Rwanda Medical Journal RMJ

ORIGINAL ARTICLE Open Access

Neonatal surgical mortality and morbidity at the University Teaching Hospital of Kigali, a tertiary university hospital in Rwanda: analysis of predicting factors

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ABSTRACT

INTRODUCTION: Globally, high morbidity and mortality is associated with neonatal surgical conditions. This study aimed to determine the factors influencing the mortality in neonates with surgical conditions at Centre Hospitalier Universitaire de Kigali (CHUK).

METHOD: This was a prospective study from October 2019 to March 2020. Analysis of patients was divided based on a diagnosis of gastroschisis versus non-gastroschisis conditions. Odds ratios were calculated at a confidence interval of 95%. Factors with p-value <0.05 on bivariate analysis were considered.

RESULTS: Eighty-two neonates were enrolled. 45.1% were admitted within the first 24 hours of life, 61% were males, 26.9% were preterm, and 51.2% had birth weight less than 2500g. Gastroschisis (n=43, 52.4%) was the most common diagnosis, followed by intestinal atresia (12.2%). The overall mortality rate was 57%. Mortality was more likely to occur among neonates with gastroschisis compared to neonates with non-gastroschisis surgical conditions (76.7% vs 35.9%, OR=5.893, p<0.001). Among neonates with gastroschisis, factors associated with mortality were the failure of initiation of enteral feeding (100%, p=0.002) and sepsis (82.5%, p=0.001).

Among neonates with non-gastroschisis surgical conditions, factors associated with mortality were prematurity (87.5%, OR:24, p=0.001), low birth weight (72.7% vs 21.4%, p=0.003), initiation of enteral feeding at more than 48 hours (33.3% vs 25.8%, p=0.006), sepsis (64.7% vs 13.6%, OR:11.61, p<0.001), and need of mechanical ventilation (63.6% vs 25%, OR:5.25, p=0.024,).

CONCLUSION: Neonatal surgical mortality is still a burden and has many predicting factors. Improvement and advocacy are needed to reduce neonatal mortality.

Keywords: Neonatal surgical conditions, Factors, Morbidity, Mortality.

INTRODUCTION

Neonatal surgical conditions occur in 1 in 5000 live births worldwide, contributing to high morbidity and mortality among neonates [1]. Compared with older children, neonates present a wide

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Received: 14th November 2022; **Initial decision given:** 03rd February 2023; **Revised manuscript received:** 26th February 2023; **Accepted:** 28th April 2023.
 Publisher: Rwanda Biomedical Centre (RBC)/Rwanda Health Communication Center, P. O. Box 4586, Kigali. ISSN: 2079-097X (print); 2410-8626 (online)

Citation for this article: V. Maniraguha; P. Robin; J. Rickard et al. Neonatal surgical mortality and morbidity at theUniversity Teaching Hospital of Kigali, a tertiary university hospital in Rwanda: Analysis of predicting factors. Rwanda Medical Journal, Vol. 80, no. 2, p. 35-43, 2023. https://dx.doi.org/10.4314/rmj.v80i2.4

divergence in physiology, anatomy, immunity, and response to stress. When neonates have a surgical illness, their metabolism becomes dysregulated and can predispose them to mortality or morbidity in a hospital, such as surgical site infection, sepsis, malnutrition, and the need for postoperative mechanical ventilation. Studies have reported factors contributing to neonatal mortality, including prematurity, sepsis, low birth weight, and malnutrition [2–5].

Ugwu et al. [6] assessed the challenges and types of surgical problems found in the neonatal period. Most (89%) surgical conditions were congenital abnormalities [6]. Neonatal surgical conditions contribute significantly to neonatal admissions and mortality in developing countries. Surgical conditions in neonates presented a mortality rate of 11.8%. The same study on neonatal surgery in sub-Saharan Africa reported high mortality in congenital malformations. In Nigeria, however, there was an improvement during the last decade in managing neonates with surgical conditions [6,7]. Morbidity and complications are often serious and life-threatening secondary to physiological disorders. Mortality from neonatal surgery was reported as 48% in Cameroon and 62.2% in Nigeria [8,9].

In Rwanda, there are 36 district hospitals, 4 provincial hospitals, and 8 referral hospitals. As the system is organized, neonates judged to need surgical management are transferred to Centre Hospitalier Universitaire Kigali (CHUK), the largest referral hospital with a specialized surgical pediatric unit for neonatal surgical management. However, there is no study done to explore neonatal surgical mortality and morbidity. Therefore, this study aimed to determine the factors influencing mortality in neonates with surgical conditions at CHUK.

METHODS

This was a prospective observational study of patients with neonatal surgical pathologies over 6 months (October 2019- March 2020). A surgical neonate was defined as any neonate with a surgical condition who needed a surgical consult.

The study was conducted at CHUK, which has one pediatric surgery ward with 15 beds, two pediatric surgeons, a pediatric surgery fellow, and one pediatric anesthesiologist. The pediatric intensive care unit has only 3 beds with 3 mechanical ventilation machines at CHUK.

We enrolled all surgical neonates and followed patients during the hospital stay, from admission until hospital discharge or 30 days' postoperative. All neonates were admitted through the neonatology and emergency unit of the pediatrics department.

Data was collected using an established questionnaire and entered into Microsoft Excel. Variables were organized as demographic data (age, gender, referring province), social data (insurance), laboratory data (full blood count (FBC), electrolyte, blood culture), and clinical data (mode of delivery, gestational age, birth weight, vital signs, diagnosis, procedure, intraoperative events, duration of surgery, postoperative disposition, postoperative complications, length of hospital stay, death and survivor).

Low birth weight was defined as weight < 2500g. Duration of surgery was the time elapsed between induction of anesthesia and recovery from anesthesia as recorded by the anesthesiologist. Total parenteral nutrition (TPN) was reported as a binary variable. Any surgical neonate who was given TPN was recorded positively.

For patients with gastroschisis, early initiation of enteral feeding was defined as starting feeding within 7 days from birth; intermediate initiation of enteral feeding was defined as starting feeding in 7-14 days of life; late enteral feeding initiation was defined as starting feeding in >14 days of life. For patients with non-gastroschisis conditions, early enteral feeding was defined as the initiation of feed within 48 hours post-operatively. Enteral feeding included feeding orally or through a nasogastric tube.

The primary outcome was mortality in the hospital. Sepsis, surgical site infection (SSI), and malnutrition were defined based on clinical assessment and documentation of the pediatrician or pediatric surgeon. Postoperative mechanical ventilation was considered as a need for postoperative re-intubation or continuous intubation post-surgery.

Ethical approval of 450/CMHS IRB/2019 as a reference number was obtained from the institutional review board of the University of Rwanda and CHUK ethics committee prior to study enrollment with a reference number of EC/CHUK/164/2019. A consent form was signed before starting to collect data for all recruited surgical neonates. Data were stored on a password-protected computer, and patient information was

de-identified prior to data analysis and used only for the purpose of this study.

Data were analyzed using IBM SPSS software version 25. Patients' characteristics were analyzed and presented as frequency and percentages. The means and standard deviations (SD) were presented for continuous variables. Due to the high number of neonates with gastroschisis and its unique management, the analysis of patients was divided based on a diagnosis of gastroschisis versus non-gastroschisis conditions.

Chi-square and Fisher's exact tests were used to calculate the association between variables, and the student t-test was used for means comparison in scale variables. An association between variables was considered significant if the p-value was less than 0.05. Odds Ratios (OR) were calculated, and a 95% confidence interval (95% CI) was presented. A bivariate analysis was used to separately evaluate factors associated with mortality in the patients with gastroschisis and those with non-gastroschisis surgical conditions.

RESULTS

During our study period, 486 neonates were admitted at CHUK, with 276 (56.8%) admitted immediately after birth in the neonatology unit and 210 (43.2%) admitted through the pediatric emergency department. Among these admissions, 82 (16.9%) were admitted due to a surgical condition and were included in this study. Among the 82 neonates included in this study, 78 (95.1%) were admitted through the emergency department, and only 4 (4.9%) were born in CHUK. Neonates with gastroschisis occupied 52.4% of all neonatal surgical conditions.

Table 1 shows the demographic characteristics of the enrolled neonates with surgical conditions. Among the provinces of origin in the country, the eastern province represented 28% of all admitted neonates with surgical conditions. The mean birth weight was 2536.5±570.1g (min: 1500g-max: 4200g), and more than half (51.2%) had low birth weight. The mean age of life at presentation was 3.9±5.8 days with a male preponderance (male to female ratio of 3:2). The majority of neonates were born at term (73.2%) and by spontaneous vaginal delivery (78%). The majority of patients (91.5%) had community health insurance. Only 2 neonates did not have health insurance.

Table 2 shows that the most common surgical condition was gastroschisis (52.4%) followed by intestinal atresia (12.2%), anorectal malformations (9.8%), and omphalocele (6.1%).

More than half (57%) of neonates with surgical conditions died. The mortality rate was 76.7% and 35.9% among neonates with gastroschisis and neonates with non-gastroschisis conditions, respectively.

The clinical characteristics of neonates with gastroschisis are presented in Table 3. Among neonates with gastroschisis, 72% had low birth weight, 32% were premature, and 32% were transferred from the eastern province. All neonates who had gastroschisis underwent surgically sterile procedures, including silo-bag placement and daily manual bowel reduction at the bedside. No neonate with gastroschisis underwent surgery in the operating room under anesthesia. Nearly half (48.8%) of patients with gastroschisis never initiated enteral feeding, and only 3 (7%) received total parenteral nutrition. As complications, 20.9% developed malnutrition, 93% had sepsis and 34.9% needed ventilation.

Factors associated with mortality among neonates with gastroschisis were lack of initiation of enteral feeding ($p<0.001$) and the presence of sepsis ($p=0.001$).

The clinical characteristics of neonates with non-gastroschisis surgical conditions are presented in Table 4. Among neonates with non-gastroschisis surgical conditions, more than 76% were born by spontaneous vaginal delivery, and 71.8% were born with normal birth weight. Kigali city was the most common province of origin. In total, 26 (66.7%) neonates were operated on for a mean operative time of 116.7 ± 69.7 minutes. Intraoperative complications included the need for vasopressors and cardiac arrest in one neonate. More than two-thirds (71.8%) were admitted to the pediatric ward. More than 79% initiated enteral feeding within the first 48 hours postoperatively.

The most common complication among neonates with non-gastroschisis surgical conditions was sepsis (43.6%), followed by the need for mechanical ventilation (28.2%).

Factors associated with mortality among neonates with non-gastroschisis surgical conditions were prematurity (87.5% vs 22.6%, OR:24.0, 95%CI: 2.509-229.561, p=0.001), low birth weight (72.7%

Table 1: Patient characteristics

		Total population	Gastroschisis Cases	Other surgical conditions
		N (%)	N (%)	N (%)
Age at admission	<24 hours	37 (45.2)	34 (79)	3 (7.7)
	24-48 hours	23 (28)	9 (21)	14 (35.9)
	>48 hours	22 (26.8)	0 (0)	22 (56.4)
Gender	Male	50 (61)	23 (53.5)	27 (69.2)
	Female	32 (39)	20 (46.5)	12 (30.8)
Mode of delivery	Spontaneous Vaginal Delivery	64 (78)	34 (79.1)	30 (76.9)
	Cesarian section	18 (22)	9 (20.9)	9 (23.1)
Gestational age at delivery	Term	60 (73.2)	29 (67.4)	31 (79.5)
	Preterm	22 (26.8)	14 (32.6)	8 (20.5)
Birth weight	<2500g	42 (51.2)	31 (72.1)	11 (28.2)
	≥2500g	40 (48.8)	12 (27.9)	28 (71.8)
Province	Kigali	17 (20.7)	7 (16.3)	10 (25.6)
	Northern	10 (12.2)	2 (4.7)	8 (20.5)
	Southern	13 (15.9)	9 (20.9)	4 (10.3)
	Eastern	23 (28.0)	14 (32.6)	9 (23.1)
	Western	19 (23.2)	11 (25.6)	8 (20.5)
Medical Insurance	Yes	80 (96.6)	41 (95.3)	39 (100)
	No	2 (2.4)	2 (4.7)	0 (0)
Hospital ward	Pediatric ward	67 (81.7)	39 (90.7)	28 (71.8)
	Pediatric Intensive Care Unit (PICU)	11 (13.4)	1 (2.3)	10 (25.6)
	Neonatology unit	4 (4.9)	3 (7)	1 (2.6)
Operated	Yes	26 (31.7)	0 (0)	26 (66.7)
	No	56 (68.3)	43 (100)	13 (33.3)
TPN	Yes	6 (7.3)	3 (7)	3 (7.7)
	No	76 (92.7)	40(93)	36 (92.3)
Complications	Surgical Site Infections	6 (7.3)	0 (0)	6 (23.1)
	Sepsis	57(69.5)	40 (93)	17 (43.6)
	Malnutrition	14 (17)	9 (20.9)	5 (12.8)
	Ventilation	26 (31.7)	15 (34.9)	11 (28.2)
	Death	47 (57.3)	33 (76.7)	14 (32.6)

vs 21.4%, p=0.003), initiation of enteral feeding at more than 48 hours (33.3% vs 25.8%, p=0.006), sepsis (64.7% vs 13.6%, OR:11.611, 95%CI:2.410-55.939, p=0.001) and need for mechanical ventilation (63.6% vs 25.0%, OR:5.250, 95%CI: 1.175-23.457, p=0.024).

DISCUSSION

This study aimed to assess the predicting factors of neonatal surgical mortality and evaluate the outcomes of neonates with surgical conditions at CHUK. Prematurity, low birth weight, failure of enteral feeding initiation, malnutrition, sepsis, and

need for mechanical ventilation were associated with mortality in neonates with surgical conditions. The proportion of neonates with surgical conditions was significant, with 16.9% of all causes of neonatal admission compared to Nigeria (6.2%) [7].

Table 2: Diagnosis

Diagnosis	N	%
Gastroschisis	43	52.4
Intestinal atresia	10	12.2
Ano-Rectal Malformations/ Imperforated anus	8	9.8
Omphalocele	5	6.1
Meconium plug	4	4.9
Inguinal hernia	2	2.4
Dry gangrene	1	1.2
Necrotizing Enterocolitis	1	1.2
Esophageal Atresia-Tracheo-Esophageal Fistula	1	1.2
Annular pancreas	1	1.2
Pyomyositis	1	1.2
Ranula oral cyst	1	1.2
Ischemic upper limb	1	1.2
Burn	1	1.2
Femur fracture	1	1.2
Hirschsprung disease	1	1.2
Total	82	100

The increased rate of neonatal surgical conditions in this study could be explained by our study site being the only hospital in the country that has a neonatal surgical unit which may increase the numerator of neonates with surgical conditions without an equivalent increase in the number of all neonatal admissions.

Mortality occurred among 57% of neonates with surgical conditions at CHUK. This is comparable to the results of the study from the Children's Hospital at Westmead (Australia), which also showed 54.8% of mortality among neonates with surgical conditions but higher than the results from a facility-based study in Nigeria showing that among all admitted neonatal surgical conditions 42.6% had neonatal death [6,10].

The most common conditions found in our study were related to gastroschisis, an abdominal wall defect that can be identified during the prenatal period using ultrasound technology. Prenatal care in Rwanda is delivered at health facilities (health centers and secondary and tertiary hospitals), and 98% of women attend some prenatal visits, but only 68.9% of neonates are delivered at health facilities [11]. A number of women are still giving birth at home (29%). This is different from the United States, where >95% of pregnant women attend prenatal visits and deliver at health facilities [12]. A very low percentage (4%) of pregnant women meet a doctor in prenatal care at the level of hospitals. Others are being seen by midwives who cannot perform prenatal ultrasounds at health centers [11]. This explains the fact that the overwhelming majority of congenital deformities, such as omphalocele and gastroschisis, are discovered at birth.

Gastroschisis has a poor outcome in affected neonates mainly because of its pathophysiology and clinical characteristic of leaving the bowels exposed to air with eventual insensible loss of fluid and electrolytes, further worsening the neonatal clinical status [13]. The management of gastroschisis typically involves resuscitation, nutrition support, pediatricians, neonatal and critical care nurses, pediatric surgeons, and pediatric anesthesiologists within an appropriate environment to deliver neonatal critical care. Primary skin or fascial closure under general anesthesia or bedside preformed silo-bag placement with serial manual reduction and delayed closure showed to offer a good prognosis [13,14]. Assessment of clinical outcomes of surgical sutured and sutureless closure of gastroschisis revealed the same outcome on survival; thereby, all gastroschisis cases didn't undergo surgery in the operating room under anesthesia in our study [15,16]. The majority of neonates with gastroschisis were given intravenous fluids, bedside silo bag placement, serial bowel reduction with delayed closure, and admitted to general wards. Despite all efforts to manage gastroschisis cases, gastroschisis presented a high mortality rate in our hospital.

Initiation of early feeding in patients with gastroschisis is associated with lower mortality, shorter hospital stay, and better weight gain [17,18]. Our results demonstrated a significant negative association between the timing of enteral feeding initiation and neonatal mortality. Delay to initiate enteral feeding depended on the severity of the condition by poor bowel function with high

bowel intolerance. Neonatal death was lower among neonates for whom enteral feeding was initiated in less than 7 days of life. Early feeding stimulates gastric mucosa adaptation, allowing full enteral feeding earlier [17].

Prematurity was significantly associated with surgical neonatal mortality in non-gastroschisis surgical conditions. Similarly, prematurity was strongly associated with neonatal mortality in India as well as in Mexico [19]. Immunity and metabolism of preterm neonates are less strong than neonates, and this makes them vulnerable [20]. Among neonates with non-gastroschisis surgical conditions, there was a significant positive

Table 3. Determinants of survival among neonates with gastroschisis

		Status at discharge N (%)				
		Survivor	Died	p-value	OR	95% CI
Province	Kigali	3 (42.9)	4 (57.1)	0.466	-	
	Northern	1 (50.0)	1 (50.0)			
	Southern	2 (22.2)	7 (77.8)			
	Eastern	3 (21.4)	11 (78.6)			
	Western	1 (9.1)	10 (90.9)			
Gender	Male	6 (26.1)	17 (73.9)	0.637	1.412	[O.335-5.944]
	Female	4 (20)	16 (80)			
Gestational Age	Term	9 (31)	20 (69)	0.112	5.143	[0.579-45.693]
	Preterm	1 (7.1)	13 (92.9)			
Age at admission	<24 hours	9 (26.5)	25 (73.5)	0.332	2.88	[0.315-26.360]
	24-48 hours	1 (11.1)	8 (88.9)			
	>48 hours	0 (0)	0 (0)			
Birth weight	<2500	7 (22.6)	24 (77.4)	0.866	0.875	[0.185-4.141]
	=>2500	3 (25)	9 (75)			
Disposition	Ward	9 (23.1)	30 (76.9)	0.789		
	Pediatric Intensive Care Unit	0 (0)	1 (100)			
	Neonatal Unit	1 (33.3)	2 (66.7)			
Initial enteral feeding	Yes	10 (45.5)	12 (54.5)	**0.000**	-	
	No	0 (0)	21 (100)			
Early enteral feeding (N=22)	≤ 7 days	7 (53.8)	6 (46.2)	0.342	0.429	[0.073-2.500]
	> 7 days	3 (33.3)	6 (66.7)			
Total Parenteral Nutrition given	Yes	0 (0)	3 (100)	0.323	-	
	No	10 (25)	30 (75)			
Malnutrition	Yes	0 (0)	9 (100)	0.063	-	
	No	10 (29.4)	24 (70.6)			
Sepsis	Yes	7 (17.5)	33 (82.5)	**0.001**	-	
	No	3 (100)	0 (0)			

OR: Odds Ratio; CI: Confidence Interval

association between birth weight and neonatal survival. This is in agreement with the study conducted in Ghana describing the negative effect of low birth weight in neonates with surgical conditions [14].

Malnutrition was a predicting factor of mortality among neonates with non-gastroschisis conditions. The corresponding result also reported malnutrition among the factors predisposing to neonatal surgical mortality [21]. Malnutrition is

Table 4. Determinants of survival among neonates with non-gastroschisis surgical conditions

		Survivor N (%)	Died N (%)	p-value	OR	95% CI
Province	Kigali	9 (90)	1 (10.0)	0.310	-	-
	Northern	5 (62.5)	3 (37.5)			
	Southern	2 (50)	2 (50.0)			
	Eastern	4 (44.4)	5 (55.6)			
	Western	5 (62.5)	3 (37.5)			
Gender	Male	18 (66.7)	9 (33.3)	0.617	1.429	0.353-5.788
	Female	7 (58.3)	5 (41.7)			
Gestational Age	Term	24 (77.4)	7 (22.6)	**0.001**	24.000	2.509-229.561
	Preterm	1 (12.5)	7 (87.5)			
Age at admission	<24 hours	1 (33.3)	2 (66.7)	0.326	-	-
	24-48 hours	8 (57.1)	6 (42.9)			
	>48 hours	16 (72.7)	6 (27.3)			
Birth weight	<2500g	3 (27.3)	8 (72.7)	**0.003**	0.102	0.021-0.509
	≥2500g	22 (78.6)	6 (21.4)			
Disposition	Ward	19 (67.9)	9 (32.1)	0.362	-	-
	Pediatric Intensive Care Unit	6 (60)	4 (40.0)			
	Neonatal Unit	0 (0)	1 (100)			
Operated	Yes	19 (73.1)	7 (26.9)	0.098	0.316	0.078-1.271
	No	6 (46.2)	7 (53.8)			
Enteral Feeding	<48 hours	23 (74.2)	8 (25.8)	**0.006**	-	-
	≥48 hours	2 (66.7)	1 (33.3)			
	No feeding	0 (0)	5 (100)			
Total Parenteral Nutrition given	Yes	1 (33.3)	2 (66.7)	0.248	4.000	0.329-48.656
	No	24 (66.7)	12 (33.3)			
Surgical Site Infections	Yes	5 (83.3)	1 (16.7)	0.518	0.467	0.044-4.895
	No	14 (70)	6 (30.0)			
Malnutrition	Yes	1 (20.0)	4 (80.0)	**0.028**	9.600	0.951-96.922
	No	24 (70.6)	10 (29.4)			
Sepsis	Yes	6 (35.3)	11 (64.7)	**0.001**	11.611	2.410-55.939
	No	19 (86.4)	3 (13.6)			
Ventilation	Yes	4 (36.4)	7 (63.6)	**0.024**	5.250	1.175-23.457
	No	21 (75.0)	7 (25.0)			

OR: Odds Ratio; CI: Confidence Interval

associated with increased intestinal permeability and a decrease in villous height in the postoperative period. All of these lead to poor gastrointestinal tract intolerance and functions, increasing the risk of sepsis and infections. In general, malnutrition can be reversed by enteral feeding or parenteral nutrition support. In the period of our study, TPN was not well available due to the cost and availability of resources. Different studies reported TPN to decrease neonatal malnutrition as nutritional support and increase survival rate [22,23].

Sepsis and the need for mechanical ventilation were the significant factors associated with mortality in non-gastroschisis conditions. This is similar to the findings from other resource-limited settings highlighting sepsis and the need for mechanical ventilation as significant predictors of neonatal death [2]. The lack of adequate ventilation, specifically for neonatal ventilation in resource-limited settings, may also impact neonatal survival, leading to higher mortality rates [14]. In the bivariate analysis, sepsis was associated with mortality significantly regardless of the type of diagnosis, and this is in line with the findings from Nigeria and Alexandria [1,6].

During the analysis looking at predictors of mortality in our patient population, sepsis was significantly associated with neonatal death. The higher likelihood of having neonatal sepsis among neonates with gastroschisis could be explained by the clinical aspect of gastroschisis that exposes bowel surfaces to the external environment leading to an inflammatory process making the neonates more susceptible to microbial invasion. Additionally, the poorly developed gastrointestinal tract (mucosal integrity) of preterm neonates leads to feeding intolerance and the development of malnutrition and susceptibility to infection, a composite of which is also associated with neonatal mortality [24,25]. Surgical neonatal sepsis is still a burden in our hospital and represents a high number of neonatal mortality rates, as presented in our study

The main limitation of our study is the relatively small sample size and being a facility-based study, which limits its generalizability to represent the country and also lowers the statistical power. Also, our study was not powered enough to exclude confounders such as malrotation, atresia, necrosis, and perforation from causes of mortality among neonates with gastroschisis. Yet, these conditions are documented to complicate 25% of gastroschisis [13].

CONCLUSION

This study showed that neonatal surgical mortality is still a health burden with factors such as infections/sepsis. This suggests the need to look for the sources of infections or sepsis among all surgical neonates and assess if the infection prevention and control protocol is well implemented. These could help to improve neonatal surgical mortality due to sepsis. Here, further research on the source of sepsis is needed.

We recommend encouraging pregnant women to attend prenatal visits regularly and get scanned to rule out congenital anomalies for the fetus's well-being. This will improve in having a high number of premature and low birth weight neonates.

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