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Adeline Boatin[1], Deen Garba[2], Michala Sawyer[3], Kaitlyn James[1], Joseph Ngonzi[4], Henry Lugobe[4], Blair Wylie[5], and Kwame Adu-Bonsaffoh[6]

[1]Massachusetts General Hospital
[2]The University of North Carolina at Chapel Hill School of Medicine
[3]Planned Parenthood Federation of America
[4]Mbarara University of Science and Technology
[5]Beth Israel Deaconess Medical Center
[6]University of Ghana Medical School

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Abstract

Background: Intrapartum decision-making for women with a previous caesarean section (CS) is complex due to competing risks of trial of labour after cesarean (TOLAC) and elective repeat CS (ERCS). Objective: Determine rates of TOLAC and vaginal birth after cesarean (VBAC) in sub-Saharan Africa (SSA) and estimate rates of adverse events associated with TOLAC versus ERCS. Search Strategy: We searched PubMed, MEDLINE, CAB, EMBASE, and African-specific databases. Selection Criteria: We included studies with at least one previous CS conducted in SSA. Data Collection and Analysis: We extracted data on study design, planned and actual delivery mode, and maternal and perinatal outcomes. We calculated median TOLAC and VBAC rates pooled mean uterine rupture rate and compared uterine rupture rates and mortality between TOLAC and ERCS. Main Results: From 51 included studies, the median TOLAC and VBAC rates, weighted for sample size, were 75% (IQR: 40-100%) and 34% (IQR: 24-44%) , respectively; and the weighted mean uterine rupture rate was 1.3% (SD: 1.6%). The uterine rupture rate [1.2% vs 0.2%, OR 1.54 (95% CI 0.63-3.75)] and maternal mortality [0.3% vs <0.1%, OR 0.77 (95% CI 0.30-1.98)] did not differ significantly between TOLAC and ERCS groups, respectively, however perinatal mortality was higher for the TOLAC group (5% vs 1%, OR 3.3 ; 95% CI 1.5-6.9) Conclusions: We found high rates of TOLAC and moderate rates of VBAC across SSA, with a perinatal but no maternal benefit to ERCS compared to TOLAC. Further research is needed to understand delivery outcomes in this population of women.

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Adeline A. Boatin[1,2,], Deen L. Garba[3], Michala Sawyer[4], Kaitlyn James[1], Joseph Ngonzi[5], Henry Mark Lugobe[5], Blair J. Wylie[2, 6], Kwame Adu-Bonsaffoh[7,8].

1. Department of Obstetrics and Gynecology, Massachusetts General Hospital, Boston, USA
2. Harvard Medical School, Boston, USA
3. University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA
4. Planned Parenthood of America, Massachusetts, USA
5. Department of Obstetrics and Gynecology, Mbarara University of Science and Technology, Mbarara, Uganda
6. Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Beth Israel Deaconess Medical Center, Boston, USA

7. Department of Obstetrics and Gynecology, Korle-Bu Teaching Hospital, Accra, Ghana
8. Department of Obstetrics and Gynecology, University of Ghana Medical School, Accra, Ghana

Corresponding author: Adeline A. Boatin

Email: adeline_boatin@mgh.harvard.edu; 55 Fruit Street, Boston, MA, 02114

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Data Collection and Analysis: W e extracted data on study design, planned and actual delivery mode, and maternal and perinatal outcomes. We calculated median TOLAC and VBAC rates pooled mean uterine rupture rate and compared uterine rupture rates and mortality between TOLAC and ERCS.

Main Results: From 51 included studies, the median TOLAC and VBAC rates, weighted for sample size, were 75% (IQR: 40-100%) and 34% (IQR: 24-44%) , respectively; and the weighted mean uterine rupture rate was 1.3% (SD: 1.6%). The uterine rupture rate [1.2% vs 0.2%, OR 1.54 (95% CI 0.63-3.75)] and maternal mortality [0.3% vs <0.1%, OR 0.77 (95% CI 0.30-1.98)] did not differ significantly between TOLAC and ERCS groups, respectively, however perinatal mortality was higher for the TOLAC group (5% vs 1%, OR 3.3 ; 95% CI 1.5-6.9)

Conclusions: We found high rates of TOLAC and moderate rates of VBAC across SSA, with a perinatal but no maternal benefit to ERCS compared to TOLAC. Further research is needed to understand delivery outcomes in this population of women.

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Introduction

Currently, 21.1% of women deliver by caesarean section (CS) worldwide, and this is projected to rise to 28.5% by 2030, representing an estimated 38 million CS annually.[1] While sub-Saharan Africa (SSA) has seen the slowest rise in rates, the regional average of 5% masks significant variation across the continent, ranging from 1.4% to 50.7%.[1] Analysis of CS rates by subgroup indicates that the contribution of women with a prior caesarean to overall rates has increased substantially in SSA.[2] As CS rates continue to rise, this subgroup of women will likely grow further due to the domino effect associated with repeat CS and continued high fertility rates across SSA.[3]

Intrapartum management for women with a prior caesarean is complex owing to the risk of uterine rupture balanced against the risk of repeat surgery. While uterine rupture rates are higher in women with a prior caesarean, repeat surgery also carries risks and may further complicate future pregnancies with increasing risks of abnormal placentation and surgical complications with each subsequent surgery.[4,5] Practice patterns associated with the trial of labour after caesarean (TOLAC) versus elective repeat caesarean (ERCS) have thus fluctuated over time in response to emerging evidence around these competing risks. In the late 1990s, new evidence surrounding uterine rupture led to significant practice changes in the United States and many

developed countries: rates of vaginal birth after caesarean (VBAC) dropped from 62% in studies completed before 1996 to 42% in studies conducted after 1996.[4] However, similar data examining potential changes in practice patterns in SSA is limited.

There is inadequate evidence to guide decision-making and the ideal management for women with a prior CS in SSA. Extrapolating from clinical outcomes and studies of TOLAC vs ERCS in high-income countries is problematic due to the substantially different circumstances under which intrapartum care is delivered in the SSA. Indeed, studies examining outcomes after CS in SSA demonstrate maternal and perinatal mortality rates 40-50 times higher than those observed in high-income countries and maternal morbidity rates as high as 17%.[6,7] This increased mortality and morbidity may reflect gaps in the ability to adequately monitor women and foetuses through a trial of labour or limitations in expedient surgical management should complications occur, raising concerns about the safety of TOLAC in SSA.[8,9]

There are no recent reviews synthesising the available evidence on trial of labour rates and associated clinical outcomes among women with a prior CS in SSA.[10] We performed this systematic review to summarise evidence and address this gap in the literature. Our objectives were to determine rates of TOLAC and VBAC in SSA and estimate the rates of adverse maternal and perinatal events associated with TOLAC vs ERCS. We further aimed to assess if practice patterns related to management of women with a prior CS varied by subregion within SSA and whether there have been changes in practice patterns over time in sub-Saharan Africa.

Methods

Search Strategy and Inclusion Criteria

We searched PubMed, MEDLINE, CAB, EMBASE, African Index Medicus, and CINAHL databases from inception (1966) until July 28th, 2020, to identify all studies in women with a prior CS conducted in SSA. We also reviewed reference lists of included articles and available systematic reviews to identify additional articles. Specific search terms included vaginal birth after caesarean, trial of labour after caesarean, caesarean section/delivery, abdominal delivery, and trial of labour. Unpublished studies were not included in this search. Full details of the search strategy are available in Table S1.

We included studies from full-text published studies in either English or French. Studies had to report information on participants with at least one prior CS presenting for delivery in a subsequent pregnancy. We included articles reporting planned and actual mode of delivery and delivery outcomes, including maternal, fetal and neonatal outcomes. We included studies with a range of study designs, including randomised controlled trials, cohort studies, case-control studies, cross-sectional studies and case series and be conducted in a range of clinical settings. We excluded articles with a study setting outside of SSA and those focusing on a narrower subset of women within the desired population, e.g., only women with multiple gestations or with a hypertensive disorder of pregnancy.

Study Selection

The review was conducted using a prospective protocol and reported per PRISMA guidelines. The study protocol was registered with PROSPERO (CRD42020175434), where the review protocol is available. Studies were selected for inclusion in two stages using Covidence © (2020). First, at least two authors (AAB, KAB, MS and DG) independently reviewed the titles and abstracts against inclusion criteria. Studies were excluded at this stage if they did not assess mode of delivery after a history of prior CS or were not carried out in SSA. Secondly, at least two independent reviewers (AAB, KAB, MS and DG) reviewed the full text of articles against inclusion criteria for final exclusion.

Data Extraction and Quality Assessment

Data extraction for included studies was performed independently by at least two authors (AAB, KAB, MS and DG) using REDCap electronic data capture tools hosted at Massachusetts General Hospital, Boston USA.[11] Data on the location, study year, clinical setting, study design, study population, planned and actual

mode of delivery, and any reported maternal and neonatal outcomes were extracted. A third reviewer resolved disagreements between reviewers until consensus was reached.

Quality assessment of studies was performed using the methodological index for non-randomized studies (MINORS) (Table S2)[12]. This tool was developed for quality assessment in surgical research, where it is anticipated that most studies will be observational or non-randomized. Studies are rated on 12 items and assess clarity in the aims, inclusion criteria, and endpoints of the study, as well as the extent to which studies had a prospective design, comparison group, reported and described definitions, length of follow-up of outcomes, and included appropriate statistical analysis. Studies received ratings of "Not Reported" (0 points), "Reported but inadequate" (1 point), and "Reported and adequate" (2 points). A score of 16 or greater represents a high-quality study. At least two authors (AAB, KAB, MS and DG) independently rated studies and where a disagreement occurred, consensus was reached through discussion with a third independent author. Studies were not excluded based on quality assessment, but sensitivity analyses were performed using studies with a score [?]16, indicating a high-quality study.

Data Analysis

For studies with consecutive enrolment and where data was presented on the planned mode and actual mode of delivery for all subjects, we calculated the median TOLAC rate and median VBAC rate across studies, using frequency weights for study sample size. The primary clinical outcome assessed was uterine rupture. Secondary outcomes were maternal mortality and perinatal (stillbirth and neonatal) mortality. We estimated the overall rate of these adverse outcomes across all births for which this data was available to generate estimates across all available studies, also weighted for study sample size. We further compared uterine rupture rate, maternal mortality and perinatal mortality (stillbirth and neonatal mortality) between TOLAC and ERCS in studies where comparison groups were available and calculated the pooled odds ratios of adverse outcomes with 95% confidence intervals. For this comparison, a random-effects model was used to combine the studies while accounting for heterogeneity. We used forest plots to graphically summarise the pooled results. We performed sensitivity analyses using studies with a MINORS score of [?]16.

We performed subgroup analyses to evaluate TOLAC and VBAC rates over time and compared rates in studies published before and after January 1st, 1996 using the rank-sum test to assess for differences by region and changing practice patterns and trends. We choose 1996, as a comparison date as the last published metanalysis of TOLAC in SSA included studies up to 1995.[10] This year also corresponds to a period when a marked decline in the rates of TOLAC and VBAC was seen in the other regions of the world due to emerging data on risks of uterine rupture following trial of labour.[13]

All statistical calculations were performed with STATA, version 13 (StataCorp, College Station, TX USA).

Results

Our search strategy yielded 1383 published articles, of which 51 studies from 20 countries in SSA were included. (Figure 1). Fourteen studies (27%) used prospective data collection, 27 (53%) were retrospective and 10 (20%) were unclear (Table S3). Most studies (n=44, 86.3%) were conducted in a tertiary or university hospital setting. Twenty studies (39.2%) were conducted before and including 1996, and 31 (60.8%) studies after 1996. Most studies (n=31, 60.8%) included women with only one prior caesarean delivery. MINORS scores are presented in Table S3. The mean MINORS score was 14.8 +-3.7, with a range of 6-22 across all studies. Twenty-three (23) studies had MINORS score [?] 16.

TOLAC and VBAC rates

The study sample size ranged from 34 to 10,718 women, with a total of 32,070 births included in this review. The weighted median TOLAC rate was 75% (IQR 40-75%) and ranged from 21.9% to 100%. The overall median VBAC rate was 34% (IQR 24-40%) and ranged from 3.4% to 85%.

Thirty-one studies included women with only one prior caesarean, comprising 26, 482 births. Among this group, the overall weighted median TOLAC rate was 75% (IQR: 40-75%), range: 21.9-100%), and median

VBAC rate 34% (IQR 24-34%), ranging from 14.2-84.7%. In studies conducted before and after 1996, overall weighted median TOLAC rates were 63% and 75% (p=0.41) and median VBAC rates were 52% and 34%, respectively (p=0.14).

There were 18 comparative studies, i.e., where management with TOLAC was compared to ERCS, comprising 22,938 deliveries. Study details and delivery outcomes are summarised in Table 1. The overall weighted median TOLAC rate in this subset was 75% (IQR 39-75%), ranging from 21.9% to 98.2%, and the median VBAC rate was 34% (IQR 24-34%), ranging from 3.4 to 84%.

Maternal and Perinatal Outcomes.

Forty-seven studies presented data on maternal outcomes including uterine rupture (n=39), uterine dehiscence (n=16), maternal mortality (n=44), blood transfusion (n=10), and hysterectomy (n=17) (Table 2). Forty-five studies presented data on perinatal outcomes including stillbirth (n=20), neonatal mortality (n=18), perinatal mortality (stillbirth and neonatal mortality combined) (n=18), low Apgar score (n=22), and neonatal ICU admission (n=11) (Table 2).

Although 43 studies reported on uterine rupture or dehiscence, very few provided a definition (n= 4, 9%) distinguishing between rupture and dehiscence, and definitions varied across studies. Given difficulty separating the two conditions and inconsistencies, we combined uterine rupture and dehiscence to obtain a single summary estimate. Over the 29,823 deliveries amongst studies reporting uterine ruptures or dehiscence, there were 386 cases of uterine rupture or dehiscence for an overall weighted mean of 1.3% (+- SD 1.6). There was regional variation in uterine rupture/dehiscence rates, with the lowest reported rate of 1.3% in West Africa and the highest rate of 8.8% in Central Africa. (Table 3)

Seventeen studies provided data on maternal and/or perinatal outcomes with a TOLAC and ERCS comparison group, representing 22,599 births in 8 countries (Figure 2). Pooled uterine rupture/dehiscence rate in this group (n=11 studies) was 1.4% in the TOLAC group and 0.2% in the ERCS group. However, the risk for uterine rupture did not differ from TOLAC vs ERCS (OR 1.54 (0.63-3.75 95% CI)). This did not differ when restricted to the nine studies which reported only on women with one prior CS [OR 1.70 (0.63-4.6 95%CI)] or with a MINORS score [?] 16 [OR 1.77 (0.56-5.56 95% CI)].

Maternal mortality rates did not differ by TOLAC vs ERCS (n=13 studies) (0.3% vs <0.1%, OR 0.77 (0.30-1.98) with similar findings in studies restricted to women with only one prior CS or with a MINORs score > 16. Only six studies reported on perinatal mortality by comparison group. No studies with TOLAC and ERCS comparison groups separated stillbirth and neonatal mortality. Pooled rates demonstrated that perinatal mortality was higher in women undergoing TOLAC (5%) compared to ERCS (1%), OR 3.3 (1.5-6.9 95%CI).

Regional and temporal variation

Most studies were conducted in WestAfrica, with the majority, 31% (n=26), carried out in Nigeria alone (Table 3). There was relatively little representation from Central Africa (n=4). Median TOLAC rates were highest in Central Africa at 91.6%, compared to 49% in Eastern Africa, which had the lowest rate. Adverse outcomes also varied with higher reported rates of perinatal mortality in the one study from Central Africa (115), compared to the sub-regional average for Western Africa (2.2%), and higher reported rates of uterine rupture/dehiscence (8.8% vs 1.3%) respectively. In studies conducted before and after 1996, median TOLAC rates were 90% and 76% (p=0.41), and median VBAC rates were 50% and 36%, respectively (p=0.14), respectively (Figure 3).

Discussion

Main Findings

This systematic review summarised rates and outcomes associated with delivery after a prior CS in SSA. Overall, we found relatively high rates of TOLAC across the sub-region, with a median rate of 80%. Rates of VBAC were more variable median rates of 34-48% depending on study criteria. Maternal and perinatal

outcomes were reported infrequently and with inconsistent definitions. Among those studies reporting outcomes, we found a uterine rupture rate of approximately 1%, maternal mortality ratio of 200 per 100,000 live births and perinatal mortality rate of 5 per 1000 births. There was no significant difference between TOLAC and ERCSfor rates of uterine rupture or maternal mortality. However perinatal mortality was significantly higher in the TOLAC group compared to the ERCS group. We found lower TOLAC and VBAC rates in studies after 1996 compared to those in 1996 or earlier; however, this did not reach statistical significance. . We also found sub-regional variation in the number of studies of TOLAC with relatively few in Central and East Africa and higher reported rates of adverse outcomes in Central and East Africa compared to South and West Africa.

Interpretation

Global TOLAC and VBAC rates vary greatly. TOLAC rates range from as low as 5% in nationwide studies from Japan to rates of 66-72% in Denmark and the Netherlands.[14–17] The TOLAC rates found in our review were higher than those in other regions of the world but similar to the findings by a prior SSA metanalysis from 1998, where the average rate was 69%. However, the VBAC rates we found were generally lower compared to other regions, where rates range from 60-89%, with the exception of two studies from China and Denmark, where the rates were 14% and 8%, respectively.[15–21] These differences could be due to variations in study design and inclusion criteria but could reflect practice patterns, and may reflect a greater ability to screen for and select TOLAC candidates with a higher likelihood of success due to more robust antenatal care in regions of the world with more comprehensive health care services. It is also possible that the threshold for abandoning TOLAC and moving to repeat cesarean delivery is lower in hospitals delivering this care in SSA, as there are barriers to the close monitoring needed during TOLAC and challenges of access to expedient surgical management should complications occur.

Overall, we found a uterine rupture rate of 1.3% across all reporting studies, suggesting this is a relatively low occurrence among women with a previous CS in SSA. However, this rate is several times higher than the overall rupture rates of 0.3-0.6% reported in other regions,[15,17,21,22] but lower than rates of 2.1-2.7% reported in China.[18] Overall pooled maternal and perinatal mortality rates were also higher than mortality rates associated with TOLAC and ERCD in other regions of the world.[14–17,19–21,23] In particularly, the pooled perinatal mortality rate of 5% among the TOLAC group in comparative studies is markedly higher than the rates reported in other regions of the world, where with the exception of one study from China reported perinatal mortality rates are less than 1%. [14,15,17–19,22–24]Importantly, however, the higher rate of perinatal mortality found in the TOLAC group compared to ERCS calls for further research to understand if this finding remains true in more extensive studies, across all groups of women and settings, and if outcomes are modifiable based on antenatal screening and triage patterns and intrapartum care delivery.

Further research is needed to understand the differences in regional rates, particularly the variation in uterine rupture rates (range from 1.3% to 8.8%). There are several potential reasons for these differences. With less ability to adequately screen and counsel women with prior caesareans due to limited resources and more limited access to antenatal care, it is possible that more women with a relative contraindication to TOLAC, e.g., two or more prior caesareans, undergo TOLAC. Furthermore, women may arrive late to hospitals for adequate monitoring of TOLAC or may even avoid going to the hospital to avoid a repeat cesarean. Finally, at the hospital, there may be more limited ability to monitor women adequately, appropriately triage women to repeat cesarean when TOLAC is unsuccessful, and move expediently to surgery once the decision has been made [ref].

Strengths and Limitations

Most studies included in this review were retrospective, and many lacked an adequate control or comparison group. In several studies, outcomes were compared by actual rather than the intended mode of delivery, making it hard to ascertain differences that can inform future clinical decision-making. Many studies also failed to report on adverse outcomes, and there was substantial heterogeneity in the inclusion and exclusion criteria and the definitions used for reporting. Additionally, most studies were performed in tertiary or

university hospitals; thus, our findings in this context may not be generalisable to district or general hospitals where most facility-based deliveries in SSA occur. Regional generalizability may also be limited as most studies were conducted in West Africa and relatively few in Southern Africa.

More consistent reporting is needed across studies to gain a more nuanced and reliable understanding of outcomes in this population of women. In prior work, we have summarised that based on existing patterns of care-seeking behaviour throughout sub-Saharan Africa, comparison with the two groups TOLAC vs ERCS may be incomplete and rather, three groups of analysis are preferable 1) TOLAC – i.e. women who present in labour and are allowed to continue labouring in the hospital, or women who are induced or augmented 2) – Emergency RCD - i.e. women presenting in labour and whose initial plan on arrival to the hospital is for CD and 3) Elective RCD – women whose initial plan is for a scheduled non-laboured CD.[25] We recommend considering the use of this reporting in future studies aiming to understand delivery outcomes among women in a prior cesarean delivery. We also recommend at a minimum that reported adverse outcomes include maternal and perinatal (both stillbirth and neonatal) mortality and uterine rupture rates, including other maternal and perinatal adverse events such as rates of hysterectomy, ICU admission, and blood transfusion wherever possible.

Conclusion

In summary, we found high rates of TOLAC but relatively low to moderate rates of VBAC across SSA with high variability of these rates across the sub-region and with a perinatal but no maternal benefit to ERCS compared to TOLAC. Maternal and Perinatal mortality and morbidity rates were higher when compared to mortality and morbidity rates for women with a prior cesarean in other regions. Improved study methodology and consistent reporting are needed in future studies to enhance our understanding of delivery outcomes in this population of women.

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Disclosure of Interests

There are no conflicts of interest to disclose

Author contributions

AAB and KAB conceived the study and study design. AAB, KAB, MS and DG performed the title, abstract and full-text screening and data extraction. AAB and KJ performed data analysis. AAB wrote the initial draft of the manuscript. AAB, DG, MS, KJ, JN, HML, BW and KAB discussed the results, provided interpretation, reviewed the manuscript and provided critical comments.

Ethical approval

There was no human subject contact for this study and ethical approval not required.

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Data availability

Templates for data collection forms, data extracted from included studies and data used for analyses are available from authors upon reasonable request.

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`Figure 2- Outcomes .docx` available at https://authorea.com/users/409272/articles/619058-trial-of-labour-after-caesarean-section-in-sub-saharan-africa-a-systematic-review-and-meta-analysis

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`Figure 3 TOLAC and VBAC Rates over time .docx` available at https://authorea.com/users/409272/articles/619058-trial-of-labour-after-caesarean-section-in-sub-saharan-africa-a-systematic-review-and-meta-analysis