Impact of the introduction of a low-cost uterine balloon tamponade (ESM-UBT) device for managing severe postpartum hemorrhage in India: a comparative before-and-after study

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Synopsis: Introduction of a uterine balloon tamponade device for managing severe postpartum hemorrhage in health facilities in India significantly reduced maternal death and/or invasive procedures.

Type of article: clinical article

Abstract

Objective: To evaluate the impact of introducing a uterine balloon tamponade (ESM-UBT) device for managing severe postpartum hemorrhage (PPH), mainly due to uterine atony, in health facilities in India on the rates of PPH-related maternal death and invasive procedures for PPH control.

Methods: We used a quasi-experimental, difference-in-difference (DID) design to compare changes in the rates of a composite outcome (PPH-related maternal death and/or artery ligation, uterine compression sutures, or hysterectomy) among women delivering in 9 intervention facilities compared with those delivering in 2 control facilities, before and after the introduction of ESM-UBT.

Results: The study sample included 214,123 deliveries (N=78,509 before ESM-UBT introduction; N=47,211 during ESM-UBT introduction; and N=88,403 after ESM-UBT introduction). After introduction of ESM-UBT, there was a significant decline in the rate of the primary composite outcome in intervention facilities (21.0 to 11.4 per 10,000 deliveries; difference -9.6, 95% confidence interval -14.0 to -5.4). Change in the rate of the primary composite outcome was not significant in control facilities (11.7 to 17.2 per 10,000 deliveries; difference 5.4, 95% confidence interval -3.9 to 14.9). DID analyses showed there was a significant reduction in the rate of the primary composite outcome in intervention facilities relative to control facilities (adjusted DID estimate -15.0 per 10,000 points, 95% confidence interval -23.3 to -6.8; *P*=0.005).

Conclusion: Introduction of the ESM-UBT in health facilities in India was associated with a significant reduction in PPH-related maternal death and/or invasive procedures for PPH control.

1 INTRODUCTION

Postpartum hemorrhage (PPH) remains the leading cause of maternal mortality worldwide [1]. In India, PPH accounted for over one quarter of the ~35,000 maternal deaths that were estimated for the year 2017 [2,3]. In addition, women surviving PPH are at increased risk for experiencing short-term health complications including anemia, disseminated intravascular coagulation, sepsis, and neurological, renal, or respiratory organ dysfunction, and long-term consequences such as renal failure, infertility, and emotional health problems, among others [4-6].

Uterine atony is the most common cause of PPH, but it can also be caused by injuries of the birth canal, retained placental tissue, abnormal placentation or maternal bleeding disorders [7]. Clinical interventions recommended by the World Health Organization for PPH treatment include use of uterotonics, uterine massage, administration of isotonic crystalloids, tranexamic acid, bimanual uterine compression, external aortic compression, use of non-pneumatic anti-shock garments, uterine balloon tamponade (UBT), uterine artery embolization, and surgical interventions such as uterine compression sutures, arterial ligation, and hysterectomy [8,9].

UBT is currently recommended for arresting bleeding among women with PPH due to uterine atony unresponsive to uterotonics and initial therapies to avoid invasive procedures such as arterial embolization, uterine compression sutures, pelvic vessel

ligation, and hysterectomy [8-13]. A recent systematic review and meta-analysis reported that UBT has a high success rate (86%) for treating severe postpartum hemorrhage, mainly due to uterine atony and placenta previa, with a low frequency of complications [14].

A few before-and-after studies, conducted in obstetrics units of French hospitals, have assessed the effectiveness of UBT introduction into protocols for management of severe PPH [15-17]. To date, no before-and-after study has evaluated the impact of introducing UBT for the management of severe PPH in low- and/or middle-income countries. Since commercial UBT devices are unaffordable in most resource-limited settings, our team have addressed this problem by developing the "Every Second Matters for Mothers and Babies-Uterine Balloon Tamponade" (ESM-UBT) device [18-22]. The ESM-UBT device is an ultra-low-cost, high-quality, US FDA approved, easy to use condom-catheter UBT, which is as efficacious and safe as Bakri balloon for treating PPH [14,23].

The aim of this study was to evaluate the impact of introducing the ESM-UBT device for managing severe PPH in health facilities in India on the rates of PPH-related maternal death and invasive procedures.

2 MATERIALS AND METHODS

2.1 Study design

We used a quasi-experimental, difference-in-difference (DID) design to compare changes in the rates of PPH-related maternal death and surgical interventions among women who delivered in intervention facilities compared with those in control facilities before and after the introduction of the ESM-UBT device and package for managing severe PPH. The DID

design makes use of longitudinal data from treatment and control groups to estimate the effect of a specific intervention by comparing the changes in outcomes over time between a population that is enrolled in a program (the intervention group) and a population that is not (the control group). The differences in the outcomes preintervention and postintervention are calculated for both the intervention and control groups and then compared [24]. Differences between the intervention and control groups are attributed to the effect of the intervention.

2.2 Setting

The study was conducted between January 2017 and July 2018 in 12 medical college referral hospitals located in Maharashtra and Madhya Pradesh, two of the most populous states in India. The project team purposively selected 10 medical college hospitals in these states as intervention facilities. These facilities were chosen at convenience because they were university hospitals with motivated Obstetrics and Gynecology department chiefs, high-quality data, and active research programs, and geographically spread out across the two states. One of these hospitals withdrew at mid-study due to a change of its director. Two medical college hospitals with similar characteristics to those of the intervention facilities were then purposively chosen as control facilities.

2.3 ESM-UBT device and package

Over the past 11 years investigators from the Massachusetts General Hospital (MGH) and Harvard University designed, developed, and implemented the ESM-UBT package which includes identification of and support to champions, didactic and hands on training, wall charts, memory aids, course flipcharts and facility manuals, policy support, and ESM-UBT devices [18-22]. The ESM-UBT device has undergone rigorous evaluation and

approval by the US FDA and consists of a size-24 silicone urinary catheter, condoms, O-rings, a Luer-lock one-way valve, a 60cc syringe, and a highly adherent adhesive to secure the ESM-UBT device. The ESM-UBT device components are packaged in a kit that additionally contains an illustrated checklist and data collection card. To place an ESM-UBT device, the condom is rolled out and secured to the end of the catheter with four twists of the O-ring, the balloon is then placed inside the uterus and rapidly filled with clean water using the 60cc syringe until the bleeding stops. The device is carefully secured with the adhesive. A dose of a broad-spectrum prophylactic antibiotic is recommended, and providers are instructed to leave the ESM-UBT device in place for 6–24 hours after placement. ESM-UBT devices are removed after a mother is stable by slow deflation with simultaneous close monitoring for potential resumption of bleeding.

2.4 Interventions

During the second week of January 2017, Obstetrics and Gynecology department chiefs and senior faculty from each of the initial 10 intervention facilities were trained over two days to become ESM-UBT master trainers by MGH/Harvard faculty at the Mahatma Gandhi Institute of Medical Sciences in Sewagram, Maharashtra, India. Master trainers were asked to lead provider training programs at their home facilities over the ensuing weeks and months until all skilled birth attendants in their facilities were trained. Trainees were instructed to use the UBT within the context of the established national guidelines for managing PPH, which include the use of oxytocin, methergine, misoprostol, bimanual uterine compression, and external aortic compression, among others. All these interventions, along with other resuscitation measures, should occur prior to placement of the UBT. Placement of the UBT should occur if these interventions fail and hemorrhage

continues uncontrolled. The control facilities only followed the previously mentioned standard practices for managing severe PPH throughout the study.

2.5 Outcome measures

The prespecified primary outcome was a composite of PPH-related maternal death and/or invasive procedures for hemorrhage control (artery ligation, uterine compression sutures, or hysterectomy). Secondary outcomes included PPH-related maternal death, hysterectomy, and other invasive procedures (artery ligation and/or uterine compression sutures).

2.6 Data sources

Data on the number of deliveries, PPH-related maternal deaths, and emergency procedures for controlling PPH (artery ligation, uterine compression sutures, and hysterectomy) were obtained retrospectively from each of the 11 facilities for the 12 months preceding implementation of the ESM-UBT package. Comparable data were prospectively collected for 19 months after ESM-UBT package implementation among the 9 intervention facilities and retrospectively obtained from the 2 control medical college hospitals. The intervention training period was set at 7 months to allow for ESM-UBT package implementation and integration, and to allow for balanced time intervals among comparison groups. Due to logistical and budget difficulties, data on maternal sociodemographic and obstetric characteristics in the intervention and control groups were only obtained for women delivering in the two months preceding introduction of the ESM-UBT package. Sample size calculation could not be performed because there were no prior studies that reported on rates of the composite primary outcome in intervention and control facilities.

2.7 Data management and analysis

The comparability of the study groups was determined by assessment of their baseline characteristics before the introduction of the ESM-UBT package. Categorical variables were expressed as counts and percentages, whereas continuous variables were expressed as means and standard deviations. Women delivering during the 7-month ESM-UBT package introduction period (January to July 2017) were excluded from the main analyses. Women delivering in the 12 months preceding introduction of the ESM-UBT package (January to December 2016) and those delivering in the 12 months succeeding upon completion of the ESM-UBT package introduction (August 2017 to July 2018) were included in the main analyses. We used multivariable linear regression models to compare the changes in the rates (per 10,000 deliveries) of the outcomes assessed between the intervention and control facilities. The regression coefficients estimated for the interaction terms between intervention status and the post-ESM-UBT package introduction period represent the mean difference in the outcome between intervention and control facilities before and after the introduction of the ESM-UBT package (i.e., the difference-in-difference estimate). The intervention effect was measured by the difference in rate difference per ten thousand points with 95% confidence interval (CI). Adjusted models controlled for facility and month.

P values <0.05 were considered statistically significant. All analyses were performed using Stata version 14.0 (StataCorp, College Station, Texas).

2.8 Ethics approval

Ethical approval was obtained from the Partners Human Research Committee (protocol number 2012P002112; Massachusetts General Hospital, Boston, MA, USA) and the

Mahatma Gandhi Institute of Medical Sciences (No.MGIMS/IEC/OBGY/10/2017). The study was reviewed by the India National Ministry of Health, Division of Maternal and Child Welfare and the India Council on Medical Research. The ESM-UBT device was submitted, reviewed, and approved through the Government of India National Healthcare Innovation Portal.

3 RESULTS

Among the 11 study facilities there were 78,509 deliveries before ESM-UBT package introduction (65,712 in the 9 intervention facilities and 12,797 in the 2 control facilities), 47,211 deliveries during the 7-month ESM-UBT package introduction period (40,045 in the 9 intervention facilities and 7166 in the 2 control facilities), and 88,403 deliveries (73,835 in the 9 intervention facilities and 14,568 in the 2 control facilities) after the ESM-UBT package introduction, for a total of 214,123 deliveries included in the study overall (Figure 1). The total number of UBTs inserted in the 9 intervention facilities was 7 before the ESM-UBT package introduction, 105 during the ESM-UBT package introduction, and 134 after the ESM-UBT package introduction. The corresponding numbers in the 2 control facilities were 1, 0, and 2, respectively.

Table 1 compares the sociodemographic and obstetric characteristics of women delivering in the two months preceding introduction of the ESM-UBT package between intervention and control facilities. The most notable difference was in socioeconomic status with a higher proportion of mothers below poverty line in control facilities than in intervention facilities (67% vs 48%). The rates of cesarean delivery and births assisted by a trainee obstetrician were slightly higher in intervention facilities than in control facilities. There were no major differences between the study groups in mean maternal age,

gestational age at birth and birthweight, parity, plurality of pregnancy, and the rate of low birthweight. The mean number of labor rooms and delivery beds was a little higher in hospitals in the intervention group (2.4 and 11.2, respectively) than in those in the control group (2.0 and 9.0 respectively). Relative to hospitals in the control group, hospitals in the intervention group had higher mean annual number of deliveries during 2014-2016 (6201 and 7280, respectively).

Figure 2 displays the trends of unadjusted rates (per 10,000 deliveries) of the primary composite outcome in the intervention and control facilities. Before the introduction of the ESM-UBT package, the rates of the primary composite outcome were higher in the intervention facilities than in the control facilities. Nevertheless, the rates followed the same trends in both the intervention and control facilities. The rates of the primary composite outcome markedly declined in the intervention facilities during the ESM-UBT package introduction period and maintained relatively stable and lower than those of the control facilities during the 12-month period after ESM-UBT package introduction. The rates of the primary composite outcome fluctuated during the three periods assessed in the control facilities. However, overall, the rates of the primary composite outcome increased slightly during and after the introduction of the ESM-UBT package.

Table 2 provides rates and per 10,000 points changes in the primary and secondary outcomes in both intervention and control facilities, before and after introduction of the ESM-UBT package, as well as unadjusted and adjusted DID estimates with 95% CIs. After introduction of the ESM-UBT package in the intervention facilities, there was a significant decline in the rates of the primary composite outcome (21.0‰ to

11.4‰; difference -9.6, 95% CI -14.0 to -5.4), hysterectomy (6.2‰ to 3.4‰; difference -2.9, 95% CI -5.4 to -0.6), and other invasive procedures (21.9‰ to 10.0‰; difference -11.9, 95% CI -16.3 to -7.8). The change in maternal death rate was not significant (3.5‰ to 3.4‰; difference -0.1, 95% CI -2.2 to 1.9). Changes in the rates of the primary composite outcome, maternal death, hysterectomy, and other invasive procedures were not significant in control facilities. In the adjusted DID analyses, which describe the association between the introduction of the ESM-UBT package and the rates of primary and secondary outcomes, negative DID estimates would indicate a greater decline in the rate of these outcomes in intervention facilities relative to control facilities. There was a significant reduction in the rate of the primary composite outcome in intervention facilities relative to control facilities (adjusted DID estimate -15.0‰ points, 95% CI -23.3 to -6.8; P=0.005). Adjusted DID estimates indicated that, relative to control facilities, there were no significant changes in the rates of maternal death (adjusted DID estimate -0.2‰ points, 95% CI -6.2 to 5.7), hysterectomy (adjusted DID estimate -2.80‰ points, 95% CI -7.2 to 1.7), and other invasive procedures (adjusted DID estimate -7.5‰ points, 95% CI -19.5 to 4.4) in intervention facilities in the post-ESM-UBT package introduction period.

4 DISCUSSION

In this study, we found that the introduction of the ESM-UBT device and package for the management of severe PPH in medical college referral hospitals located in Maharashtra and Madhya Pradesh, India, was associated with a significant 15‰ point decrease in the rate of a composite outcome of PPH-related maternal death and/or invasive procedures for hemorrhage control compared with hospitals in which the ESM-UBT package was not introduced. This represents a 71% decrease in the rate of the composite outcome relative

to the period before the ESM-UBT package introduction. The rates of the individual components of the primary composite outcome decreased in the intervention facilities in the post-ESM-UBT package introduction period; however, we did not detect a significant difference in the rates of change between the intervention and control groups.

Prior studies have reported a significant reduction in the use of invasive procedures for PPH control such as arterial embolization, arterial ligation, and uterine compression sutures among women delivering in French hospitals after introduction of Bakri UBT in protocols for severe PPH management [15-17,25]. Our before-and-after study is the first to report that the introduction of UBT for the management of severe PPH reduces maternal death and/or invasive procedures among women delivering in hospitals in a low middle-income country. The largest contributors to this reduction were artery ligation, uterine compression sutures, and hysterectomy. These findings are in agreement with those from the French studies. Given we only collected data for the 12-month after ESM-UBT package introduction period, it could be too early to detect the impact of this intervention on maternal death.

The Sustainable Development Goal 3 target of a reduction of the global maternal mortality ratio to 70 of every 100,000 live births by 2030 will not be possible without addressing PPH at every level worldwide. While in our study we found that the introduction of a quality and affordable UBT device lowers maternal deaths and emergency operative procedures across referral facilities in India, most women that lose their lives from PPH globally do so outside of referral facilities, where operative interventions are often not available. Additionally, in this time of Pandemic fewer women are able to access higher levels of care for delivery services. While placement of a UBT

in a woman with severe PPH at a referral facility may save her from an emergency operation, intervening in a woman with PPH in similar dire straits outside of a referral facility may directly save her life. Given that ESM-UBT devices have been shown easy to use by all levels of cadres, safe, low-cost, and effective, scale across all settings where women deliver with the assistance of a trained birth attendant should be strongly considered.

The strengths of this study lie in the DID design used, the rigorous methodology used, its large sample size, and the performed sub-analyses to evaluate if intervention had similar/different effect on components of the primary outcome. Moreover, the parallel trend in outcome, the most critical assumption to ensure internal validity of DID models [24], was fulfilled in our study. It requires that in the absence of intervention, the difference between the “intervention” and “control” group is constant over time. Visual inspection of Figure 2 shows the trends of primary composite outcome rates in the intervention and control facilities were parallel before introduction of the ESM-UBT package. Our study is subject to some potential limitations. First, the study design is quasi-experimental, not randomized, allowing for potential differences between groups not otherwise considered. Second, we were unable to control for sociodemographic and obstetric characteristics before introduction of the ESM-UBT package because these data could not be collected for all women. However, we did not expect the distribution of these variables to change markedly within the two study groups, so our DID analysis should have been able to eliminate any unmeasured confounding due to these factors. Third, it is possible that other unmeasured changes in the facilities during the study period, such as turnover in staff, change of policies or facility management, may have influenced study results. We did not

identify any such changes that were major enough to explain the beneficial effect we found. Fourth, we were not able to measure the causes of PPH and the rates of blood transfusion and admission to the intensive care unit before and after introduction of ESM-UBT package.

In conclusion, this large before-and-after DID study showed for the first time that introduction of a low-cost UBT in the management of severe PPH reduces PPH-related maternal death and/or invasive procedures for PPH control in hospitals in low/middle-income countries. Since a low-cost UBT is a highly cost-effective intervention for controlling severe PPH [26], its implementation and scaling up should be considered in low-resource settings around the world.

AUTHOR CONTRIBUTIONS

TFB conceived of the research program, participated and oversaw implementation and data acquisition, and contributed to manuscript writing/editing; PVS was in-country lead, organized all implementation efforts, and contributed to editing; PP had a leading role in data acquisition efforts and contributed to editing; LG provided data management oversight and contributed to editing; AC-A contributed to data analysis, and manuscript writing/editing; and MG helped direct all aspects of implementation, was vital in data acquisition and contributed to editing.

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CONFLICTS OF INTEREST Dr. Burke is president of the Ujenzi Charitable Trust, which holds the US FDA Registration for the ESM-UBT device. However, neither Dr. Burke, nor the Ujenzi Charitable Trust hold any financial interests in the ESM-UBT device. No other authors have a conflict of interest.

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FIGURE LEGENDs

Figure 1. Flowchart

Figure 2. Trends of unadjusted rates (per 10,000 deliveries) of the primary composite outcome[a] in the intervention and control facilities. The introduction period of the ESM-UBT package is shown in gray

FIGURE 1

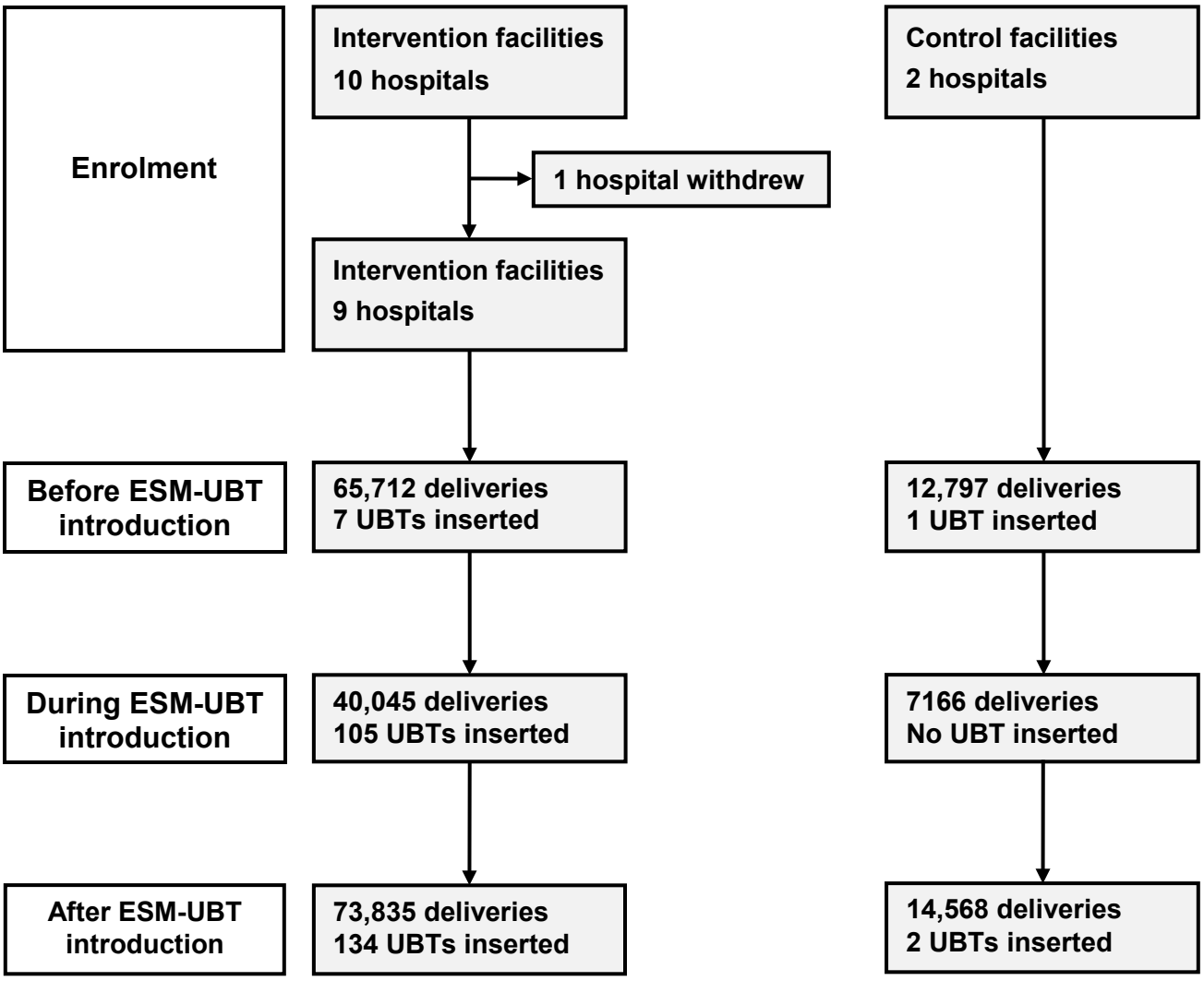
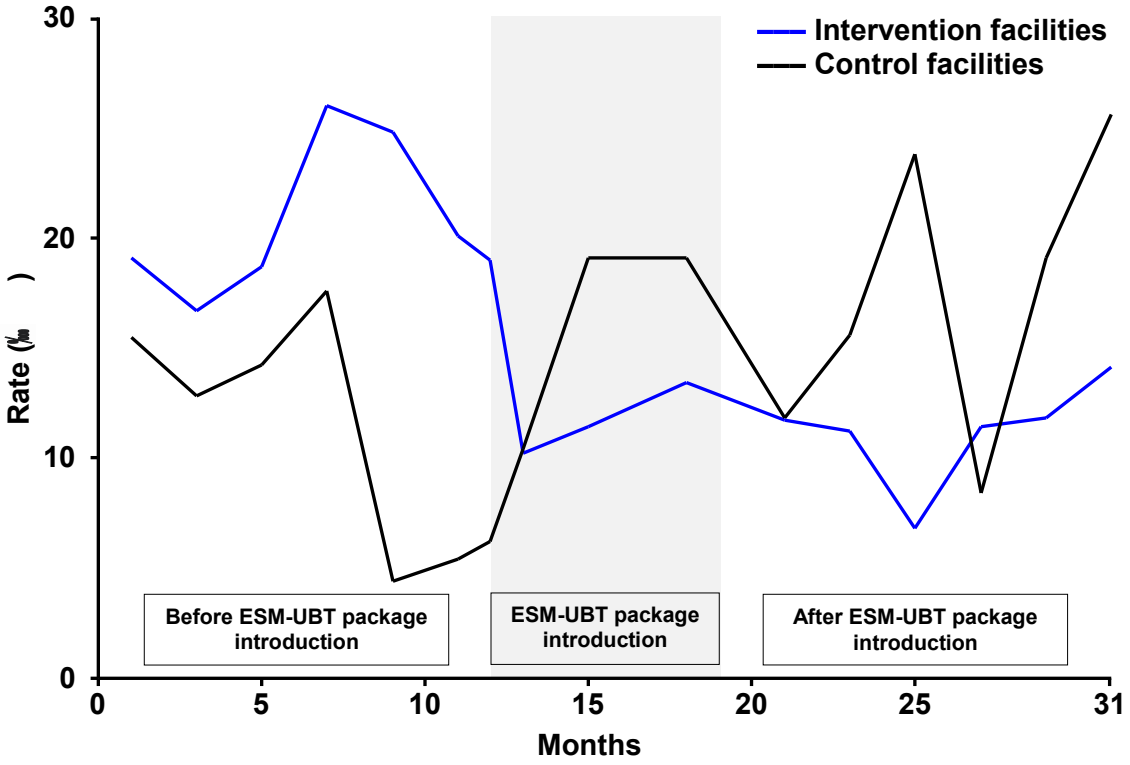


Figure 2



[a]Occurrence of any of the following events: maternal death, hysterectomy, artery ligation, or uterine compression sutures.

TABLE 1. Sociodemographic and obstetric characteristics of women delivering in the two months preceding introduction of the ESM-UBT device and package[a]

Characteristic	Intervention facilities (N=11,250)	Control facilities (N=2234)
Maternal age (years)	25.9 ± 5.4	24.0 ± 3.3
Socioeconomic status		
Women below poverty line	5441 (48.2%)	1507 (67.4%)
Parity		
Nulliparous	4299 (38.2%)	955 (42.7%)
Parous	6951 (61.8%)	1279 (57.3%)
Gestational age (weeks)	37.3 ± 2.5	37.6 ± 2.5
Plurality of pregnancy		
Singleton	11116 (98.8%)	2191 (98.1%)
Twin	132 (1.2%)	43 (1.9%)
Triplet	2 (0.02%)	0 (0%)
Mode of delivery		
Vaginal delivery	7008 (62.3%)	1527 (68.4%)
Cesarean delivery	4242 (37.7%)	707 (31.6%)
Birth attendant		
Consultant Ob/Gyn	2371 (21.1%)	646 (28.9%)
Trainee Ob/Gyn	8649 (76.9%)	1588 (71.1%)
Nurse	230 (2.0%)	0 (0%)
Birthweight (kg)	2.6 ± 0.5	2.6 ± 1.3
Birthweight <2.5 kg	3344/11386 (29.4%)	742/2277 (32.6%)

Abbreviations: ESM-UBT, Every Second Matters for Mothers and Babies-Uterine Balloon Tamponade; Ob/Gyn, obstetrician and gynecologist.
[a]Data are presented as mean ± standard deviation or as number (percentage).

Table 2. Unadjusted and adjusted changes in primary and secondary outcomes associated with ESM-UBT device and package introduction

Outcomes	Intervention facilities			Control facilities			Difference-in-difference Per 10,000 points (95% CI)[b]			
	Before UBT introduction[a] (N=65,712 deliveries)	After UBT introduction[a] (N=73,835 deliveries)	Difference (95% CI) Per 10,000 points	Before UBT introduction[a] (N=12,797 deliveries)	After UBT introduction[a] (N=14,568 deliveries)	Difference (95% CI) Per 10,000 points	Unadjusted analysis	*P* value	Adjusted Analysis[c]	*P* value
Composite[d]	138 (21.0)	84 (11.4)	-9.6 (-14.0 to -5.4)	15 (11.7)	25 (17.2)	5.4 (-3.9 to 14.9)	-15.1 (-21.8 to -8.1)	0.005	-15.0 (-23.3 to -6.8)	0.005
Maternal death	23 (3.5)	25 (3.4)	-0.1 (-2.2 to 1.9)	5 (3.9)	6 (4.1)	0.2 (-5.5 to 5.6)	-0.3 (-3.4 to 2.9)	0.90	-0.2 (-6.2 to 5.7)	0.93
Hysterectomy	41 (6.2)	25 (3.4)	-2.9 (-5.4 to -0.6)	11 (8.6)	13 (8.9)	0.3 (-7.4 to 7.7)	-3.2 (-6.9 to 0.5)	0.18	-2.8 (-7.2 to 1.7)	0.22
Other invasive procedures[e]	144 (21.9)	74 (10.0)	-11.9 (-16.3 to -7.8)	16 (12.5)	12 (8.2)	-4.3 (-12.9 to 3.5)	-7.6 (-17.7 to 2.4)	0.37	-7.5 (-19.5 to 4.4)	0.35

Abbreviations: CI, confidence interval; UBT, uterine balloon tamponade.
Data are presented as number (‰).
[a]The before ESM-UBT package introduction period is defined as January to December 2016, and the after ESM-UBT package introduction period is defined as August 2017 to July 2018. The ESM-UBT package introduction period, defined as January to July 2017, was excluded from comparisons.
[b]Difference-in-difference estimates represent the differential change in the outcome from before ESM-UBT package introduction to after ESM-UBT package introduction periods in intervention facilities relative to control facilities.
[c]Adjusted for facility and month.
[d]Occurrence of any of the following events: maternal death, hysterectomy, artery ligation, or uterine compression sutures.
[e]Artery ligation and/or uterine compression sutures.