ORIGINAL RESEARCH ARTICLE

AOGS
Acta Obstetricia et Gynecologica Scandinavica

Augmentation of labor with oxytocin and its association with delivery outcomes: A large-scale cohort study in 12 public hospitals in Nepal

Helena Litorp[1,2] ⓘ | Avinash K. Sunny[3] ⓘ | Ashish Kc[1,4] ⓘ

[1]Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden

[2]Department of Global Public Health, Karolinska Institutet, Stockholm, Sweden

[3]Golden Community, Lalitpur, Nepal

[4]Society of Public Health Physicians Nepal, Kathmandu, Nepal

Correspondence
Helena Litorp, Department of Women's and Children's Health, Uppsala University, Sjukhusvagen 7, 753 09 Uppsala, Sweden.
Email: helena.litorp@kbh.uu.se

Abstract

Introduction: The use of oxytocin to augment labor is increasing in many low-resource settings; however, little is known about the effects of such use in contexts where resources for intrapartum monitoring are scarce. In this study, we sought to assess the association between augmentation of labor with oxytocin and delivery outcomes.

Material and methods: We conducted a cohort study in 12 public hospitals in Nepal, including all deliveries with and without augmentation of labor with oxytocin, but excluding elective cesarean sections, women with missing information on augmentation of labor, and women without fetal heart rate on admission. Bivariate and multivariate logistic regression calculating the crude and adjusted risk ratio (aRR) with corresponding 95% CI were performed, comparing (a) intrapartum stillbirth and first-day mortality (primary outcome); and (b) intrapartum monitoring, mode of delivery, postpartum hemorrhage, bag-and-mask ventilation of the newborn, Apgar score, and neonatal death before discharge (secondary outcomes) among women with and without oxytocin-augmented labor.

Results: The total cohort consisted of 78 931 women, of whom 28 915 (37%) had labor augmented with oxytocin and 50 016 (63%) did not have labor augmented with oxytocin. Women with augmentation of labor had no increased risk of intrapartum stillbirth and first-day mortality (aRR 1.24, 95% CI 0.65-2.4), but decreased risks of suboptimal partograph use (aRR 0.71, 95% CI 0.68-0.74), suboptimal fetal heart rate monitoring (aRR 0.50, 95% CI 0.48-0.53), and emergency cesarean section (aRR 0.62, 95% CI 0.59-0.66), and increased risks of bag-and-mask ventilation (aRR 2.1, 95% CI 1.8-2.5), Apgar score <7 at 5 minutes (aRR 1.65, 95% CI 1.49-1.86), and neonatal death (aRR 1.93, 95% CI 1.46-2.56).

Conclusions: Although augmentation of labor with oxytocin might be associated with beneficial effects, such as improved monitoring and a decreased risk of cesarean section, its use may lead to an increased risk of adverse perinatal outcomes. We urge

for a cautious use of oxytocin to augment labor in low-resource contexts, and call for evidence-based guidelines on augmentation of labor in low-resource settings.

1 | INTRODUCTION

Augmentation of labor is the process of stimulating the frequency, duration, and intensity of uterine contractions after the onset of labor either by intravenous oxytocin infusion or artificial rupture of membranes, and it is used to treat prolonged labor and potentially avert cesarean section (CS). The World Health Organization (WHO) recommends that oxytocin to augment labor should only be used when there is a valid indication and potential benefit, when the mother is closely monitored in terms of fetal heart rate and uterine contractions, and the mother is not left unattended.[1] However, ambiguous use of oxytocin to augment labor has been reported from both high- and low-resource settings, which has raised concern regarding its potential harmful effects.[2-7]

Although augmentation of labor may be effective to shorten the first and second stages of labor,[8-10] little to no effect has been demonstrated on CS rates.[8-13] During uterine contractions, the maternal spiral arteries are compressed and placental perfusion is strangulated. As oxytocin increases the intensity of uterine contractions and decreases the resting time between contractions,[14] it has been suggested that augmentation of labor with oxytocin increases the risk of fetal asphyxia.[15] Although previous studies have reported increased risk of uterine hyperstimulation[8,11,12] and fetal heart rate anomalies[8,12] during augmentation of labor with oxytocin, several large randomized controlled trials in high-resource contexts have failed to establish an association between augmentation of labor with oxytocin and adverse perinatal outcomes.[8-12] In spite of reports of an increasing use of oxytocin to augment labor in low-resource contexts,[2,3,5,16] no previous studies have, to our knowledge, explored the effects of oxytocin to augment labor in terms of potential benefits and harms in such settings, where intrapartum surveillance is often substandard.[17-19] In this large-scale study in 12 public hospitals in Nepal, we sought to assess the association between augmentation of labor with oxytocin and delivery outcomes, including; (a) intrapartum stillbirth and first-day mortality (primary outcome); and (b) intrapartum monitoring, mode of delivery, postpartum hemorrhage, bag-and-mask ventilation of the newborn, Apgar score, and neonatal death before discharge (secondary outcomes).

2 | MATERIAL AND METHODS

We conducted a cohort study using data collected on all deliveries between 14 April 2017 and 17 October 2018 in 12 public hospitals in

---

> **Key Message**
>
> In this large-scale cohort study in 12 public hospitals in Nepal, augmentation of labor with oxytocin was associated with improved intrapartum monitoring and decreased risk of emergency cesarean section, but an increased risk of adverse perinatal outcomes.

Nepal. The study was based on secondary data from a large stepped-wedged randomized controlled trial conducted to evaluate the effect of a quality improvement intervention on perinatal care in Nepal (NePeriQIP), specifically targeting the quality of neonatal resuscitation of non-breathing newborns.[20,21]

2.1 | Setting

Nepal is a low-income country that, despite a number of social challenges and struggles to build up its midwifery workforce,[22] has made impressive improvements in maternal and child outcomes during the last decades.[23] The under-5 mortality rate has declined from 91/1000 live births in 2001 to 38/1000 live births in 2014,[24] and the maternal mortality ratio has declined from 553/100 000 live births in 2000 to 186/100 000 live births in 2017.[25] Although only 69% of women undergo the recommended number of four or more antenatal care visits, 84% of women attend antenatal care at least once during their pregnancy and 58% of births are assisted by a skilled birth professional.[26] Of the total births in Nepal in 2016, CS accounted for 9%.[26]

Hospitals included in the current study had between 1000 and 11 000 deliveries per year, were government-funded referral centers for maternal and newborn care, and had similar resources to provide comprehensive emergency obstetric care. With a total number of deliveries of about 100 000 in the 12 hospitals, the NePeriQIP data collection accounted for almost 29% of the total health facility deliveries in Nepal during the study period. Despite most of them being in the flatlands, the hospitals were different in terms of service coverage and diverse in relation to ethnicity, language, and religion. Mid-Western Regional and Seti Zonal Hospitals were located in the most disadvantaged regions in Nepal in terms of literacy, access to services, and life expectancy. Bheri Zonal Hospital in Nepalgunj had a large number of minority Muslim communities, whereas in Bharatpur, some of the

most fringe communities came for maternal and sick newborn services. The hospitals' labor units were led by skilled birth attendants, fetal heart rate monitoring was performed using Pinard fetoscope or hand-held Doppler, and the guidelines on fetal heart rate monitoring at the hospitals were in adherence with WHO guidelines (ie, to be performed for 60 seconds every 15-30 minutes in the first stage of labor and for 60 seconds every five minutes in the second stage of labor).[27] If fetal heart rates are outside the normal range (110-160 beats per minute), the guidelines stipulate monitoring should be extended to cover three consecutive uterine contractions. Oxytocin was readily available for induction or augmentation of labor at all the hospitals, as it is listed as an emergency drug under the Free Essential Drug List in Nepal,[28,29] and was administered either with a motor-driven pump or an infusion drip.[30] For augmentation of labor, national clinical guidelines recommend that the initial oxytocin infusion rate is set at 1-4 milliunits/minute (2-8 drops/minute) and that the infusion rate is gradually increased at intervals of at least 20 minutes until a contraction pattern of three to four contractions per 10 minutes is established.[30] With either method of infusion, the guidelines stipulate that frequency, strength, and duration of uterine contractions, as well as the fetal heart rate, be carefully monitored. However, the guidelines provide no recommendation to increase fetal heart rate monitoring if the woman has labor augmented with oxytocin.[30] No pain relief during labor was offered in any of the hospitals.

2.2 | Participants

We included all women consenting to participate in the NePeriQIP study[20,21] who were admitted with recorded fetal heart rate and for whom oxytocin to augment labor (yes vs no) was registered in the data collection form. Women with missing data on oxytocin use, women who had absent or no recording of fetal heart rate on admission, and women who underwent elective CS were excluded from the analyses.

2.3 | Data collection and management

As part of the NePeriQIP data collection, a data surveillance system was established in all the hospitals to collect data on deliveries.[20,21] For obstetric variables, data were extracted from the Maternity Registers and medical records by trained data collectors using a data retrieval form. For sociodemographic variables, data were collected by the same data collectors through semi-structured interviews with mothers before discharge. Completed forms were then assessed by a data coordinator at the hospital for completeness and accuracy before being entered digitally into the data base by the data entry and management team. For entering and cleaning data, we used the Census and Survey Processing System.

2.4 | Variables and outcomes

The exposure variable was oxytocin to augment labor (yes vs no) as registered in the data collection form. The primary outcome variable was intrapartum-related mortality defined as intrapartum stillbirth (no breathing 10 minutes after delivery) or neonatal death within the first 24 hours of life (yes vs no). Secondary outcomes included suboptimal partograph use (partograph completely or partially filled vs not filled), suboptimal fetal heart rate monitoring (fetal heart rate monitoring performed according to protocol,[27] or fetal heart rate monitored more than once during labor vs fetal heart rate monitored only once during labor or not at all), bag-and-mask ventilation of the infant after birth (yes vs no), Apgar score <7 at 5 minutes (yes vs no), emergency CS (yes vs no), instrumental delivery (yes vs no), postpartum hemorrhage (yes vs no), and neonatal death before discharge (yes vs no). We chose to include intrapartum monitoring, that is partograph use and surveillance of fetal heart rate, as outcome variables because we wanted to assess whether women who had labor augmented with oxytocin had been properly monitored given the potential increased risk of adverse obstetric outcomes associated with augmentation of labor.[8,11,12,15]

2.5 | Statistical analyses

The cleaned data were exported to Statistical Package for Social Sciences (SPSS) version 25 (IBM Corp.) for analysis. We used descriptive statistics to compare the socio-economic and obstetric characteristics of women with and without augmentation of labor with oxytocin, and applied the Pearson chi-squared test for categorical variables and the independent t test for continuous
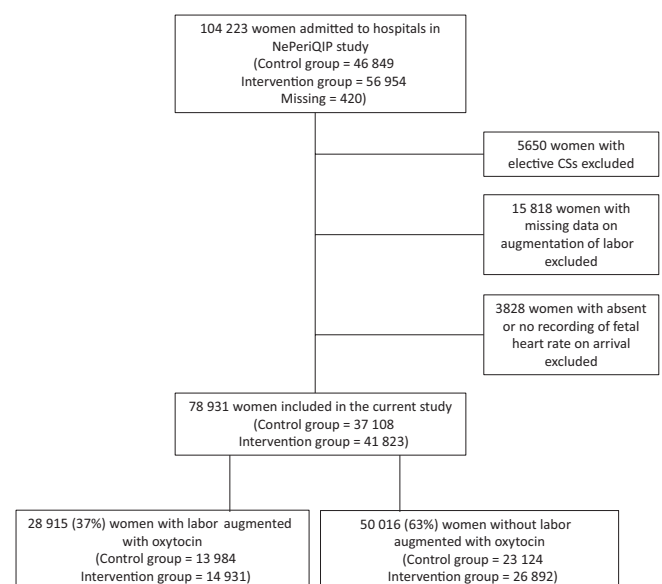
FIGURE 1 Flow chart of inclusion of participants. NePeriQIP, Nepal Perinatal Quality Improvement Project; CS, cesarean section

TABLE 1 Characteristics of women with and without augmentation of labor with oxytocin in 12 public hospitals in Nepal. Includes only women admitted with fetal heart rate

	Oxytocin to augment labor				
	Yes N = 28 915		No N = 50 016		P value[a]
Characteristic	N	%	N	%	
Maternal age (SD)	23.6 (4.1)		24.0 (4.3)		<.001
Ethnicity					
Advantaged group	14 410	50%	25 540	51%	.001
Disadvantaged group	14 505	50%	24 476	49%	
Missing	0	0%	0	0%	
Education level					
Illiterate	944	3.2%	1888	3.8%	<.001
Literate	2076	7.1%	3855	7.7%	
Basic education	3650	13%	6526	13%	
Secondary	14 896	51%	22 656	44%	
Higher	1637	5.6%	3281	6.2%	
Missing	5711	20%	11 810	24%	
Parity					
Para 0	15 573	54%	21 903	44%	<.001
Para 1	8859	31%	17 912	36%	
Para ≥2	4480	16%	10 195	20%	
Missing	3	0%	6	0%	
Gestational age					
22-27 weeks	268	0.9%	1831	3.7%	<.001
28-32 weeks	397	1.4%	1619	3.3%	
33-36 weeks	3317	11%	6484	13%	
37-41 weeks	21 909	76%	35 342	71%	
42-45 weeks	947	3.3%	1415	2.8%	
Missing	2133	7.3%	3325	6.6%	
Inclusion of study participants across hospitals					
Western Regional Hospital	3180	11%	5831	12%	<.001
Midwestern Regional Hospital	1537	5.3%	3791	7.6%	
Bardiya District Hospital	36	0.1%	1063	2.1%	
Bharatpur Zonal Hospital	6856	24%	9676	19%	
Seti Zonal Hospital	3348	12%	6983	14%	
Nuwakot District Hospital	145	0.5%	1156	2.3%	
Koshi Zonal Hospital	3214	11%	5376	11%	
Rapti Subregional Hospital	1651	5.7%	3743	7.5%	
Prithiva Chandra Hospital	118	0.4%	651	1.3%	
Lumbini Zonal Hospital	4912	17%	5781	12%	
Bheri Zonal Hospital	3309	11%	4181	8.4%	
Pyuthan District Hospital	609	2.1%	1784	3.6%	
Fetal heart rate at admission					
Normal	28 863	99.8%	49 877	99.7%	.007
Abnormal	52	0.2%	139	0.3%	

(Continues)

TABLE 1 (Continued)

| Characteristic | Oxytocin to augment labor | | | | | P value[a] |
| | Yes N = 28 915 | | No N = 50 016 | | | |
	N	%	N	%		
Stage of labor at admission						
Not in labor	4433	15%	9528	19%		<.001
Latent phase of labor	16 055	56%	23 020	46%		
First stage of labor	7659	27%	14 593	29%		
Second stage of labor	766	2.6%	2755	5.5%		
Missing	2	0%	120	0.20%		
Induction of labor						
No	16 044	56%	31 758	64%		<.001
With prostaglandins	6146	21%	7604	15%		
With amniotomy	662	2.3%	1204	2.4%		
With oxytocin	3940	14%	3175	6.3%		
Missing	2123	7.3%	6275	13%		
Complications during pregnancy or labor						
Multiple pregnancy	256	0.9%	537	1.1%		.011
Premature rupture of membranes	127	0.3%	84	0.3%		<.001
Severe anemia	33	0.1%	123	0.2%		<.001
Chorioamnionitis	5	0%	5	0%		<.001
Hypertensive disorders	71	0.2%	148	0.3%		<.001
Antepartum/intrapartum hemorrhage	6	0%	56	0.1%		<.001
Birthweight						
<2500 g	3743	13%	9491	19%		<.001
>2500 g	23 095	80%	37 200	74%		
Missing	2076	7.2%	3325	6.6%		
Sex of the baby						
Male	15 607	54%	26 969	54%		.88
Female	13 308	46%	23 047	46%		
Missing	0	0%	0	0%		

[a]Pearson chi-squared test for categorical variables and the independent *t* test for continuous variables.

variables to determine statistically significant differences between the groups. We considered a *P*-value <.05 as statistically significant. We further compared primary and secondary outcomes between exposed and unexposed using the Pearson chi-squared test and bivariate logistic regression, and used multivariate logistic regression to adjust the estimate for variables previously reported to be confounders for the outcome under investigation, for example maternal age, ethnicity, educational level, gestational age, complications during pregnancy, mode of delivery, birthweight etc.[31,32] We presented the results as crude and adjusted risk ratios (aRR) including 95% CI. Results on outcome measures were also stratified as per hospital level (high-, medium-, and low-volume) as defined by the NePeriQIP randomization process,[21] in order to explore the generalizability of findings across hospital settings. Missing data were excluded from the analyses.

2.6 | Ethical approval

Written informed consent was obtained from the mothers before inclusion in the NePeriQIP study and confidentiality was guaranteed. The study was approved by the Ethical Review Board of Nepal Health Research Council (reference number 26-2017) on 16 March 2017. For the current study, the researchers worked with a database coded as per the patient's identity.

3 | RESULTS

There were 104 223 women admitted to the hospitals included in the NePeriQIP study during the study period. After exclusion of women with elective CS (5650, 5.4%), missing data on oxytocin to

augment labor (15 814, 15%), and absent or no recording of fetal heart rate on arrival (3828, 3.7%), the total cohort consisted of 78 931 women of which 28 915 (37%) had labor augmented with oxytocin and 50 016 (63%) did not have labor augmented with oxytocin (Figure 1). Women who had labor augmented with oxytocin were more often younger, more often from a disadvantaged ethnic group, had a higher level of education, were more often giving birth to their first child, had higher gestational age, were more often admitted to the high-volume hospitals, were more often induced with prostaglandins or oxytocin, were less likely to have experienced complications during pregnancy or delivery, and more often gave birth to a normal-weight infant (Table 1). The overall proportion of women who had labor augmented with oxytocin was higher in high-volume than in medium- and low-volume hospitals (Table 2).

Details of delivery outcomes and intrapartum monitoring among women with and without augmentation of labor with oxytocin are presented in Table 3. After multivariate regression analyses accounting for socio-economic and obstetric characteristics, including events during pregnancy and delivery (Table 4), we found that women with augmentation of labor had no increased risk of intrapartum stillbirth and first-day mortality (aRR 1.24, 95% CI 0.65-2.4), but a lower risk of suboptimal partograph use (aRR 0.71, 95% CI 0.68-0.74), a lower risk of suboptimal fetal heart rate monitoring (aRR 0.50, 95% CI 0.48-0.53), and a lower risk of CS (aRR 0.62, 95% CI 0.59-0.66). On the other hand, they had a higher risk of instrumental delivery (aRR 2.60, 95% CI 2.40-2.80), a higher risk of bag-and-mask ventilation of the newborn (aRR 2.10, 95% CI 1.80-2.50), a higher risk of Apgar score <7 at 5 minutes (aRR 1.65, 95% CI 1.49-1.86), and a higher risk of neonatal death before discharge (aRR 1.93, 95% CI 1.46-2.56). Overall, results were similar regardless of hospital level (high-, medium-, and low-volume), except for results in low-volume hospitals related to suboptimal partograph use, emergency CS, postpartum hemorrhage, bag-and-mask ventilation, Apgar score <7 at 5 minutes, and neonatal death before discharge, of which some failed to reach statistical significance in the multivariate analyses (see Supplementary material, Tables S1-S3).

4 | DISCUSSION

In this large-scale cohort study exploring the association between oxytocin to augment labor and delivery outcomes in 12 public hospitals in Nepal, we found no difference in intrapartum stillbirth and first-day mortality between women with and without augmentation of labor with oxytocin. On the other hand, after multivariate analyses accounting for socio-economic and obstetric characteristics and events, we found that women who had labor augmented with oxytocin had a lower risk of suboptimal intrapartum monitoring and CS, but a higher risk of instrumental delivery, bag-and-mask ventilation, Apgar score <7 at 5 minutes, and neonatal death before discharge.

The main strength of our study was the large sample size collected in 12 public hospitals distributed over the country and in

TABLE 2 Proportion of women receiving oxytocin to augment labor in high-, medium-, and low-volume hospitals

Hospital	Number and percentage of deliveries with labor augmented with oxytocin N = 28 915	
	N	%
High-volume hospitals	18 162	41%
Bharatpur Zonal Hospital	6856	42%
Lumbini Zonal Hospital	4912	46%
Koshi Zonal Hospital	3214	37%
Western Regional Hospital	3180	35%
Medium-volume hospitals	9845	35%
Seti Zonal Hospital	3348	32%
Bheri Zonal Hospital	3309	44%
Rapti Sub-regional Hospital	1651	31%
Mid-Western Regional Hospital	1537	29%
Low-volume hospitals	908	16%
Pyuthan District Hospital	609	25%
Prithivi Chandra Hospital	118	15%
Nuwakot District Hospital	145	11%
Bardiya District Hospital	36	3.3%

total accounting for almost a third of Nepal's facility births during the study period, which make our results generalizable and applicable to many other health-care settings in low-income countries. The data collection teams were organized to secure data quality data, and repeated validity checks were undertaken. Nevertheless, missing data were a problem in some variables. For example, more women than reported most likely suffered from obstetric complications such as hypertensive disorders. It is, however, difficult to speculate on whether either of the groups under comparison had a larger underreporting of complications than the other, and how this might have affected the results. The current study was based on secondary data from the NePeriQIP study,[20] hence, there is a risk that the study was under-powered to detect an association between augmentation of labor and our primary outcome. The results on secondary outcomes, such as intrapartum monitoring, mode of delivery, and adverse perinatal outcomes do, however, add valuable evidence to the current literature, hence the study still serves its purpose. Although all hospitals were referral centers with similar resources to provide emergency obstetric care, the use of oxytocin to augment labor differed across hospital levels, with higher use of augmentation of labor in high-volume hospitals. To account for this, we stratified results by hospital level, which produced similar results as for the total cohort. Lastly, another limitation of our study was that it provided no information on the clinical events that proceeded the decision to augment labor with oxytocin, whether oxytocin was used according to guidelines,[30] whether there was a problem with uterine hyperstimulation, or what dosage of oxytocin was used;

TABLE 3 Delivery outcomes and intrapartum monitoring among women with and without augmentation of labor with oxytocin in 12 public hospitals in Nepal. Includes only women admitted with fetal heart rate

Delivery outcomes and intrapartum monitoring	Oxytocin to augment labor				
	Yes N = 28 915		No N = 50 016		P-value[a]
	N	%	N	%	
Primary outcome					
Intrapartum stillbirth and first day mortality among newborns					
Yes	64	0.2%	130	0.3%	.28
No	28 851	99.8%	49 886	99.7%	
Secondary outcomes					
Progress of labor recorded in partograph					
Yes, completely filled	10 092	35%	12 968	26%	<.001
Yes, partially filled	8423	29%	14 817	30%	
No	10 400	36%	22 231	44%	
Fetal heart rate monitoring performed during labor					
Yes, as per protocol	15 069	52%	20 881	42%	<.001
Yes, sporadically (>once)	8739	30%	12 798	26%	
Yes, only once	4350	15%	11 868	24%	
No	757	2.6%	4469	8.9%	
Mode of delivery					
Spontaneous vaginal	23 338	81%	38 708	77%	<.001
Instrumental vaginal	1891	6.5%	1049	2.1%	
Emergency cesarean section	3561	12%	9688	19%	
Assisted breech delivery	111	0.4%	297	0.6%	
Postpartum hemorrhage					
Yes	67	0.2%	155	0.3%	.046
No	28 848	100%	49 861	100%	
Bag-and-mask ventilation					
Yes	439	1.6%	346	0.7%	<.001
No	27 637	96%	48 261	99%	
Apgar score					
<7 at 5 minutes	1136	3.9%	1553	3.1%	<.001
>7 at 5 minutes	27 773	96%	48 447	97%	
Neonatal death					
Dead at discharge	234	0.8%	422	0.8%	.60
Alive at discharge	28 590	99%	49 419	99%	

[a]Pearson chi-squared test.

nor did we have data on important obstetric complications such as anal sphincter injury[33,34] and uterine rupture,[35] which might have been more common in the group of women who had labor augmented with oxytocin.

In line with previous publications on the effect of augmentation of labor with oxytocin, which have reported small or statistically non-significant associations between augmentation of labor and adverse perinatal outcomes,[8-12] our large-scale study found no increased risk of intrapartum stillbirth and first-day mortality. On the other hand, we found an increased risk of neonatal resuscitation, low

Apgar score, and neonatal death before discharge among women who had labor augmented with oxytocin, which suggests that oxytocin to augment labor might have harmful effects when used in low-resource contexts. Although our conflicting results regarding perinatal outcomes might be due to a type II bias, as described above, Bakker et al, who analyzed low pH in the umbilical cord artery at birth among women who had labor augmented with oxytocin, suggest the association between augmentation of labor and fetal acidosis is most likely the result of increased uterine activity and not of the oxytocin itself.[35] This is also in line with a UK case-control

TABLE 4 Bivariate and multivariate logistic regression analyses of delivery outcomes and intrapartum monitoring among women with and without augmentation of labor with oxytocin in 12 public hospitals in Nepal. Includes only women admitted with fetal heart rate

| Delivery outcomes and intrapartum monitoring | Oxytocin to augment labor | | | | |
	No	Yes Crude RR	95% CI	Yes Adjusted RR	95% CI
Primary outcome					
Intrapartum stillbirth and first day mortality	1.0	0.85	0.63-1.15	1.24[a]	0.65-2.40
Secondary outcomes					
Suboptimal partograph use	1.0	0.70	0.69-0.72	0.71[b]	0.68-0.74
Suboptimal fetal heart rate monitoring	1.0	0.44	0.43-0.46	0.50[c]	0.48-0.53
Emergency cesarean section	1.0	0.57	0.55-0.60	0.62[d]	0.59-0.66
Instrumental delivery	1.0	2.70	2.50-2.90	2.60[d]	2.40-2.80
Postpartum hemorrhage	1.0	0.75	0.56-0.99	0.80[e]	0.55-1.20
Bag-and-mask ventilation	1.0	2.20	1.90-2.60	2.10[a]	1.80-2.50
Apgar score < 7 at 5 minutes	1.0	1.30	1.20-1.40	1.65[a]	1.49-1.86
Neonatal death before discharge	1.0	0.96	0.82-1.10	1.93[a]	1.46-2.56

[a]Adjusted for maternal age, ethnicity, educational level, parity, gestational age, fetal heart rate at admission (normal vs absent), induction of labor, complications during pregnancy or labor, birthweight, suboptimal partograph use, suboptimal fetal heart rate monitoring, and mode of delivery.

[b]Adjusted for maternal age, ethnicity, educational level, parity, gestational age, fetal heart rate at admission (normal vs absent), induction of labor, complications during pregnancy or labor, birthweight, and suboptimal fetal heart rate monitoring.

[c]Adjusted for maternal age, ethnicity, educational level, parity, gestational age, fetal heart rate at admission (normal vs absent), induction of labor, complications during pregnancy or labor, birthweight, and suboptimal partograph use.

[d]Adjusted for maternal age, ethnicity, educational level, parity, gestational age, fetal heart rate at admission (normal vs absent), induction of labor, complications during pregnancy or labor, birthweight, suboptimal partograph use, and suboptimal fetal heart rate monitoring.

[e]Adjusted for maternal age, ethnicity, educational level, parity, gestational age, fetal heart rate at admission (normal vs absent), induction of labor, complications during pregnancy or labor, birthweight, and mode of delivery.

study, which found that oxytocin did not increase base-line fetal heart rate or short-term variability when given according to a routine regimen.[14] As our study provides no information on whether indications of augmentation of labor with oxytocin were valid, to what extent clinical guidelines were adhered to, and if study participants were subjected to uterine hyperstimulation, we recommend that future studies from low-resource settings should focus on health-care professionals' monitoring of uterine contractions during augmentation of labor with oxytocin, the role of hyperstimulation in relation to adverse perinatal outcomes, and evaluation of clinical guidelines for labor augmentation. Such evidence will be imperative to ensure a cautious use of oxytocin to augment labor.[3,5,36] The lack of statistically significant associations between augmentation of labor and adverse perinatal outcomes found in low-volume hospitals was most likely due to a smaller sample size in these hospitals.

As emphasized by the WHO,[1] augmentation of labor should only be performed if the mother is properly monitored. A positive effect of augmentation of labor with oxytocin in our setting was that it seemed to have triggered an increased commitment among health-care professionals, resulting in better partograph use and fetal heart rate monitoring than among those women who did not have labor augmented with oxytocin. The quality of intrapartum monitoring was, however, far from meeting the WHO standards, as reported from other low-resource settings,[17-19] and the majority of women only had fetal heart rate monitoring performed sporadically or once. In contrast to previous studies that have reported a limited effect of augmentation of labor with oxytocin on CS rates,[8-13] women in our study who received augmentation of labor with oxytocin had a significantly lower risk of CS than women who received no augmentation of labor, even after adjusting for socio-economic and obstetric characteristics and events. These results are in line with an intervention study in Zanzibar, where the CS rate increased as the total oxytocin use to argument labor dropped from 22% to 12%, although the authors do not interpret the oxytocin drop to have had a casual effect on the CS rate.[3] Given the global concern of CS overuse,[31,37-39] our results highlight that augmentation of labor, as part of active management of labor, has a potential to avert unnecessary operations.

5 | CONCLUSION

Although augmentation of labor with oxytocin in low-resource settings might be associated with beneficial effects such as improved partograph use, improved fetal heart rate monitoring, and a lower risk of CS, its use may also lead to an increased risk of adverse perinatal outcomes such as bag-and-mask ventilation, low Apgar score, and neonatal death. We urge for a cautious use of oxytocin to augment labor in low-resource contexts, and call for future studies to evaluate and suggest guidelines for augmentation of labor suitable for low-resource settings, to ensure optimal outcomes for mothers and newborns.

CONFLICT OF INTEREST
None.

ORCID
Helena Litorp https://orcid.org/0000-0001-7164-598X
Avinash K. Sunny https://orcid.org/0000-0002-9965-181X
Ashish Kc https://orcid.org/0000-0002-0541-4486

REFERENCES

1. World Health Organization. *WHO recommendations for augmentation of labour*. Geneva: World Health Organization; 2014. ISBN 978 92 4 150736 3.
2. Oladapo OT, Souza JP, Fawole B, et al. Progression of the first stage of spontaneous labour: a prospective cohort study in two sub-Saharan African countries. *PLoS Medicine*. 2018;15:e1002492.
3. Maaløe N, Housseine N, Meguid T, et al. Effect of locally tailored labour management guidelines on intrahospital stillbirths and birth asphyxia at the referral hospital of Zanzibar: a quasi-experimental pre-post study (The PartoMa study). *BJOG*. 2018;125:235-245.
4. Bernitz S, Oian P, Rolland R, Sandvik L, Blix E. Oxytocin and dystocia as risk factors for adverse birth outcomes: a cohort of low-risk nulliparous women. *Midwifery*. 2014;30:364-370.
5. Kalisa R, Rulisa S, van den Akker T, van Roosmalen J. Is prolonged labor managed adequately in rural Rwandan hospitals? *Afr J Reprod Health*. 2019;23:27-34.
6. Le Ray C, Fraser W, Rozenberg P, et al. Duration of passive and active phases of the second stage of labour and risk of severe postpartum haemorrhage in low-risk nulliparous women. *Eur J Obstet Gynecol Reprod Biol*. 2011;158:167-172.
7. Nyfløt LT, Sandven I, Stray-Pedersen B, et al. Risk factors for severe postpartum hemorrhage: a case-control study. *BMC Pregnancy Childbirth*. 2017;17(1):17.
8. Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev*. 2011;7:CD007123.
9. Wei S, Wo BL, Qi H-P, et al. Amniotomy and early oxytocin for prevention of, or therapy for, delay in first stage spontaneous labour compared with routine care. *Cochrane Database Syst Rev*. 2013;8:CD006794.
10. Dencker A, Berg M, Bergqvist L, Ladfors L, Thorsen LS, Lilja H. Early versus delayed oxytocin augmentation in nulliparous women with prolonged labour—a randomised controlled trial. *BJOG*. 2009;116(4):530-536.
11. Budden A, Chen LJ, Henry A. High-dose versus low-dose oxytocin infusion regimens for induction of labour at term. *Cochrane Database Syst Rev*. 2014;10:CD009701.
12. Bor P, Ledertoug S, Boie S, Knoblauch NO, Stornes I. Continuation versus discontinuation of oxytocin infusion during the active phase of labour: a randomised controlled trial. *BJOG*. 2016;123:129-135.
13. Brown HC, Paranjothy S, Dowswell T, Thomas J. Package of care for active management in labour for reducing caesarean section rates in low-risk women. *Cochrane Database Syst Rev*. 2013;9:CD004907.
14. Aye CY, Redman CW, Georgieva A. The effect of augmentation of labour with syntocinon on the fetal CTG using objective computerised analysis: a nested case-control study. *Eur J Obstet Gynecol Reprod Biol*. 2014;176:112-118.
15. Jonsson M, Norden-Lindeberg S, Ostlund I, Hanson U. Acidemia at birth, related to obstetric characteristics and to oxytocin use, during the last two hours of labor. *Acta Obstet Gynecol Scand*. 2008;87:745-750.
16. Mukamurigo J, Dencker A, Nyirazinyoye L, Ntaganira J, Berg M. Quality of intrapartum care for healthy women with spontaneous onset of labour in Rwanda: A health facility-based, cross-sectional study. *Sex Reprod Healthc*. 2019;19:78-83.
17. Mgaya AH, Litorp H, Kidanto HL, Nystrom L, Essen B. Criteria-based audit to improve quality of care of foetal distress: standardising obstetric care at a national referral hospital in a low resource setting, Tanzania. *BMC Pregnancy Childbirth*. 2016;16:343.
18. Kc A, Wrammert J, Clark RB, Ewald U, Malqvist M. Inadequate fetal heart rate monitoring and poor use of partogram associated with intrapartum stillbirth: a case-referent study in Nepal. *BMC Pregnancy Childbirth*. 2016;16:233.
19. Kruk ME, Leslie HH, Verguet S, Mbaruku GM, Adanu RMK, Langer A. Quality of basic maternal care functions in health facilities of five African countries: an analysis of national health system surveys. *Lancet Glob Health*. 2016;4:e845-e855.
20. Kc A, Ewald U, Basnet O, et al. Effect of a scaled-up neonatal resuscitation quality improvement package on intrapartum-related mortality in Nepal: a stepped-wedge cluster randomized controlled trial. *PLoS Medicine*. 2019;16(9):e1002900.
21. Kc A, Bergström A, Chaulagain D, et al. Scaling up quality improvement intervention for perinatal care in Nepal (NePeriQIP); study protocol of a cluster randomised trial. *BMJ Glob Health*. 2017;2(3):e000497.
22. Bogren MU, van Teijlingen E, Berg M. Where midwives are not yet recognised: a feasibility study of professional midwives in Nepal. *Midwifery*. 2013;29(10):1103-1109.
23. Barker CE, Bird CE, Pradhan A, Shakya G. Support to the Safe Motherhood Programme in Nepal: an integrated approach. *Reprod Health Matters*. 2007;15(30):81-90.
24. Ministry of Health. *Nepal´s Every Newborn Action Plan*. Kathmandu: Government of Nepal; 2016.
25. World Health Organization. *Trends in maternal mortality 2000 to 2017: estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division*. Geneva: World Health Organization; 2019. ISBN 978-92-4-151648-8.
26. Ministry of Health. *Nepal Demographic and Health survey*. Kathmandu: Government of Nepal; 2016.
27. World Health Organization. *WHO recommendation on intermittent fetal heart rate auscultation during labour*. Geneva: World Health Organization; 2018.
28. Ministry of Health. *National List of Essential Medicines*. Kathmandu: Governemnt of Nepal; 2009.

29. Poudyal AK, Shrestha B, Onta SR. Availability and use of oxytocin in health facilities in Nepal. *J Inst Med*. 2014;36(1):3-8.

30. Ministry of Health. *Reproductive Health Clinical Protocol for Medical Officers*. Kathmandu: Government of Nepal; 2007.

31. Sobhy S, Arroyo-Manzano D, Murugesu N, et al. Maternal and perinatal mortality and complications associated with caesarean section in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet*. 2019;393:1973-1982.

32. Altman MR, Lydon-Rochelle MT. Prolonged second stage of labor and risk of adverse maternal and perinatal outcomes: a systematic review. *Birth*. 2006;33:315-322.

33. Rygh AB, Skjeldestad FE, Korner H, Eggebo TM. Assessing the association of oxytocin augmentation with obstetric anal sphincter injury in nulliparous women: a population-based, case-control study. *BMJ Open*. 2014;4:e004592.

34. Tunestveit JW, Baghestan E, Natvig GK, Eide GE, Nilsen ABV. Factors associated with obstetric anal sphincter injuries in midwife-led birth: a cross sectional study. *Midwifery*. 2018;62:264-272.

35. Bakker PC, Kurver PH, Kuik DJ, Van Geijn HP. Elevated uterine activity increases the risk of fetal acidosis at birth. *Am J Obstet Gynecol*. 2007;196(4):313.e1-313.e6.

36. Gurung R, Jha AK, Pyakurel S, et al. Scaling Up Safer Birth Bundle Through Quality Improvement in Nepal (SUSTAIN)-a stepped wedge cluster randomized controlled trial in public hospitals. *Implement Sci*. 2019;14(1):65.

37. Betran AP, Ye J, Moller AB, Zhang J, Gulmezoglu AM, Torloni MR. The increasing trend in caesarean section rates: Global, Regional and National Estimates: 1990–2014. *PLoS One*. 2016;11:e0148343.

38. Boatin AA, Schlotheuber A, Betran AP, et al. Within country inequalities in caesarean section rates: observational study of 72 low and middle income countries. *BMJ*. 2018;360:k55.

39. Betrán AP, Temmerman M, Kingdon C, et al. Interventions to reduce unnecessary caesarean sections in healthy women and babies. *Lancet*. 2018;392:1358-1368.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Litorp H, Sunny AK, Kc A. Augmentation of labor with oxytocin and its association with delivery outcomes: A large-scale cohort study in 12 public hospitals in Nepal. *Acta Obstet Gynecol Scand*. 2021;100:684–693. https://doi.org/10.1111/aogs.13919