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CLINICAL ARTICLE

Maternal and neonatal outcomes of hospital vaginal deliveries in Tibet

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Abstract

Introduction: To determine the outcomes of vaginal deliveries in three study hospitals in Lhasa, Tibet Autonomous Region (TAR), People's Republic of China (PRC), at high altitude (3650 m). *Methods:* Prospective observational study of 1121 vaginal deliveries. *Results:* Pre-eclampsia/gestational hypertension (PE/GH) was the most common maternal complication 18.9% ($n=212$), followed by postpartum hemorrhage (blood loss ≥ 500 ml) 13.4%. There were no maternal deaths. Neonatal complications included: low birth weight (10.2%), small for gestational age (13.7%), pre-term delivery (4.1%) and low Apgar (3.7%). There were 11 stillbirths (9.8/1000 live births) and 19 early neonatal deaths (17/1000 live births). *Conclusion:* This is the largest study of maternal and newborn outcomes in Tibet. It provides information on the outcomes of institutional vaginal births among women delivering infants at high altitude. There was a higher incidence of PE/GH and low birth weight; rates of PPH were not increased compared to those at lower altitudes.

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1. Introduction

Reported maternal mortality ratios (MMR) and neonatal mortality rates (NMR) remain higher in the Tibet Autonomous Region (TAR) than in the remainder of the People's Republic of China [1–3]. Postpartum hemorrhage (PPH) and pre-eclampsia (PE) are the leading causes of maternal deaths in China and the TAR [4]; while birth asphyxia is a leading cause of neonatal mortality [5].

Approximately 80% of people in the TAR live at high altitude, defined as greater than 2500 m or 8200 ft [6]. Living at high altitude during pregnancy has been associated with an increased incidence of pre-eclampsia (PE), gestational hypertension (GH), low birth weight newborns [7–9] and pre-term deliveries [10]. A study comparing pre-eclampsia rates between women living at low and high altitude in Colorado found that 16% of women delivering at 3100 m had pre-eclampsia compared to only 3% of women delivering at 1260 m [8].

Previous studies in Colorado and South America have found that altitude has a negative effect on birth weight, independent of other risk factors [9,11–14]. Jensen and Moore [11] reported on birth weights in the Colorado mountains at altitudes between 915 m to 3350 m; they found that birth weight decreases by 100 g for every 1000-meter elevation increase. Although mean birth weight decreases as altitude increases, there is no evidence that increasing altitude is associated with a decrease in gestational age [8,9,14–16].

This paper reports on an observational study conducted by the Global Network for Women's and Children's Health Research, a collaboration between U.S. investigators (University of Utah and the University of California, San Francisco (UCSF)), Tibetan investigators, RTI International, and the National Institute of Child Health and Human Development program scientists. This article describes maternal and neonatal outcomes of 1121 consecutive vaginal deliveries in Lhasa, Tibet at an altitude of 3650 m.

2. Methods

2.1. Study sites and participants

The observations were conducted between January 2004 and May 2005 at three maternity hospitals, the Mentzikhang Traditional Tibetan Medicine and Astrology Hospital (Mentzikhang Hospital), Lhasa Municipal Hospital and the Lhasa Maternal and Child Health Hospital). Eligibility criteria were women with a singleton intrauterine pregnancy of $\geq$28 weeks gestation. Women who delivered by Cesarean section were excluded. The majority of women in this study resided at altitudes between 3300 m and 4500 m.

As there was limited experience with biomedical research in the three study hospitals, two years of ethnographic research and relationship building between the U.S. and Tibetan investigators and the community preceded the observational study [17].

2.2. Definitions specific to this study

Prenatal care is at least one pregnancy related visit to a health professional during the current pregnancy. *Pre-eclampsia* (PE) and *gestational hypertension* (GH) were combined as *PE/GH*, documentation of blood pressure before pregnancy was not available and proteinuria was not routinely recorded. *PE/GH* was a systolic BP $\geq$140 mm Hg or a diastolic BP $\geq$90 mm Hg taken in a seated position on admission to the hospital or one hour postpartum.

Gestational age was determined preferentially by an ultrasound performed in the first half of pregnancy. If no early ultrasound report was available, *gestational age* was calculated from the first day of the woman's last menstrual period, or, if not known, by measuring her fundal height. Term newborns, 37–41 weeks were considered to be *small for gestational age* (SGA) if their birth weight was less than the 10th percentile for their gestational age adjusted for sex, based on the 1963 Lubchenco growth curves [18]. *Low Apgar* was <7 at 5 min.

2.3. Data collection

The IRBs of UCSF, the University of Utah, RTI and the Mentzikhang Hospital approved the study protocol. Informed consent was not required for this observational study. The use of the blood collection drape, while not standard protocol, was not considered by the hospitals or IRBs to need consent, as there was no diagnostic or therapeutic actions taken based on its use.

Demographic information and medical and obstetric history were obtained by clinician data collectors who interviewed patients on admission or obtained data from patient medical records. Labor and delivery progress, complications, medications, and maternal and neonatal outcomes were recorded concurrently with patient care. All data were recorded on a standardized data collection form. Postpartum blood loss was measured, using a closed-end blood collection drape (BRASSS®-V Drape™ Blood Collection Receptacle, Excellent Fixable Drapes, Madurai, India) [19] for one hour following the delivery of the placenta. The blood drape was placed under the women's buttocks prior to delivery and the collection pouch was opened following the delivery of the placenta. At the end of the one hour blood collection period, blood and clots that pooled under the mother were swept into the drape, the bottom of the drape was cut open, and the contents emptied into a solid graduated cylinder, measured, and the amount recorded in ml.

Data collection forms were reviewed for accuracy by hospital study staff before being submitted to the research office for data entry into Epi Info™ version 3.3 [20] and transmitted electronically using BLAST software [21] to the Data Coordinating Center (RTI).

2.4. Statistical analysis

Data were transferred to SAS version 9.0 [22]. Descriptive statistics were generated for participant demographics, health care received, and outcomes. Continuous variables were categorized based on the distribution of the data and clinical relevance. Relationships between categorical variables were evaluated by examining cross-tabulations, unadjusted odds ratios, chi-square and Fisher's exact tests. Relationships between continuous variables were

evaluated by examining means, standard deviations, and quartiles.

3. Results

3.1. Maternal

The maternal sample included 1121 women (Mentzikhang Hospital = 187, Lhasa Municipal Hospital = 551 and Lhasa MCH = 383). Results are shown in Table 1. Women who did not receive prenatal care were more likely to have a LBW infant (OR 2.8, 95% CI: 1.9–4.3, $p<0.001$). There were no maternal deaths.

Of the 336 (30%) maternal complications, PE/GH was the most common 18.9% (N=212). A higher proportion of Han Chinese women had PE/GH ($n=37$, 25.3%) compared to Tibetan women ($n=166$, 17.7%, OR 1.58; 95% CI: 1.03–2.42; $p=0.03$). Women who had PE/GH had an increased incidence of PPH (OR 1.49; 95% CI: 0.99–2.23; $p=0.05$). These women were also more likely to have a LBW newborn (13.4%, $n=28$) or an SGA newborn (15.7%, $n=31$). There was a significant four-fold increased risk of PPH for women with a third stage of labor lasting ≥15 min (OR 4.2; 95% CI: 2.2–7.8; $p<0.001$).

Of the 614 (54.8% of the total) women who received an uterotonic postpartum (oxytocin (48.7%), misoprostol (4.6%), or ZB 11, a traditional Tibetan uterotonic (1%), 96.1% (590) received the medication within one hour after the birth of the baby. Of these, 389 (65.9%) received the uterotonic with or immediately following the delivery of the placenta. Only 154 (26.1%) women received an uterotonic between delivery of the baby and delivery of the placenta.

Table 1 Maternal clinical characteristics and complications of women delivering vaginally ($n=1121$) in hospital in Lhasa, TAR, PRC, Jan 2004–May 2005

Variable	Total *n* (%)
Total enrolled	1121
Age (years) [a]	26.8 (4.5)
Parity [a]	0.5 (0.9)
Gravida [a]	1.8 (1.1)
Ethnicity	
Tibetan	938 (83.7)
Han Chinese	146 (13.0)
Other	37 (3.3)
Prenatal care	880 (78.5)
Episiotomy	553 (49.3)
Perineal tear	207 (18.5)
Cervical tear	83 (7.4)
Blood loss (ml) [a]	282.2 (209.9)
PPH (≥500 ml)	150 (13.4)
Categorized blood loss	
0–499 ml	971 (86.6)
500–999 ml	126 (11.2)
≥1000 ml	24 (2.1)
Maternal complication [b]	336 (30.0)
PE/GH	212 (18.9)
Retained placenta	34 (3.0)

[a] Mean (S.D.).
[b] Some women had more than one maternal complication.

Table 2 Characteristics of stillborn and live born infants delivered vaginally ($n=1121$) in hospital in Lhasa, TAR, PRC, Jan 2004–May 2005

Variable	Value *n* (%)
Total enrolled	1121
Neonatal outcome	
Live birth, alive at discharge	1091 (97.3)
Death prior to discharge	19 (1.7)
Stillbirth	11 (1.0)
Sex	
Male	572 (51.1)
Female	548 (48.9)
Mean gestational age (wks) [a]	39.4 (1.7)
Categorized gestational age (wks)	
<37 (pre-term)	46 (4.1)
37–41 (term)	1039 (92.7)
≥42 (post-term)	36 (3.2)
Mean birth weight (grams) [a]	3,000.0 (463.4)
Categorized birth weight (grams)	
<1500	7 (0.6)
1500–2499	108 (9.6)
2500–3499	835 (74.5)
≥3500	171 (15.3)
Newborn complications	200 (17.8)
Low Apgar (<7 at 5 min) [b]	41 (3.7)
SGA [c]	145 (13.7)

[a] Mean (S.D.).
[b] Apgar score provided for live births only ($n=1110$).
[c] SGA ($n=1062$).

3.2. Newborns

Of 1121 vaginal deliveries, there were 11 stillbirths. Newborn characteristics and outcomes are described in Table 2. The early neonatal mortality rate was 17/1000 live births; the stillbirth rate was 9.8/1000 live births.

One hundred forty-five (13.7%) newborns were SGA. Han Chinese newborns ($n=34$; 24.5%) were more than twice as likely to be SGA than Tibetan newborns ($n=103$; 11.6%) (OR 2.5, 95% CI: 1.6–3.9, $p<0.0001$).

4. Discussion

This study is the first large-scale maternal and newborn observational study of hospital births in Tibet, although smaller observational studies examining effects of altitude on pregnancy processes and outcomes between Tibetans and Han Chinese have previously been published [23–25].

PE/GH was a major complication for mothers. These data may confirm previous findings that women delivering at high altitude have higher rates of PE/GH than women delivering at lower altitudes [7–11]. Nineteen percent of women in this study experienced PE/GH compared to a 6 to 8% incidence in the United States [26]. While there may be many other characteristics that are dissimilar between US parturients and the women in this study, a recent study conducted in Suzhou in eastern China near sea level found the rate of PE/GH to be only 10.8% [27]. Studies conducted in Colorado and Bolivia [7–10] also reported that PE/GH occurred more frequently in women residing at higher altitudes than women residing at lower altitudes [7–9,23].

To the researchers' knowledge there are no published data on rates of postpartum hemorrhage of women who reside and deliver at high altitude. Researchers found the 13.4% rate of PPH, mainly using expectant management (as there was no protocol of active management of third stage labor), to be similar to rates of PPH at lower altitudes. A study conducted in Kyrgyzstan at an altitude of 1953 m found a 12% incidence of PPH or blood loss $\geq$400 ml [28]. A recent randomized controlled clinical trial, in India, at lower altitudes, comparing misoprostol to placebo in preventing PPH found a 13.2% rate of PPH in the placebo group [29].

It has been previously documented [8–10,13,16,18,30] that birth weight at high altitude tends to be lower than birth weight at sea level. Yip found a 10% reduction in the mean birth weight in newborns of women residing at high altitude in the United States compared to lower altitudes [16]. The mean birth weight of newborns in this sample was 3000 g compared to 3228.8 g in a low altitude Chinese sample [27]. A previous, smaller study in Tibet found the mean birth weight of newborns at 3000 to 4000 m to be 3008 g [23]. The data preclude identification of specific mechanisms for this lower birth weight, although others have speculated on reduced maternal arterial oxygenation during pregnancy [16,31].

These data also showed that the mean gestational age of newborns (39.4 weeks) born at high altitude is similar to the gestational age of newborns born at lower altitude in China (39.2 weeks) [27]. Other studies conducted at low and high altitudes in Colorado and South America comparing neonatal outcomes between low and high altitude residences also found very little difference in rates of pre-term deliveries [9,10,14,25] further supporting the argument that lower birth weight at high altitude is more likely a result of intrauterine growth restriction than lower gestational age [9,16,25].

5. Limitations

A major limitation of this study is the use of a convenience sample. Because data were collected only on women who delivered vaginally in three urban hospitals in the capital city, the findings are not generalizable to the many Tibetan women who deliver at lower level rural health facilities, by Cesarean section, or at home. It is likely that women delivering in hospitals in Lhasa are different from women delivering at home in nomadic areas or in rural villages. Study participants more likely had more prenatal care, more years of education, and may be better nourished than women who deliver at home or in rural villages. Because the researchers have no preconception data, very limited antepartum data, and few intrapartum laboratory assessments, they are unable to comment regarding the underlying mechanisms of these observations. Specifically lacking is information on maternal proteinuria. Since urinalysis for protein was not recorded, it is not clear whether patients had GH or PE.

While differences in adverse outcomes were found between women and newborns in this sample and outcomes in women and newborns at lower altitudes, it is possible that the increased adverse outcomes are unrelated to altitude and/or are not only related to altitude but also to other differences between the study groups.

As this was an observational study the researchers did not institute a specific protocol for administration of uterotonics, individual providers prescribed uterotonics as they deemed necessary. Different uterotonics were administered by a variety of routes and at a variety of times, from shortly after the delivery of the baby to, at or shortly after, the delivery of the placenta (66% of those receiving an uterotonic).

The authors acknowledge that the Lubchenco data were collected more than 40 years ago prior to the use of obstetric ultrasound and that the study population was of different racial and ethnic make up and probably of different nutritional status than that described in the current study. However, the Lubchenco data were collected at 5200 ft and are the best available moderate altitude gestational age–birth weight data.

One aspect of the protocol, the measurement of blood loss only after the placenta was delivered, rather than measuring from the birth of the baby, may make our measurements less comparable to other recent measured blood loss studies [29,32].

The neonatal mortality rate was calculated only on newborns that died in the study hospitals prior to discharge. The average hospital stay for postpartum women is three to five days and no data were collected on newborns after the mother's discharge from the hospital.

6. Conclusions

This is the largest study to date examining maternal and newborn outcomes in Tibet. It provides information on the health status of pregnant women and infants. This population had a relatively higher incidence of PE/GH and LBW compared to those at lower altitudes. Although rates of PPH were not increased in this sample, it is still a major cause of maternal morbidity in Tibet [1]. Further research is necessary both to determine etiologies for these outcomes as well as interventions that might decrease their incidence.

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