources of bias were independently evaluated by two authors (GB and SLS). Discrepancies were resolved via discussions with a third senior author (PIC). The methodological quality of included studies was evaluated by using the Newcastle-Ottawa scale (NOS) [40]. Scale ranges are from 0 to 9, with 0 being the lowest. NOS assessment includes three domains: the selection of the study groups (0–4 points), the comparability of the groups (0–2 points), and the ascertainment of the outcome or the effect of interest (0–3 points). The certainty of the evidence was graded into four levels (high, moderate, low or very low) according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines [41].

2.5. Statistical analysis

Dichotomous outcomes were pooled using the DerSimonian-Laird random-effect model to measure crude pooled estimates. When available, adjusted odd ratios (aOR) and relative standard errors were extracted, derived in logarithmic scale and pooled using a

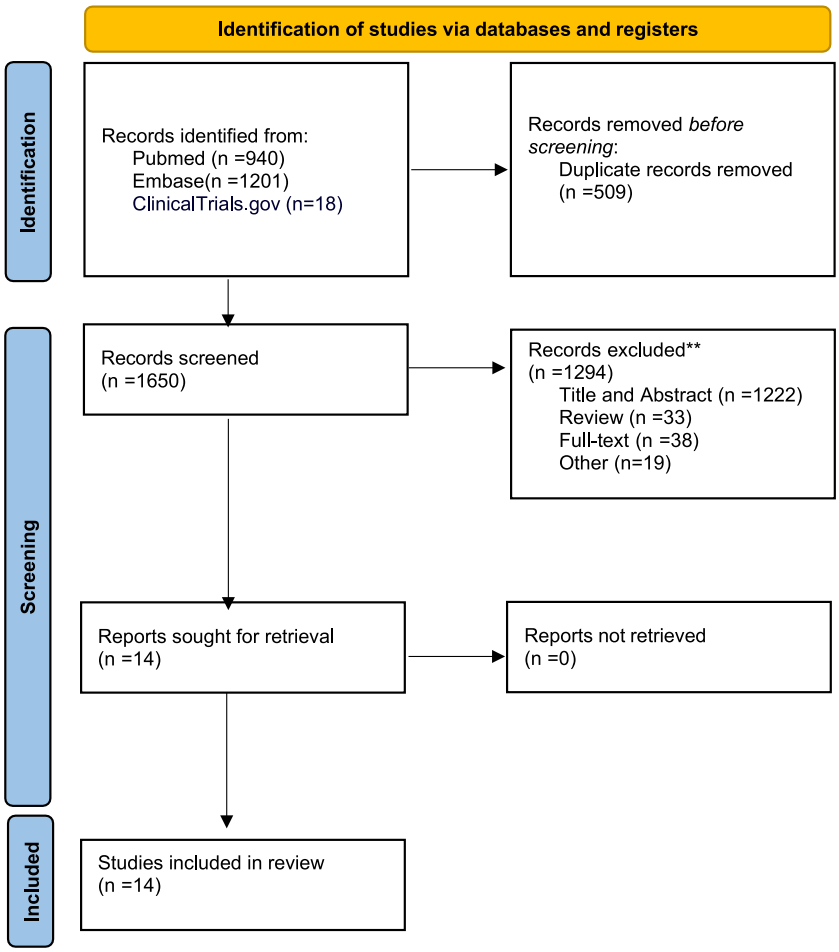

Fig. 1. PRISMA 2020 flow diagram of studies included in the meta-analysis.

DerSimonian-Laird generic inverse variance method. Adjustments for confounding variables for each included study are detailed in Table 1. Sensitivity analysis of highest quality studies was also considered to deal with clinical and statistical heterogeneity. More so, when relevant subgroups could be identified, subgroup analyses were carried out, as appropriate. Results were reported as OR and corresponding 95 % confidence intervals (95 % CIs). Forest plots and summary tables were used to display ORs of interest and 95 % CI

Table 2
Meta-analyses of studies collecting occurrence of type III FGM/C and obstetric outcomes using random effect model.

Outcome	No of studies	FGM III, n	no FGM, n	OR (95 % CI)	I [44]	*p value*
PPH	9	14,112	23,333	1.83 (1.03–3.24)	93 %	0.04
Crude[a]	4	6875	34,573	1.76 (1.42–2.17)	0 %	0.006
Adjusted[b]	6	6960	8004	2.76 (1.38–5.51)	95 %	0.04
Sensitivity - NOS>7[c]	5	6920	15,548	1.16 (0.42–3.18)	81 %	0.77
Subgroup case/cont-cross.sect[d]	5	7192	7785	2.53(0.81.7.94)	94 %	0.11
Subgroup cohort[e]						
Caesarean delivery	9	8307	16,781	1.65(0.70–3.89)	94 %	0.25
Crude[a]	5	7761	34,647	1.11(0.75–1.66)	66 %	0.59
Adjusted[b]	5	6960	8004	1.80(0.65–4.98)	89 %	0.26
Sensitivity - NOS>7[c]	4	1115	8996	1.89(0.22–16.31)	97 %	0.56
Subgroup case/cont-cross.sect[d]	5	7192	7785	1.51(0.64,3.59)	89 %	0.35
Subgroup cohort[e]						
Episiotomy	7	7310	24,170	3.07(0.90, 10.50)	98 %	0.07
Crude[a]	4	6875	34,573	1.56(1.03, 2.35)	52 %	0.04
Adjusted[b]	3	6367	7029	7.53(1.19, 47.54)	96 %	0.03
Sensitivity - NOS>7[c]	5	7078	15,664	3.77(0.77, 18.39)	98 %	0.10
Subgroup case/cont-cross.sect[d]	2	232	8506	1.98(1.31,3.00)	0 %	0.001
Subgroup cohort[e]						
Instrumental delivery	6	2031	9040	1.11(0.65, 1.92)	20 %	0.70
Crude[a]	2	190	1791	0.89(0.44,1.82)	8 %	0.76
Adjusted[b]	2	180	333	1.80(0.27, 11.87)	25 %	0.54
Sensitivity - NOS>7[c]	4	1619	8926	1.00(0.53,1.90)	32 %	1.00
Subgroup case/cont-cross.sect[d]	2	412	114	1.95(0.40,9.50)	30 %	0.41
Subgroup cohort[e]	3	418	362	2.31(0.69,7.74)	0 %	0.17
Subgroup low-income[f]	3	1613	8678	0.95(0.53,1.68)	27 %	0.86
Subgroup high-income[g]						
Perineal tears	4	397	588	2.62(0.70, 9.87)	86 %	0.15
Crude[a]	2	190	1791	1.20(0.51,2.83)	0 %	0.67
Adjusted[b]	3	239	472	4.24(1.09,16.46))	66 %	0.04
Sensitivity - NOS>7[c]	2	164	364	2.60(0.15, 43.60)	75 %	0.51
Subgroup case/cont-cross.sect[d]	2	233	224	3.29(0.65,16.64)	80 %	0.15
Subgroup cohort[e]						
OASIS	6	7384	23,835	0.54(0.22,1.32)	73 %	0.18
Crude[a]	2	836	131	0.97(0.31,3.07)	41 %	0.96
Adjusted[b]	2	6361	6781	0.56(0.05,6.17)	80 %	0.64
Sensitivity - NOS>7[c]	3	6914	15,300	0.39(0.13,1.14)	77 %	0.08
Subgroup case/cont-cross.sect[d]	3	470	8535	0.84(0.27,2.68)	73 %	0.77
Subgroup cohort[e]						
Prolonged 2nd stage of labour	4	901	518	2.77(0.65,11.75)	80 %	0.17
Crude[a]	3	239	472	5.19(1.00,26.85)	66 %	0.05
Sensitivity - NOS>7[c]	2	668	294	6.74(0.03,1306.95)	92 %	0.48
Subgroup case/cont-cross.sect[d]	2	233	224	2.65(1.17,6.02)	0 %	0.02
Subgroup cohort[e]						
Apgar score less than 7	5	1851	536	1.33(0.45,3.91)	63 %	0.61
Crude[a]	2	65	387	4.19(1.64,10.70)	0 %	0.003
Sensitivity - NOS>7[c]	3	1554	368	0.60(0.28,1.32)	0 %	0.21
Subgroup case/cont-cross.sect[d]	2	297	168	4.09(1.68,9.98)	0 %	0.002
Subgroup cohort[e]	3	303	416	3.70(1.57,8.67)	0 %	0.003
Subgroup low-income[f]	2	1548	120	0.57(0.25,1.29)	0 %	0.18
Subgroup high-income[g]						
Perinatal death	4	1912	510	0.99(0.40,2.45)	0 %	0.99
Crude[a]	2	364	390	1.11(0.35,3.50)	0 %	0.86
Subgroup low-income[f]	2	1548	120	0.83(0.19,3.59)	0 %	0.81
Subgroup high-income[g]						

Abbreviations: *FGM* female genital mutilation, *PPH* postpartum haemorrhage, *CD* caesarean delivery, *OASIS:* Obstetric Anal Sphincter Injuries.
[a] Meta-analysis of studies providing unadjusted data.
[b] Meta-analysis of studies providing data adjusted for confounders (adjustments and confounders are listed in Table S1).
[c] Sensitivity analysis including studies that met seven or more of the nine recommended items in the NOS scale.
[d] Subgroup analysis including cross-sectional/case-control studies.
[e] Subgroup analysis including cohort studies.
[f] Subgroup analysis including low-income country studies.
[g] Subgroup analysis including high-income country studies.

for the analysed outcomes. Meta-regression adjusting for potentially relevant covariates was considered in presence of significant confounders affecting the outcome and related heterogeneity, as well as available data. Heterogeneity was assessed using the I^2 and Q statistics. The I^2 values of 25, 50 and 75 % represented low, moderate and high heterogeneity, respectively. When the number of articles exceeded 10, a funnel plot was employed to assess publication bias using Egger's method, as recommended by the Cochrane Manual. A p-value of < 00.05 indicated statistical significance. Data analysis was conducted using Review Manager version 5.4 and STATA version 17.

3. Results

3.1. Search results

The initial literature search resulted in 2141 records. After reviewing titles and abstracts, we identified 38 articles eligible for full-text screening. We excluded twenty-four articles as not comparing FGM/C type III vs no FGM. Overall, fourteen studies met eligibility criteria for quantitative meta-analysis. Fig. 1 illustrates the flowchart depicting the study selection process.

3.2. Characteristics of included studies

Studies included a total population of 15,320 of patients with FGM/C type III and 59,347 women with no FGM. We included seven cross-sectional studies [27,29,30,37,42,43], six cohort studies [20,31–36], and one case-control study [28]. Studies were conducted in both in low- and high-income countries. Overall, more than half of the studies came from African countries [20,27,29,32,37,34,33], three studies came from Europe [42,30,35], two studies from Australia [43,36], and only one study was conducted in Asia [28]. All studies reported their inclusion criteria according to the 2020 FGM/C WHO classification system [1].

The most widely described obstetric outcomes in women who had undergone FGM/C type III were postpartum haemorrhage and caesarean delivery (37,445 and 25,088 participants in 9 studies, respectively). Other prominent outcomes included episiotomy (31,480 participants in 7 studies), instrumental delivery (11,071 in 6 studies), perineal tears (985 participants in 4 studies), as well as OASI (31,219 participants in 6 studies), and prolonged 2nd stage of labour (1419 participants in 4 studies). Neonatal outcomes were reported only in six studies [29,30,37,35,34,33] including Apgar score less than 7(2357 participants in 5 studies) and perinatal death (2422 participants in 4 studies).

3.3. Risk of bias of the studies

According to the NOS scale [40], the quality assessment of included studies was generally adequate or high (median NOS score: 7; IQR: 6–8) and 8 of the 14 studies incorporated in the meta-analysis scored 7 or 8 (Supplemental Tables S1 and S2). Publication bias assessment was unnecessary due to the limited number of studies (less than 10) available for each investigated outcome. The overall level of the evidence, according to the GRADE approach [41], was low (Supplemental Fig. S1).

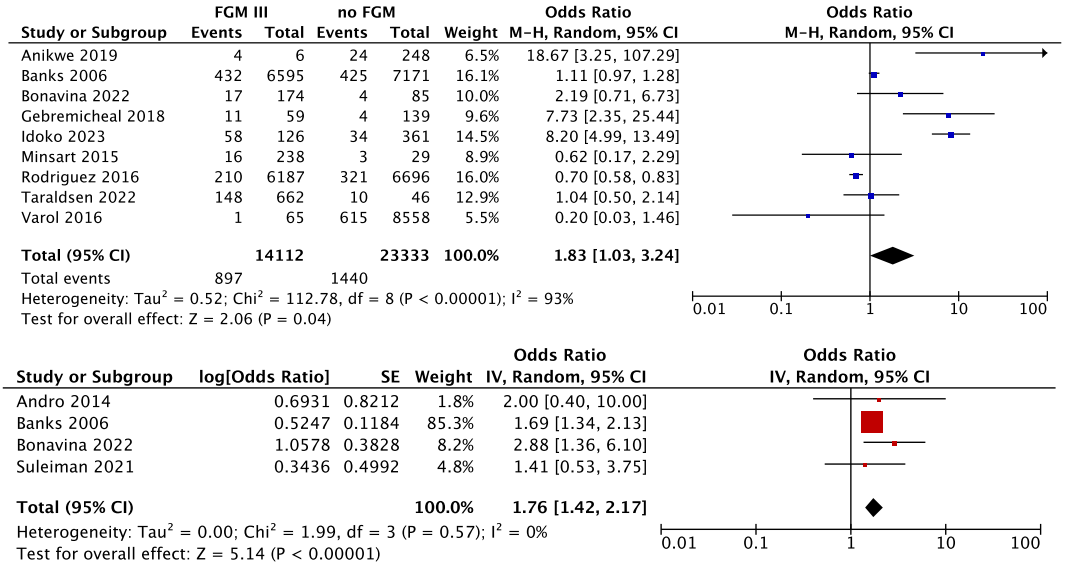

Fig. 2. A. Forest plot of studies collecting occurrence of type III FGM/C and postpartum haemorrhage using unadjusted random effect model. **B.** Forest plot of studies collecting occurrence of type III FGM/C and postpartum haemorrhage using adjusted random effect model. Figure Legend: *FGM* female genital mutilation.

3.4. Meta-analysis results

The results of the present meta-analysis on studies collecting occurrence of type III FGM/C and obstetric outcomes are summarized in Table 2.

3.4.1. Maternal outcomes

3.4.1.1. Postpartum haemorrhage. Nine studies [20,27,29,30,43,32,31,33,34] reporting the pooled crude data showed that FGM type III was associated with a significant increase in PPH compared with the unaffected matched control group (OR: 1.83, 95 % CI: 1.03–3.24, p-value: 0.04); however, heterogeneity between studies was high (I^2: 93 %, p-value=<0.000001) (Fig. 2A). The pooled analysis of data adjusted for maternal age and parity of four studies [20,42,37,32] also showed a significant association between FGM/C type III and postpartum haemorrhage (aOR: 1.76, 95 % CI: 1.42–2.17, I^2: 0 %, p-value: 0.006), contributing to a considerable reduction of heterogeneity (I^2: 0 %; Table 2; Fig. 2B). The significant increase in the risk of PPH was confirmed by sensitivity analysis including studies scoring more than 7 in the NOS scale (OR: 2.76, 95 % CI: 1.38–5.51, I^2: 95 %, p-value: 0.04; Table 2) [20,27,29,32,34,31]. The statistical significance was lost in subgroup analysis of pooled separate data from cross-sectional or case-control studies and those from cohort studies (Table 2). Meta-regression showed that nulliparity and maternal age >35 were positively ($p = 0.007$) and negatively ($p = 0.003$) correlated with PPH, respectively. However, when combining regression of these two moderators, nulliparity remained significant ($p = 0.029$), while that was not the case for maternal age>35 ($p = 0.590$) (Supplemental Figs. S2A–B).

3.4.1.2. Caesarean delivery. Pooled crude analysis of nine studies [20,43,29,32,35,28,31,33,34] showed no significant association between FGM/C type III and caesarean delivery rate, with significant heterogeneity between studies (Table 2). The sensitivity and subgroup analysis according to study design, and the pooled aOR including five studies [20,42,32,35,37] also failed to indicate significant effect of type-III FMG. Meta-regression did not produce a significant effect on nulliparity and maternal age>35 ($p = 0.269$ and $p = 0.264$, respectively).

3.4.1.3. Episiotomy. Seven studies [27,29,30,43,32,36,28] investigated the association between FGM/C type III and episiotomy. FGM/C type III was associated with a higher rate of episiotomy compared to controls. Despite pooled crude and subgroup analysis according to study design failing to show a significant difference (Table 2), a clear difference was identified according to the pooled aOR of four studies with data adjusted for confounders [20,42,37,32] (aOR: 1.56, 95 % CI: 1.03–2.35, I^2: 51 %, p-value: 0.04) (Table 2; Supplemental Fig. S3). Also, the sensitivity analysis of three studies with higher quality at NOS [27,29,32] produced a statistically significant increase summary OR (OR: 7.53, 95 % CI: 1.19–47.54, I^2: 95 %, p-value: 0.04) (Table 2). Subgroup analysis of data from case-control and cross sectional studies showed a significant risk increase for episiotomy, whereas this variable failed to show significance from those from cohort studies (Table 2). The meta-regression failed to demonstrate a significant effect of nulliparity ($p = 0.856$), while data was too scanted for analysis of maternal age>35.

3.4.1.4. Instrumental delivery. Pooled analysis of both adjusted [42,32] and unadjusted data [43,30,29,32,35,33], and the sensitivity analysis of two studies [29,32] regarding instrumental delivery failed to indicate any significant effect of type-III FMG (Table 2). Subgroup analysis according to study design and country setting also failed to show a significant difference (Table 2). Meta-regression failed to demonstrate a significant effect of nulliparity and maternal age>35 ($p = 0.18$ and $p = 0.53$, respectively).

3.4.1.5. Perineal lacerations. The association of perineal lacerations with FGM/C type III was assessed in four studies [29,32,34,28]. Both analysis of unadjusted and adjusted data failed to indicate any significant effect of type-III FMG (Table 2). Subgroup analysis according to study design also failed to show a significant difference (Table 2). However, the sensitivity analysis including three studies scoring more than 7 in the NOS scale [29,32,34], showed a statistically significant association between FGM/C type III and perineal laceration (OR: 4.24, 95 % CI: 1.09–16.46, I^2: 66 %, p-value: 0.04). Meta-regression for nulliparity and maternal age>35 was impossible due to lack of data.

3.4.1.6. Obstetric anal sphincter injuries (OASIS). Six studies [27,30,43,32,36,33] assessed the association between FGM/C type III and OASI (Table 2). Both analysis of unadjusted and adjusted data failed to indicate a significant effect of type-III FMG (Table 1). Subgroup analysis according to study design and sensitivity analysis including two studies with NOS score>7[32,36]also failed to show a significant difference (Table 2). Meta-regression for nulliparity and maternal age>35 was impossible due to lack of data.

3.4.1.7. Prolonged 2nd stage of labour. Although the crude analysis of four studies [30,29,32,34] failed to show an association between FGM/C type III and prolonged second stage of labour, type III FGM/C was found to increase the risk of prolonged second stage of labour in the sensitivity analysis of three studies with higher quality at NOS [29,32,34] (Table 2; OR 5.19, 95 % CI: 1.00–26.85, I^2: 66 %, p-value: 0.05). Subgroup analysis of data from cohort studies showed a significant risk increase for prolonged second stage of labour, whereas this variable failed to show significance of those from case-control and cross-sectional studies (Table 2). Meta-regression for nulliparity and maternal age>35 was impossible due to lack of data.

3.4.1.8. Other outcomes. Prolonged 1st stage of labour, preterm or late term delivery, meconium, premature rupture of membranes

(PROM), induction of labour and maternal death were insufficiently reported; therefore, they were not analysed.

3.4.2. Neonatal outcomes

3.4.2.1. Apgar score less than 7. Although crude analysis and subgroup analysis according to study design of five studies [30,29,34–36] failed to reveal a significant effect of FGM/C type III on Apgar score less than 7, a clear effect was identified in the sensitivity analysis of two studies with NOS score>7[34,39] (Table 2; OR: 4.19, 95 % CI: 1.64–10.70, I^2: 0 %, p-value: 0.003), with no heterogeneity between studies. Subgroup analysis of studies from low-income countries showed a significant risk increase for Apgar score below 7, whereas this variable failed to show significance for high-income countries (Table 2). Meta-regression for nulliparity and maternal age>35 was impossible due to lack of data.

3.4.2.2. Perinatal death. Pooled crude analysis of data from four low-quality studies [30,35,33,31] failed to reveal a significant effect of type III FGM/C on perinatal death (Table 2). Pooling of adjusted, sensitivity and subgroup analyses, meta-regression for nulliparity and maternal age>35 were impossible due to lack of data.

3.4.2.3. Other outcomes. Birth asphyxia, neonatal intensive care unit admission, neonatal acidemia and infant resuscitation outcomes were insufficiently reported; therefore, they were not analysed.

3.4.3. Deinfibulation

Only one study [32] at low risk of bias and three studies [30,35,28] at medium-high risk of bias were available for subgroup quantitative analysis.

3.4.3.1. Deinfibulation versus no prior FGM. Compared to women with no prior FGM, deinfibulation was not significantly associated with higher risk of postpartum haemorrhage (OR: 1.34, 95 % CI: 0.68–2.63, I^2: 14 %, p-value: 0.40), caesarean delivery (OR: 0.68, 95 % CI: 0.43–1.07, I^2: 18 %, p-value: 0.29),instrumental delivery (OR: 1.07, 95 % CI: 0.68–1.68, I^2: 0 %, p-value: 0.77), episiotomy (OR: 1.82, 95 % CI: 0.75–4.44, I^2: 87 %, p-value: 0.19), perineal tears (OR: 0.93, 95 % CI: 0.59–1.45, I^2: 0 %, p-value: 0.74), OASI (OR: 0.87, 95 % CI: 0.28–2.74, I^2: 27 %, p-value: 0.81), prolonged second stage of labour (OR: 0.94, 95 % CI: 0.35–2.51, I^2: 32 %, p-value: 0.90), Apgar score less than 7 (OR: 0.57, 95 % CI: 0.25–1.29, I^2: 0 %, p-value: 0.18), and perinatal death (OR: 0.84, 95 % CI: 0.19–3.63, I^2: 0 %, p-value: 0.81).

3.4.3.2. Antepartum versus intrapartum deinfibulation. Only two studies [30,35] at high risk of bias assessed the association between antepartum and intrapartum deinfibulation with adverse obstetric and neonatal outcomes. No significant difference was found between antepartum and intrapartum deinfibulation for outcomes such as instrumental delivery (OR: 1.10, 95 % CI: 0.82–1.47, I^2: 16 %, p-value: 0.52), Apgar score less than 7 (OR: 1.42, 95 % CI: 0.79–2.54, I^2: 0 %, p-value: 0.24), and perinatal death (OR: 0.76, 95 % CI: 0.29–2.00, I^2: 0 %, p-value: 0.58).

3.4.3.3. Deinfibulation versus no deinfibulation. Only two studies [30,35] at high risk of bias assessed the association between deinfibulated and non-deinfibulated type III FGM/C with adverse obstetric and neonatal outcomes. No significant difference was found between deinfibulated and non-deinfibulated women for outcomes such as instrumental delivery (OR: 1.68, 95 % CI: 0.15–19.29, I^2: 69 %, p-value: 0.68), Apgar score less than 7 (OR: 1.11, 95 % CI: 0.29–4.21, I^2: 0 %, p-value: 0.87), and perinatal death (OR: 0.92, 95 % CI: 0.17–5.00, I^2: 0 %, p-value: 0.93).

3.5. Assessment of heterogeneity

Nulliparity, BMI and maternal age were considered as potential moderators for obstetric outcomes. Meta regression for BMI was always impossible because available data were insufficient. For the sensitivity analysis we included studies with higher scores at NOS. In one case, when no alternative was available, RR was assimilated to adjusted OR for pooled estimates, (aRR of Banks et al. [20]).

Despite the large sample size reported in the pooled analysis, confidence intervals remain wide for some rare outcomes. Publication bias assessment was not produced due to the limited number of studies (less than 10) available for each investigated outcome [45]. Significant variability in statistical heterogeneity was noticed in the pooled data effect sizes of the outcomes, with I^2 values ranging from 0 % to 98 %. Heterogeneity was explored through adjusted pooled analyses when data were available. Sensitivity analysis included studies that met seven or more of the nine recommended items in the NOS scale. Additionally, subgroup analysis according to study design, comparing cross-sectional/case-control studies versus cohort studies, was performed. Any remaining heterogeneity could not be further investigated because of limited availability of data.

4. Discussion

4.1. 1Main findings

Our findings suggests that women with type-III FGM/C have a higher risk of experiencing adverse obstetric and neonatal outcomes

as compared to women with no FGM/C.

Specifically, type-III FMG/C appears to increase the risk for postpartum haemorrhage (about 2-fold), episiotomy (about 3-fold), perineal tears (about 2 to 3-fold) and prolonged second stage of labour (about 3-fold). On the other hand, type-III FGM/C was not significantly associated with OASI, caesarean or instrumental delivery. As for neonatal outcomes, adjusted and sensitivity analyses revealed a significantly increased risk of Apgar score <7 (about 4-fold). Analysis of the very limited evidence available, did not reveal significant differences in obstetric outcomes of women who had undergone deinfibulation compared to those who never had type-III FGM, and this knowledge, in view of our overall results, suggest a beneficial effect of deinfibulation. Finally, data were too few to detect meaningful differences between ante- and intrapartum deinfibulation.

4.2. 2Strenghts and limitations

To our knowledge, this metanalysis is the first to date evaluating the effect of FGM/C type III on obstetric outcomes. The current meta-analysis incorporates adjusted data, sensitivity and subgroup analysis, and meta-regression for proportions, allowing us to add on robustness, precision and refinement of previous pooled estimates. In addition, our review presented methodological robustness aligned with PRISMA and MOOSE guidelines, as well as with the Cochrane Handbook of Systematic Reviews for Interventions. The 2020 WHO classification system [1] was rigorously applied for type III FGM classification in all the included studies. Further, the data are all from medical records except for one study where the data is self-reported by the patients.

The main limitation of this study would be related to somehow high statistical heterogeneity of some analyses and to the high clinical heterogeneity of some individual definition of outcomes or exposures, as well as to inclusion of few low-quality studies.

Thus, the summary estimates for some outcomes should be interpreted cautiously. Further studies with larger populations are needed in the future to determine whether there are more significant associations than have thus far been revealed, including assessment of additional non-investigated factors (e.g., social or food deprivation, adolescent pregnancy, low income or education level, drugs of abuse, antenatal care, etc). Regardless of the precise magnitude of the increased risk associated with FGM/C type III, the consistency of findings indicating heightened risk for various adverse obstetric and neonatal outcomes, especially PPH, among women with FGM type III remains robust.

4.3. Interpretation

Our findings are at odds with some previous literature on FGM/C, which, however, shows controversial results. In particular, data differ substantially among the different types of FGM/C, and available studies presented significant methodological limitations failing to investigate all details of obstetric risks in each individual FGM/C subtype, thus being unable to provide reliable evidence. Four metanalyses [15–18], with very low quality of evidence, have indeed suggested that adverse obstetric and neonatal outcomes might be more common in women who had some type of genital mutilation. Nonetheless, from a clinical standpoint, the overall risk varies significantly by FGM/C type at the time of delivery, with the most extensive forms of FGM/C (type III; infibulation) carrying the greatest risk [20].

4.3.1. Obstetric outcomes

When evaluating postpartum haemorrhage in this context, we can speculate that higher rates of perineal tears and prolonged second stage of labour, combined with the gradual loss of vaginal tissue elasticity and strength secondary to scarring, may explain the higher blood loss in these women. Prolonged labour is indeed an independent risk factor for postpartum haemorrhage [26]. Interestingly, a meta-regression analysis indicated that the effect size on PPH increased with increasing rates of nulliparity among FGM/C type III women vs. controls raised. Thus, this association may be in part explained by the increased rates of tears and episiotomy in nulliparous women, together with a preexisting scarred and narrowed vaginal introitus. Moreover, the univariate meta regression potentially highlighted a higher effect on PPH with increasing rates of women under 35 in FGM/C type III compared to controls. When combining the effect of these two moderators, the nulliparity ratio still remains significant, while maternal age does not. This could be explained by the fact that nulliparity and maternal age are strictly and directly related: it is not surprising that we found a higher risk for PPH in nulliparous women who are also usually younger.

Although female genital mutilation irrespective of subtype was found to be significantly associated with caesarean delivery in three meta-analyses [15,17,18], our data showed that type-III FGM/C was not significantly correlated with higher rates of either caesarean section or instrumental deliveries. These results are not surprising and are well aligned with the knowledge the patients' characteristics and thresholds for labour anomalies are the major determinants affecting the risk of caesarean delivery [45].

Anothermeta-analysis [16] showed no differences in episiotomy rates between women with and without genital mutilations, but it noted a significant increase in severe perineal lacerations, regardless the subtype of FGM. Despite the absence of a significant effect of infibulation on the risk of OASIS, based upon our findings, a protective role towards severe obstetric perineal trauma, maybe hypothesized in view of the increased use of episiotomy in women with type III FGM, as already observed in two studies [27,32].

4.3.2. Neonatal outcomes

A prolonged second stage of labour is directly associated with an increased risk of neonatal acidemia, which can explain our findings of an increased risk of low Apgar scores [46–48]; however, we did not find an apparent association with perinatal death. One large, multicentre, prospective study including more than 23,000 women, showed that about 22 % of perinatal deaths can be attributed to FGM/C[21]. Although several studies have documented an increased risk of fetal distress in women with type III FGM/C [37,34], we

could not assess several important perinatal outcomes due to the lack of quantitative data and heterogeneity in reporting data between the included studies.

4.3.3. Deinfibulation

The significance of deinfibulation in preventing complications and improving birth outcomes of women with type III FGM/C was identified as a research priority by the WHO in 2016 [49].

In line with previous systematic reviews and metanalyses [21,22], deinfibulation can lead to comparable obstetric outcomes to those of women who have never undergone type III FGM. Moreover, there is no evidence for a significant difference between antepartum and intrapartum deinfibulation for outcomes such as instrumental delivery, Apgar score less than 7 and perinatal death, although most studies included in the analysis were of low quality and underpowered to detect statistical differences.

4.3.4. Country setting

Most women who have undergone FGM/C live in countries with limited healthcare infrastructure. Therefore, the frequency and the impact of related complications might differ, especially for important outcomes, such as PPH. However, the high heterogeneity of analysed outcomes could only be partially explained by subgroup meta-analysis for country setting. Notably, only a few outcomes seem to be highly variable depending on country setting. Thus, the risk for instrumental delivery was homogenously higher in low-income countries compared to high income one, as for the risk for Apgar<7. The lack of a consistent pattern of heterogeneity by country for any of the other outcomes is reassuring, indicating that the overall ORs for the main findings can be considered an appropriate summary of the results.

5. Conclusions

FGM/C have a profound impact on women health and wellbeing. These results consistently show an increased risk of adverse obstetric outcomes in women with FGM/C type III. Infibulation substantially increases the risk for PPH, particularly in nulliparae. Analysis of the very limited evidence available, revealed that deinfibulation can achieve similar obstetric outcomes to women who never had type III FGM. Yet, our work also highlighted the paucity of available evidence on potential effective interventions (antepartum or intrapartum deinfibulation) to prevent complications and improve birth outcomes. The difficulties in ensuring that studies with appropriate design are conducted should not justify the lack of intervention to correct infibulation before delivery, particularly when due to paucity of data availability. This meta-analysis revealed important insights about the dynamics of type-III FGM during childbirth and demonstrated the need for more evidence to support specific interventions and primary prevention policies for the millions of women at risk or already living with FGM/C. Pregnancies with diagnosis of FGM/C should be considered at high-risk of postpartum haemorrhage, episiotomy, perineal tears, prolonged second stage of labour and low Apgar score and should undergo appropriate obstetric management to address these issues accordingly.

Ethics declarations

Review and/or approval by an ethics committee was not needed for this study.

Data availability statement

Data will be made available on request by the corresponding author.

CRediT authorship contribution statement

Giulia Bonavina: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Silvia Lina Spinillo:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Alexandros Sotiriadis:** Writing – review & editing, Supervision, Methodology, Data curation. **Alessandro Bulfoni:** Writing – review & editing, Methodology. **Randa Kaltoud:** Writing – review & editing, Methodology, Data curation. **Stefano Salvatore:** Writing – review & editing, Methodology. **Massimo Candiani:** Writing – review & editing, Supervision, Methodology. **Paolo Ivo Cavoretto:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Paolo Ivo Cavoretto reports financial support and article publishing charges were provided by Heliyon. Paolo Ivo Cavoretto reports a relationship with Helyion that includes: board membership and consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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