Characteristics of Pregnant Women and Risk Factors of Their Newborn for Admission to a Neonatal Intensive Care Unit in Nepal

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ABSTRACT

Background: Nepal has progressed gradually in reducing under-5 mortality and neonatal mortality; however, they are still high at 30.8 and 19.8 per 1000 live births, respectively. Neonatal mortality constituted about 64% of the under-5 mortality in 2019, higher than the global average of 47%.

Methods: This is a prospective study among pregnant women and their newborn babies in Siddhi Memorial Hospital, Bhaktapur, Nepal, from October 2017 to April 2018. Demographic and clinical data, high vaginal swabs of pregnant mothers, and umbilical cord blood were collected. High vaginal swabs were cultured, and umbilical cord blood samples were cultured and tested for inflammatory markers. After discharge to home, neonates were followed for 28 days of life by weekly phone calls.

Results: Total number of pregnant mothers enrolled was 151. The median age was 26 years (IQR: 18-40), and the proportion of adolescent mothers was 4.7%. Half of the deliveries were done by the caesarian section, and 8.6% had gestational age <37 weeks. High vaginal swab cultures were positive in 8.2% of the samples (n=135), and *Escherichia coli* was the most common bacteria. Out of 153 newborn babies (2 were twins), 8 (5.2%) were admitted to the neonatal intensive care unit. The proportion of low birth weight was 13%, and it was independently associated with neonatal intensive care unit admission (adjusted OR=9.4, 95%CI 1.8-50.1; P value= 0.009).

Conclusions: Adolescent pregnancies and Low Birth Weight babies were commonly observed. Both of these issues need to be addressed by effective measures that would improve the current situation of maternal and child health in Nepal.

Keywords: Maternal health; morbidity neonates; Nepal; risk factors; morbidity

INTRODUCTION

The inclusion of maternal and child health as one of the Millennium Development Goals (MDGs) led to a significant improvement in the areas of maternal and child health.¹ Towards the end of the MDG era, WHO launched Every Newborn Action Plan (ENAP) in 2014 to initiate a concerted global action to reduce neonatal mortality.² The Sustainable Development Goal (SDG) 3.2 set a target of reducing the national neonatal mortality rate (NMR) to 12 or less per 1000 live births by 2030.³ Despite all the efforts, neonatal mortality remains an important global health concern; 47% of all the underfive deaths occurred within the neonatal period (28 days of life) in 2019.⁴ However, in Nepal, under-5 mortality was 30.8, and neonatal mortality was 19.8 in 2019; thus, neonatal deaths accounted for 64% of under-5 mortality, which was higher than the global average.⁵ Several factors like mothers of adolescent ages, lack of formal education, coming from the disadvantaged community has been associated with risks for neonates.^{6, 7} In this study, we aimed to identify the maternal characteristics

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during the pregnancy and delivery, and the risk factors associated with newborns for their admission to intensive care units within the first month of the neonate life.

METHODS

A prospective study was carried out in Siddhi Memorial Hospital (SMH), Bhaktapur, from October 2017 to April 2018. SMH is a non-profit making community hospital specialized in women's and children's health. All the pregnant women who attended the hospital for delivery were counseled by the hospital staff not involved in this research. The rationale, objectives, expected benefits, safety, and rights of the participants were explained to the participants.

The study was approved by the Nepal Health Research Council (Reg. no. 227/2017). Only those women or their guardians who willingly gave their written consent with signature were enrolled in the study. All the personal identifiers were made anonymous for confidentiality.

Trained research assistants collected the demographic and clinical data in a standard questionnaire in paper format at the time of enrollment, and later the data were transferred to Epi-Info 7.2 (CDC, Atlanta). In addition, trained nurses and gynecologists took two high vaginal swabs (HVS) from each pregnant woman at enrollment, and umbilical cord blood (UCB) was collected immediately after the delivery of the baby. Among the two high vaginal swabs, one was used for Gram's staining, and the other was used for culture.

The vaginal swab was cultured in blood agar (aerobically), chocolate agar (anaerobically), and in Mac-Conkey agar (aerobically) using the quadrant streaking method and incubated at 37° C for 24 hours. We focused on the isolation of pathogens only and excluded the possible contaminants.

Of the total 5 ml of umbilical cord blood collected from each participant, 1 ml was transferred to a brain heart infusion broth (BHI) for culture, and the remaining 3 ml was transferred to a plain vial and 1 ml to an ethylenediamine tetra-acetic acid (EDTA) vial, both for hematological tests. The BHI bottles were immediately taken to the laboratory after proper labeling and incubated at 37° C. The cord blood culture was carried out in a similar culture condition as for vaginal swabs, and the observation for any microbial growth was done for seven days. The identification of the clinically relevant microbial isolates from the vaginal swabs and umbilical cord blood was performed by phenotypic characterization, which involves the colonies' morphological appearance, staining reaction, and biochemical properties.⁸

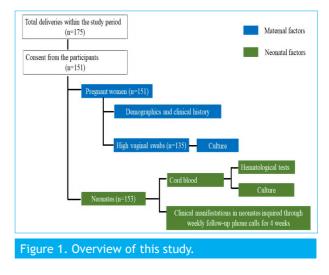
The cord blood specimens collected in EDTA vials were used to determine micro erythrocyte sedimentation rate (mESR) and immature to the total neutrophil ratio (I/T ratio). Blood samples in the plain vial were centrifuged, and serums were separated and tested for C-reactive protein by using the latex agglutination method. Complete blood cell counts were carried out using a blood sample collected in an EDTA vial using a Coulter analyzer (Beckman).

Any instances of medical attention received by neonates within 28 days of life were inquired by followed up through weekly phone calls. In addition, if the newborns were admitted to Siddhi Memorial Hospital within 28 days, clinical data were collected from the hospital's medical records.

Data from Epi-Info 7.2 were transferred to STATA 14 (Stata Corp, Texas) for statistical analysis. The categorical variables were presented as proportions, and continuous variables were shown as the medians and interquartile range. Univariate and multivariate analyses were performed to assess the association of the maternal and neonatal factors with NICU admission of the newborn. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

There were total 175 deliveries at SMH within the study period. Twenty-four pregnant women refused to participate in the study. Of the 151 women enrolled in the study, two gave birth to twins amounting to a total of 153 neonates (Figure 1).



The median age of pregnant women was 26 years, and the interquartile range (IQR) was 18 to 40 years. The proportion of adolescent mothers was 4.7%. The median gestational age was 39 weeks with an IQR of 33-42 weeks. Half of the deliveries were done by cesarean section (CS) (n=77), out of which 23 were elective CS, and 54 were emergency CS. Of 151 mothers, 79 (52.3%) were primigravidae. Characteristics of the pregnant mothers are shown in Table 1.

| Table 1. General maternal characteri | stics of mothers. |
|--------------------------------------|-------------------|
| Characteristics | N=151 (%) |
| Maternal age | |
| <20 | 7 (4.6) |
| 20-29 | 101 (66.9) |
| ≥30 | 43 (28.4) |
| Gestational age | |
| <37 weeks (preterm) | 13 (8.6) |
| 37-41 weeks (term) | 137 (90.7) |
| ≥42 weeks (post-term) | 1 (0.7) |
| Mode of delivery | |
| Vaginal | 74 (49) |
| Emergency Caesarian section | 54 (35.8) |
| Elective Cesarean Section | 23 (15.2) |
| Number of babies per delivery | |
| Single | 149 (98.7) |
| Twins | 2 pairs [4] (1.3) |
| Number of previous delivery | |
| >2 | 3 (2) |
| 1 - 2 | 69 (45.7) |
| 0 (Primi-gravida) | 79 (52.3) |
| Hyperthyroidism | |
| Yes | 3 (2) |
| No | 148 (98) |
| Hypertension | |
| Yes | 4 (2.6) |
| No | 147 (97.4) |
| HBsAg test | |
| Positive | 1 (0.7) |
| Negative | 150 (99.3) |
| Fever before delivery | |
| Yes | 3 (2) |
| No | 148 (98) |

The HVS swabs could only be collected for 135 mothers. Eleven swab cultures (8.2%) showed positive growth for pathogenic organisms. One swab yielded growth of *Escherichia coli* and *Klebsiella pneumoniae*. *Escherichia* *coli* was the most common pathogen (Table 2). Results of hematological tests and culture of umbilical cord blood samples are shown in Table 3. Ten samples (6.5%) had WBC counts >20000/mm³, and one sample was positive for *Escherichia coli*.

| Table 2. Pathogenic organisms isolated to cultures from eleven mothers (out of 135 mo | |
|---|-------------|
| Organisms | Number |
| Escherichia coli | 6 |
| Candida albicans | 2 |
| Non-albicans Candida | 2 |
| Klebsiella pnuemoniae | 1 |
| Staphylococcus aureus | 1 |
| Note: Escherichia coli and Klebsiella pneumonia | ae were co- |

isolated from one HVS culture.

| Table 3. Hematological test and cultu umbilical cord blood samples. | ire results of the |
|---|--------------------|
| WBC count/(CCM) | N=153 (%) |
| <5000 | 3 (2) |
| 5000-20000 | 140 (91.5) |
| >20000 | 10 (6.5) |
| I/T ratio | |
| ≥0.2 | 0 (0) |
| <0.2 | 153 (100) |
| micro ESR | |
| ≥13 | 0 |
| <13 | 153(100) |
| CRP | |
| >6mg/l | 0 |
| ≤6mg/l | 153 (100) |
| Cord blood culture | |
| Positive | 1 (0.7) |
| Negative | 152 (99.3) |

53.6% of newborns (n=153) were male, and the median birth weight was 3035 g (IQR: 1640-4600 g). The proportion of low birth weight was 13%, and 7 babies (4.6%) had APGAR scores at 1st minute was <7 (Table 4).

| Table 4. General characteristics of neona | tes. |
|---|-----------|
| Characteristics | N=153 (%) |
| Sex | |
| Male | 82 (53.6) |
| Female | 71 (46.4) |
| Weight at birth, gram | |
| <2500 (Low birth weight) | 20 (13) |

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| 2500-4000 (Normal) | 132 (86.3) | Ye |
|---|------------|----|
| >4000 (Overweight) | 1 (0.7) | |
| APGAR score at the 1 st minute | | H |
| <7 | 7 (4.6) | Ne |
| ≥7 | 146 (95.4) | Po |
| APGAR score at the 5 th minute | | Se |
| <7 | 1 (0.7) | Fe |
| ≥7 | 152 (99.3) | F |
| Outcome of baby birth | | M |
| Transferred to mother side (well-baby) | 140 (91.5) | Bi |
| Transferred to NICU/ward | 13 (8.5) | ≥2 |

Of 153 neonates, 5 (3.2%) were transferred to the hospital ward for observation, and 8 (5.2%) were admitted to NICU due to clinical manifestations, such as respiratory distress, assumed sepsis, hypothermia, and reduced breastfeeding. In univariate analysis, emergency CS (OR=9.1, 95%CI 1.1-78.2; *P* value=0.044) and low birth weight of the neonates (OR= 9.2, 95%CI 1.8-50.1, *P* value=0.004) were associated with the NICU admission. Due to the low sample size, the 95% CI was wide. In the multivariate analysis, low birth weight (adjusted OR=9.4, 95%CI 1.8-50.1; *P* value= 0.009) was independently associated with NICU admission (Table 5). There was no mortality in the NICU or any referral to a higher center.

| Table 5. Risk factors for NICU admission of neonates. | | | | |
|---|--------------------|------------|--------------------|------------|
| | Univariate | | Multivariate | |
| Risk factors | OR (95% CI) | P value | OR (95% CI) | P value |
| Maternal age | | | | |
| ≥20 years | 1.0 | | 1.0 | |
| <20 years | 2.1 (0.2- 19.2) | 0.502 | 2.2 (0.2- 27.7) | 0.537 |
| Gestational age (week) | | | | |
| ≥37 | 1.0 | | | |
| <37 | 4.0 (0.7- 22.2) | 0.113 | - | - |
| Type of delivery | | | | |
| Vaginal delivery | 1.0 | | 1.0 | |
| Emergency CS | 9.1 (1.1- 78.2) | 0.044 | 7.7 (0.8- 72.2) | 0.076 |
| Elective CS | 3.3 (0.2- 55.3) | 0.403 | 2.9 (0.1- 56.2) | 0.486 |
| Leaking per vagina | | | | |
| No | 1.0 | | 1.0 | |

| 4.5 (1.0- 20.3) | 0.054 | 4.5 (0.8- 24.5) | 0.083 |
|--------------------|---|---|--|
| e (n=135) | | | |
| 1.0 | | | |
| 3.5 (0.6- 20.1) | 0.154 | - | - |
| | | | |
| 1.0 | | 1.0 | |
| 1.4 (0.3- 6.2) | 0.634 | 2.0 (0.4- 10.9) | 0.427 |
| Birth weight (g) | | | |
| 1.0 | | 1.0 | |
| 9.2 (2.1- 41.0) | 0.004 | 9.4 (1.8- 50.1) | 0.009 |
| | 20.3) e (n=135) 1.0 3.5 (0.6- 20.1) 1.0 1.4 (0.3- 6.2) nt (g) 1.0 9.2 (2.1- | 20.3) 0.054 e (n=135) 1.0 3.5 (0.6-20.1) $0.1541.01.4 (0.3-6.2) 0.634nt (g)1.09.2 (2.1-0.004)$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |

About 17.0% (n=26) of the neonates received medical attention in 7 to 28 days of the neonatal period. Diarrhea, vomiting, eye infection, jaundice, umbilical infection, and ear infection were the presenting complaints. These babies were managed in outpatients taking appropriate specimens for culture and treatment. Eight samples from eye swabs, umbilical pus swabs, and ear swabs yielded bacteria. They were treated with appropriate antibiotics. For diarrhea, vomiting, and physiological jaundice, appropriate counseling were given and followed up.

DISCUSSION

In this prospective study, we assessed the epidemiological and clinical characteristics of 151 pregnant women and their 153 newborn babies in a secondary hospital in a semi-urban region of Nepal. We observed that 8.2% of pregnant women (n=135) had vaginal colonization of a pathogenic bacteria, half of the deliveries (n=151) were done by the caesarian section, and 5.2% of neonates (n=153) were admitted to NICU. In addition, low birth weight (<2500 g) was independently associated with NICU admission. We also observed that 17% of neonates presented to the outpatient department with medical complaints, such as diarrhea, vomiting, and localized infections.

In our study, 4.6% of mothers were adolescents. The proportion of adolescent mothers in Nepal was previously reported in the range of 13.1-14.4%.⁹⁻¹¹ Nepal Demographic and Health Survey 2016 data showed that 173 per 1000 adolescent women get pregnant in Nepal.¹² Furthermore, in contrast to our study carried out in a single hospital within a period of seven months with lower study subjects, the study by Gurung R et.al.,

detected 7.8% deliveries from adolescent mothers carried out in 12 hospitals in Nepal over a period of one year with a larger number of deliveries with increased risks of prolonged labor, preterm birth and small baby for the gestational week in adolescent mothers.⁶

We observed a high proportion (51%) of deliveries done by the caesarian section (CS). National Demographic and Health Survey (NDHS) data from 1996 to 2016 showed a ten-fold increase in population-based CS rate (0.9% to10.2%) and institution-based CS rate increasing from 10.4% to 16.4%.¹² The national CS rate of Nepal seems to be fairly within the range of 10-15%, as recommended by WHO.¹³ However, the CS rate might be increasing in recent years in private institutions, as seen in our study, but not in public hospitals.^{11,14,15} Besides, 23 (15.2%) of the CS deliveries were carried out on request in this study, similar to a hospital at Lalitpur, Nepal (16.2%, n=379).¹⁵ The reasons why women opt to elective CS should be studied in the future because some of those reasons may be driven by superstitions regarding auspicious dates.¹⁶ Noteworthy, elective CS without medical indications can result in adverse maternal outcomes.¹⁷

The HVS culture yielded a pathogenic organism in 11 mothers (8.1%, n=135). Out of 11, 9 women were delivered by CS. One of the babies was admitted to NICU. It is known that vaginal colonization can result in an increased risk of neonatal infections. We did not observe isolation of Streptococcus agalactiae in this study. Plausible explanations could be the lack of enrichment media (Todd Hewitt medium), selective media, and sensitive molecular assays, such as PCRbased methods. In addition, we only collected the upper vaginal swab and did not collect the lower vaginal and rectal samples that might have also contributed to a lack of detection of Streptococcus agalactiae. A recent study showed that 24 (19.2%) of 125 vaginal samples collected from pregnant women were positive for Streptococcus agalactiae in Kathmandu.18

The proportion of preterm birth in this study (8.6%) is consistent with a multicenter study (9.3%, n= 5964) and a tertiary hospital in Nepal (8.1%, n=357).^{11,19} Overall, the preterm birth rate in Nepal is comparable to the global preterm rate (10.6%). ²⁰ Thirteen percent (n=153) of newborn babies had a birth weight of less than 2,500 grams (LBW). The prevalence of LBW was previously reported in the range from 11.9% to 39.6% in Nepal.⁹ In 2015, Nepal was one of the countries with the highest prevalence of LBW newborn babies globally.²¹ Many maternal factors, including maternal physique (low height, weight, body mass index), preterm birth, hard work during pregnancy, young age of mothers, iron deficiency, maternal comorbidity, and insufficient maternal nutrition during pregnancy, are associated with LBW.^{9,10,22} Effective public health interventions are needed to curve these risk factors to reduce the prevalence of LBW in Nepal. We observed that eight (5.2%) neonates (n=153) were admitted to NICU. In risk factor analysis, LBW was independently associated with NICU admission. Respiratory distress, assumed sepsis, and hypothermia were some of the causes for NICU admission. Some of the frequent causes of NICU admission in Nepal were infections, severe neonatal jaundice, respiratory distress, perinatal asphyxia, and prematurity.²²⁻²⁴

The major limitation of this study is the small sample size because we could not extend the study more than 6 months. Our detection of vaginal colonization was limited by a swab of only the upper vagina. We did not take a rectal swab. Due to this, we could probably not detect some of the bacterial colonizers, such as *Streptococcus agalactiae*.

CONCLUSIONS

In conclusion, this study described the epidemiological and clinical characteristics of pregnant women and their newborn babies in a semi-urban setting in Nepal. Adolescent pregnancy was still observed, although it is illegal to get married before 20 years of age. LBW is common among newborns, and it is a major cause of morbidity, including admission to NICU. Caesarian delivery has been seen in an increasing trend in the recent period.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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