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Risk factors for severe early neonatal morbidity among term neonates admitted at Muhimbili National Hospital, Tanzania: A nested case control study

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Abstract: *Background:* Early-neonatal problems are most likely in the early term. The first-week accounts for 75% of the 4 million neonatal deaths worldwide. Mortality is greater for very sick neonates. More research is done on premature babies' risk of severe early-neonatal morbidity. Term neonates are healthier due to physiological maturity; their risk factors vary. A study of term neonates admitted at MNH Neonatal Care Unit within seven days of delivery identified significant morbidity risk factors.
Methods: All term neonates admitted within seven days of delivery from September to December 2014 were studied in a nested case -control study. We collected and followed up using the MAIN-score checklist. Dead morbidity items during seven days of delivery separated severe from less severe-morbid babies. Neonatal unit case notes, RCH4 cards, delivery records, and mother interviews gave data. Univariate regressions calculated severe morbidity risks and clinical significance of risk factors using odds ratios and 95% CIs. A multivariate analysis identified independent risk factors for severe morbidity. P -values under 0.05 were significant. Ethical approval came from Muhimbili National Hospital and the MUHAS Senate Research and Publication Committee.
Results: Of 2104 babies admitted to MNH-NCU during the experiment, 1624 didn't meet the requirements. Out of 463 term newborns, 220 (47.5%) suffered substantial early neonatal morbidity. Term babies had 255.7/1000 early neonatal morbidity. UTI during pregnancy and low-term birth weight independently predicted severe early neonatal morbidity.
Conclusion: Many term infants without congenital abnormalities showed high early neonatal morbidity, requiring further study. Further studies should discover more risk factors.

Keywords: Severe Early Neonatal Morbidity, Neonates, Fetal and Neonatal Factors.

Résumé: *Contexte:* Les complications néonatales précoces surviennent le plus souvent chez les nouveau-nés à terme. La première semaine représente 75 % des 4 millions de décès néonatals dans le monde. La mortalité est plus élevée chez les nouveau-nés gravement malades. La plupart des recherches se concentrent sur le risque de morbidité néonatale sévère chez les prématurés, tandis que les nouveau-nés à terme, grâce à leur maturité physiologique, présentent des facteurs de risque différents. Une étude sur les nouveau-nés à terme admis à l'unité de soins néonatals du MNH dans les sept jours suivant la naissance a identifié des facteurs de risque significatifs de morbidité.
Méthodes: Tous les nouveau-nés à terme admis dans les sept jours suivant la naissance, de septembre à décembre 2014, ont été inclus dans une étude cas-témoins emboîtée. Les données ont été collectées et suivies à l'aide de la grille MAIN-score. Les éléments de morbidité sévère au cours des sept premiers jours ont permis de distinguer les nouveau-nés gravement malades des moins sévèrement malades. Les informations prove

provenaient des dossiers de l'unité néonatale, des carnetde santé maternelle et infantile, des registres d'accouchement et des entretiens avec les mères. Des régressions univariées ont évalué le risque de morbidité sévère et la signification clinique des facteurs de risque à l'aide des odds ratios et des intervalles de confiance à 95 %. Une analyse multivariée a identifié les facteurs de risque indépendants de morbidité sévère. Une valeur de $p < 0,05$ a été considérée comme significative. L'approbation éthique a été obtenue auprès de l'hôpital national Muhimbili et du Comité de recherche et publication du Sénat de MUHAS.
Résultats: Sur 2104 nouveau-nés admis au MNH-NCU pendant l'étude, 1624 n'ont pas rempli les critères d'inclusion. Parmi les 463 nouveau-nés à terme inclus, 220 (47,5 %) ont présenté une morbidité néonatale précoce sévère, soit 255,7 pour 1000 naissances. Les infections urinaires maternelles pendant la grossesse et le faible poids de naissance à terme ont été identifiés comme des facteurs prédictifs indépendants de morbidité néonatale précoce sévère.
Conclusion: De nombreux nouveau-nés à terme sans anomalies congénitales présentent une morbidité néonatale précoce élevée, soulignant la nécessité d'études supplémentaires pour identifier d'autres facteurs de risque.

Mots-clés: Morbidité néonatale précoce sévère ; nouveau-nés à terme ; facteurs fœtaux et néonatals.

Introduction

The early neonatal period is before seven completed days of age, in which most neonatal deaths occur.[1] Worldwide, about 4 million neonatal deaths occur yearly; three-quarters of fatalities occur in the first week of life, with the highest risk on the first day.[2] Among under-five mortality, neonatal deaths increased from 37% in 2000, 41% in 2008, to 44% in 2012.[3] Over 98% of these deaths occurred in developing nations, with the highest rates in Africa.[4] The United Nations (UN) estimated that 1.6 million babies are born in Tanzania yearly. About 51,000 die in Tanzania annually, among the top five countries with the most newborn deaths in sub-Saharan Africa.[5] The neonatal mortality rate remained high at 32 per 1,000 live births, accounting for 47% of the infant mortality rate in the country. Compared to post-neonatal mortality, the slow decline in neonatal mortality calls for attention and efforts to reverse the trend.[6]

Pregnancy and delivery complications were implicated in more than half of newborn morbidity.[7] Intrapartum and immediate postnatal periods have always been essential and can pose a significant risk to both the mother and her newborn neonate.[8] Studies have shown that adverse intrapartum events were implicated in up to 23% of neonatal deaths, along with long-term impairment and disability worldwide.[9] Every year, an estimated 904000 intrapartum-related neonatal deaths occur worldwide, accounting for one-third of the early neonatal deaths, contributing to 9% of all under-5 child mortality.[8] In developing countries, nearly two-thirds of all births occur at home. Skilled care is unavailable in approximately half of the deliveries, worsening intrapartum-related morbidity and mortality. Suspected factors include maternal characteristics, pregnancy complications, intrapartum events, lack of skilled birth attendants, especially in developing countries, and neonatal factors leading to early neonatal morbidity, mortality, and long-term impairment and disability. In Tanzania, severe infections, birth asphyxia, and preterm complications are the leading causes of newborn deaths.[10] Neonates with severe neonatal morbidity were the ones at higher risk of mortality.

It can be assumed that along with every case of neonatal mortality, there were morbidity cases as well. Interventions to reduce neonatal morbidity indirectly led to a reduction in neonatal mortality. Severe morbidity of a term infant without congenital malformations is an emotionally devastating outcome for parents, caregivers, and the community.[11]

The magnitude of term neonatal morbidity admissions to NICU varies worldwide. In Canada, admission was 14.4%, while in the USA, 5-18% of term babies get admitted to NICU, and 40% of all admissions at higher-level nurseries were term babies.[12] In Northern Tanzania, 15% get admitted to the neonatal care unit (NCU).[13] This includes both term, pre-term, and post-term. Among them, neonatal deaths were around 15 percent, and the rest were treated with morbidity. At Muhimbili National Hospital, an average of 500 neonates were admitted monthly. Reasons for admissions in the MNH neonatal unit include prematurity 21.7%, birth asphyxia 21.6%, septicemia 14%, Pneumonia 1.4%, congenital anomalies 1.48%, Anemia 0.2%, routine care 31.8%, unknown 0.15, others 7.7% (MNH database 2014). Some of these neonates recover quickly and get discharged within the optimum time. However, some were born at term without congenital anomalies and still have delayed recovery and develop life-threatening conditions resulting in higher morbidity and mortality rates. Contrary to preterm and post-term, most neonates delivered at term do well and have a low prior probability of death, and severe morbidity has drawn little research attention.[11] It is the rationale that this group referred to in this study as seven extreme term neonates are the group of interest (an outcome), of which risk factors or predictors associated with their morbidity need to be established.

Methods

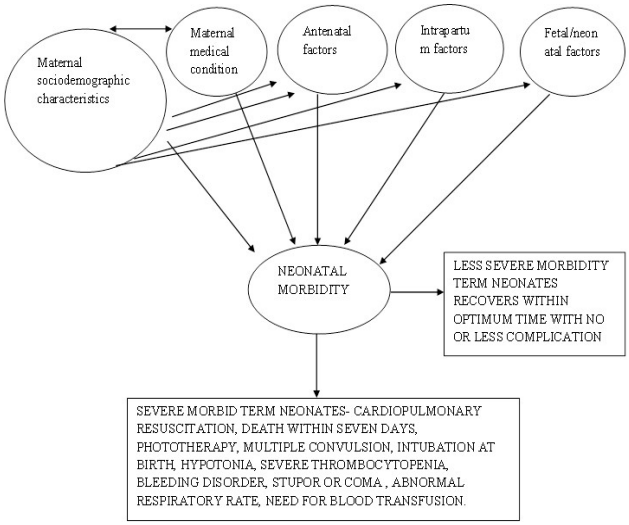
Study design and settings

A case-control study was nested in a cohort of term neonates at Muhimbili National Hospital Neonatal Care Unit. The MNH Maternity block receives most obstetric

and neonatal high-risk cases from within the hospital and referrals from private and government hospitals in Dar Es Salaam and nearby regions. It has a capacity of 356 beds, where 130 were baby cots, 22 were delivery beds, eight were maternal high-dependent unit beds, and 196 were general beds.

All term neonates admitted were followed up to their seventh day of birth, discharge, or death, depending on which came first. Neonates were then screened for indicators of severe morbidity during the period, as depicted in Figure 1 below.

Fig 1: The risk and other factors associated with neonatal morbidity.

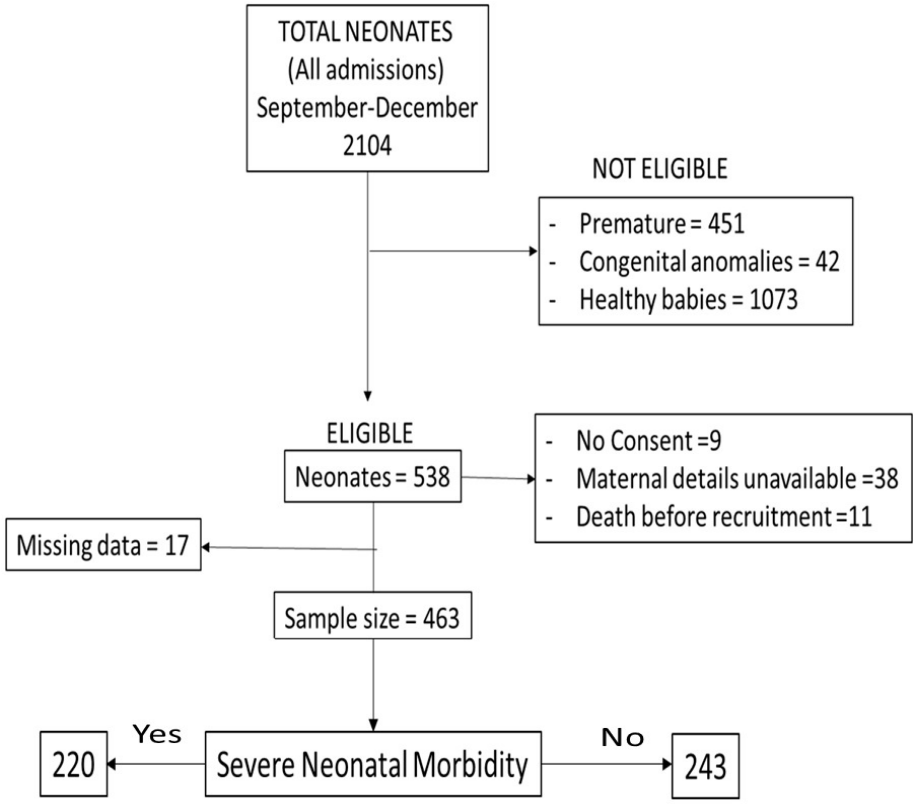


Study population Inclusion and Exclusion criteria

All ill neonates born at term or/and their mothers admitted at MNH Neonatal Care Unit, and implicitly their mothers were the target population between September and December 2014, consented and met the study inclusion criteria. Severe Early Neonatal Morbidity was defined as any admitted term neonate with at least one of the following conditions: death within the seven days of life, Multiple convulsions, Cardiopulmonary resuscitation any time before discharge, Apnea corrected by oxygen or by resuscitation, Need for intubation at birth, Hyperbilirubinemia bilirubin >250µmol/L (needing phototherapy or exchange transfusion), Hypotonia, Severe thrombocytopenia with or without the bleeding disorder, Stupor, obtundation or Coma, Abnormal respiratory rate persisting for two days or longer, Need for blood transfusion and Abnormal heart rate.

Those with gross congenital malformations, whose maternal details are not available, death, and abandoned babies were excluded from the study, as detailed in Fig 2 below.

Fig 2: The sampling design and procedure for neonates



Taking a risk estimate of 2 (odds=2: for developing severe morbidity once exposed to CS (the minimum risk by Hansen et al., 2008, a power of 80% calculated sample size is 330 (165 on each arm) using the Fleiss formula.

Data Management and Analysis

Data sources and collection tool:

A checklist was created (modified MAIN score tool), and the daily progress of the sick neonate was noted using the checklist for seven completed days, discharge or death, whichever came first. Mothers of neonates were interviewed during admission.

Resources

Training of health care providers modified MAIN score tool.

Data processing

Data was cleaned, summarized, and entered into a computer. Analysis was done using Microsoft Excel, Epi info software, and SPSS version 20.

Geographic area

The pilot study was conducted at Muhimbili National Hospital Neonatal Care Unit in Dar es Salaam after receiving ethical clearance from the Muhimbili University of Health and Allied Sciences Senate, Research and Publication Committee and permitted by the Muhimbili National Hospital, where 40 neonates and their mothers were recruited and followed up. This familiarised the research assistants with working tools, patient flow, and convenient working times. Evening hours were selected for recruitment and follow-ups when routine neonatal ward activities were minimal. An average of 2-5 eligible neonates were found to be admitted daily. Queries in the tool were identified, and amendments to the tool were made and adjusted accordingly. The original MAIN score tool was used in a pilot study, where some items were removed because they were not applicable in our setting. This resulted in a modified MAIN score tool named neonatal morbidity severity assessment tool (appended index 4).

Data analysis

Data was entered in EPI info and transferred to the SPSS computer program version 20 for analysis. An association of individual co-variates with the primary outcome (Presence of severe morbidity Yes/No) was determined on bivariate analysis. Multivariate analysis was performed to determine independent predictors of severe morbidity for term neonates by including in the final model predictor variables with a p-value of 0.1 or less on bivariate analysis. In all studies, the p-value of 0.05 or less was taken as statistically significant.

Results

Descriptive findings

Total admission was 2104 neonates. The total number of neonates who had morbidity at term with no congenital anomalies was 538. Therefore, the incidence of early neonatal morbidity at term among all admissions at Muhimbili National Hospital neonatal unit was (538/2104) x1000, which equals 255.7 per 1000 neonates. Neonates with severe morbidity were 220. Term neonates with morbidity who participated in the study were 463. Therefore, the % of babies with early neonatal morbidity at term with severe morbidity was 47.5%.

Of the 538 eligible neonates, nine did not consent,38 maternal details were unavailable,11 died before recruitment, and 17 had missing data. Therefore, the sample size analysed in our study was 463, of which 267 (57.7%) were male and 196(42.3%) were female**.** The median age of neonates was one day (Range 1-3) with SD 1.77. The Mean birth weight was 3237.62gms (Range 2100-5000) with SD 526.62. Three hundred and fifteen 315(68%) were born at MNH, and 148(32%) were from hospitals outside MNH. Of all recruited, 257 (55.5%) were born by cesarean section, and 344(74.2) were from Dar es Salaam. Majority of mothers in the study 381(82.3%) were married, multipara 266(57.5%) with primary education 244(52.5%) who were either housewives or petty traders 277(59.8). All attended antenatal clinics, of which 342(73.8%) attended four or more times. See Table 1 below.

Table 1: Socio-demographic characteristics of study participants N=463 Neonates with severe morbidity

Variables		N(%)
Age	<19	38(8.2)
	20-34	362(78.2)
	35+	63(13.6)
Marital status	Single	82(17.7)
	Married/Cohabiting	381(82.3)
Address	Temeke	127(27. 4)
	Kinondoni	108(23.3)
	Ilala	109(23.5)
	Pwani Districts	29(6.3)
	Others	89(19.2)
Occupation	Housewife	163(35.2)
	Non employed	53(11.4)
	Peasant	24(5.2)
	Petty trader	114(24.6)
	Business	43(9.3)
	Employed	66(14.3)
Education	No formal education	16(3.5)
	Primary education	244(52.7)
	Secondary education	132(28.5)
	College/University	71(15.3)
Delivery place	MNH	315(68)
	Peripheral hospital	148(32)
Neonatal gender	Male	267(57.7)
	Female	196(42.3)
Neonatal weight	200-2499g	18(3.9)
	2500-3999g	394(85.1)
	4000g	51(11)

were higher in teenage mothers than in other age groups (p=0.035). Inmost neonates with severe morbidity, their mothers were single peasants without formal education, although this was statistically insignificant, as shown in Table 2 below.

Table 2: Maternal socio-demographic characteristics with severe neonatal morbidity among neonates admitted at MNH neonatal unit. N=463

Variable	Severe morbidity NO (%)	YES (%)	P value
Age Group			
15-19	14(36.8)	24(63.2)	
20-34	201(55.5)	161(44.5)	0.035
35+	28(44.4)	35(55.6)	
Marital status			
Single	39(47.6)	43(52.4)	0.447
Married/cohabit	204(53.5)	177(46.5)	
Education level			
No formal education	6(37.5)	10(62.5)	
Std seven	126(51.6)	118(48.4)	
Secondary	71(53.8)	61(46.2)	0.568
College	40(56.3)	31(43.7)	
Occupation			
Housewife	89(54.6)	74(45.4)	
Non employed	26 (49.1)	27 (50.9)	
Peasant	6 (25)	18(75)	0.06
Petty trader	60(52.6)	54(47.4)	
Business	28 (65.1)	15 (34.9)	
Employed	34 (51.5)	32 (48.5)	

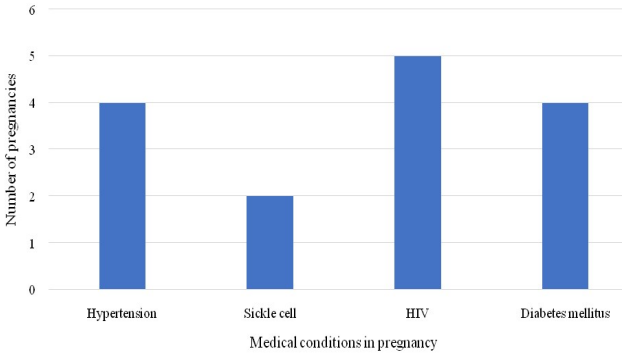
The primiparas had a primipara severe morbidity (51.6%) than those who delivered before. Mothers with previous child deaths of two or more (50%) and those women with previous abortions (48.1%) had more babies with severe morbidity. However, none of the reproductive characteristics were statistically significant (Table 3 below).

Table 3: Maternal reproductive characteristics with severe neonatal morbidity among neonates admitted at MNH neonatal unit. N=463.

Variable	Severe morbidity NO (%)	Yes (%)	P value
Parity			
Primiparas	107(48.4)	114(51.6)	0.094
Multiparas	136(56.2)	106(43.8)	
Number of parities before the index			
No	107(48.40)	114(51.60)	
1-4	131(56.20)	102(43.80)	0.246
5+	5(55.60)	4(44.40)	
Previous child death			
No	199(51.8)	185(48.2)	
1	33(57.9)	24(42.1)	0.852
2+	12(50.0)	12(50.0)	
Abortion			
No	203(52.6)	183(47.4)	0.918
Yes	40(51.9)	37(48.1)	

However, the number of mothers with medical conditions was few. Still, results showed that mothers with HIV had higher severe morbid neonates followed by non-gestational diabetes and hypertension, as revealed in Fig 3 below.

Fig 3: Maternal medical conditions with severe neonatal morbidity among neonates' mothers admitted at MNH neonatal unit from Sept-Dec 2014. N=463.



Patients attended by a doctor at ANC had fewer neonates with severe morbidity than those seen by nurses of any cadre (p=0.053). Mothers with upper urinary tract infections during pregnancy had higher rates of neonates with severe morbidity than those who did not have UTIs (p=0.001), as detailed in Table 4 below.

Table 4: Maternal socio-demographic characteristics with severe neonatal morbidity among neonates admitted at MNH neonatal unit. N=463.

Variable	Severe morbidity No (%)	Yes (%)	P value
SP given			
No	1(20.00)	4(80.00)	0.606
Yes	242(52.8)	216(47.2)	
Dewormed			
No	76(56.7)	58(43.3)	0.244
Yes	167(50.8)	162(49.20)	
ANC Attendant			
Doctor	66(60.6)	43(39.4)	0.053
Nurses of any cadre	177(50.0)	177(50.0)	
Pre-eclampsia			
No	222(51.9)	206(48.1)	0.354
Yes	21(60)	14(40)	
Eclampsia			
No	226(51.7)	211(48.3)	0.175
Yes	17(65.4)	9(34.6)	
Watery discharge			
Yes	20(66.7)	10(33.3)	0.108
No	223(51.5)	210(48.5)	
UTI			
Yes	5(20)	20(80)	0.001
No	238(54.3)	200(45.7)	
Vagina Bleeding			
Yes	10(43.5)	13(56.5)	0.375
No	233(53)	207(47)	
Malaria			
Yes	38(49.4)	39(50.6)	0.547
No	205(53.1)	181(46.9)	
Anemia			
Yes	4(50)	4(50)	0.887
No	239(52.5)	216(47.5)	
Worm infestation			
Yes	3(30)	7(70)	0.15
No	240(53)	213(47)	
Diabetes			
Yes	5(62.5)	3(37.5)	0.567
No	238(52.3)	217(47.7)	

Mothers who delivered their neonates at a peripheral hospital had more neonates with severe morbidity than those delivered at MNH (p=0.0001). Neonates referred to within 24 hours had more severe morbidity than beyond (p=0.0001), as shown in Table 5 below.

Table 5: Intrapartum events and immediate postpartum factors with severe neonatal morbidity among term neonates admitted at MNH neonatal unit. N=463.

Variable	Severe morbidity No (%)	Yes (%)	P value
Mode of delivery			
SVD	85(45.7)	101(54.3)	
LSCS	150(58.4)	107(41.6)	0.009
ABD	6(60)	4(40)	
VACUUM	2(20)	8(80)	
Assistant at delivery			
Doctor	163(57.6)	120(42.4)	
Nurse/Midwife	80(44.9)	98(55.1)	0.01
Relative	0(0)	2(100)	
Place of delivery			
Muhimbili National Hospital	190(60.3)	125(39.7)	0.0001
Peripheral Hospitals	53(35.8)	95(64.2)	
Problem during/just after delivery			
Headache			
Yes	17(73.9)	6(26.1)	0.042
No	226(51.4)	214(48.6)	
Prolonged labor			
Yes	30(41.1)	43(58.9)	0.035
No	213(54.6)	177(45.4)	
Referral duration			
Not applicable (from MNH)	191(60.4)	125(39.6)	0.0001
Within 24 hours	22(28.2)	56(71.8)	
Beyond 24hours	30(43.5)	39(56.5)	

Most neonates with severe morbidity had lower birth weight (72.2%) than those with averageable or heavy weight (p=0.014), as shown in Table 6 below.

Table 6: Neonatal factors associated with severe morbidity of term neonates admitted at MNH neonatal care unit. N=463.

Variable	Non-severe (%)	Severe (Col %)	P value
Neonatal Sex			
Male	125(46.8)	142(53.2)	0.004
Female	118(60.2)	78(39.8)	
Apgar score			
Less than seven	229(52.8)	205(47.2)	0.639
More than seven	14(48.3)	15(51.7)	
Neonatal weight (gm)			
2000-2499	5(27.)	13(72.2)	
2500-3999	204(51.8)	190(48.2)	0.014
4000+	34(66.7)	17(33.3)	

In Table 7 below, factors with a P value of 0.1 or less in bivariate analysis were entered in multivariate logistic regression. Weight of the neonate (AOR; 7.58 95%CI 1.30-44.31) and UTI in pregnancy AOR; 16.32%CI (1.65–161.43) remained independently associated with severe morbidity.

Table 7: Multivariate analysis for factors associated with severe morbidity of term neonates admitted at MNH neonatal intensive care unit. N=463

Variable	AOR	95% CI	P value
Age group			
<=19	2.27	0.19-27.14	0.028
20 – 34	.859	0.08 – 9.54	0.902
35+		1	
Parity			
Primipara	1.08	0.25 – 4.69	0.921
Multipara		1	
ANC attendant			
Doctor	0.89	0.42 – 1.9	0.761
Nurse (any cadre)	1		
Watery discharge			
Yes	2.12	0.65 – 6.96	0.215
No			
UTI			
Yes	16.31	1.65 – 161.43	0.017
No			
Mode of delivery			
Vacuum		1	0.610
SVD	0.111	0.002 – 6.49	0.289
LSCS	.09	0.001 – 6.19	0.261
ABD	0.038	0.0 – 4.732	
Assistant At Delivery			
Relative		1	0.950
Doctor	1.22	0.02 – 96.84	0.930
Nurse	0.977	0.016 – 59.27	0.991
Delivery place			
MNH	0.584	0.085- 3.99	0.583
Peripheral hospital	1		
Headache			
No	2.351	0.542 – 10.20	0.254
Yes			
Prolonged labor			
Yes	0.781	0.322 – 1.898	0.586
No	1		
Time to referral			
Beyond 24 hours			0.286
Not referred	0.966	0.13 – 7.17	0.973
Within 24 hours	2.148	0.54 – 10.20	0.132
Sex (Neonate)			
Male	1.572	0.864 – 2.859	0.138
Female	1		
Weight (grams)			
>= 4000	1		0.064
2000 – 2499	7.58	1.297 – 44.31	0.025
2500 – 3999	2.104	0.85 – 5.208	0.108

Discussion

The Morbidity Assessment Index for Newborns (MAIN) was developed as a global measure of morbidity in the

first week of life for babies with no congenital anomalies delivered at a gestation age of more than 28 weeks. The MAIN score tool was based on items of routine clinical and laboratory examinations of newborns. The MAIN score tool had already been validated for use.[14] However, this tool was seldom used in resource-poor settings.

We adopted the MAIN score index from 47 items to 37 and later re-adapted it to 27 clinically relevant items, and a modified MAIN tool was developed. A checklist of all these 27 items was administered daily for seven days. A composite of neonatal morbidity was created, and neonates were assigned their appropriate severity status. This new modified MAIN tool was significantly shortened and cheaper regarding resources. The use of the modified MAIN tool solely as a measure of severe morbidity was avoided since the new modified tool's performance had not been validated.

Our study revealed that the incidence of early neonatal morbidity at term among all admissions at the MNH Neonatal unit for four months was (538/2104) x1000, which equals 255.7 per 1000 neonates. This finding is far higher than that of other published studies. In a study of severe neonatal morbidity of term neonates without congenital anomalies in the Netherlands, the incidence was 3-4 neonates per 1000 term neonates.[11] This could be due to differences in neonatal unit setups. Only neonates with life-threatening conditions were admitted to level three neonatal care units, hence the low number. All sick neonates were mixed in the same neonatal unit in our setting. In another study comparing the morbidity of term and late pre-term neonates, the incidence of term neonates was found to be (0.3/1000) in Atlanta.[15] Developed countries are far better in quality of care than developing countries due to the availability of equipment and expertise; hence, fewer complications during antenatal, intrapartum, and immediate postpartum are expected. This could be another reason for the low incidences of severe morbidity in these two studies compared to the findings noted. The alarming incidence of neonatal morbidity of term neonates at MNH Neonatal Care Unit was possibly due to a scarcity of functioning neonatal care units at peripheral hospitals in the region and nearby regions, necessitating most cases being referred to this centre. The lack of expertise, drugs, and equipment for neonates is partly the reason for more referrals for neonatal care at MNH.

Earlier studies have defined severe morbidity in term neonates.[16, 17] We adapted these and defined our severe morbidity in term neonates as any admitted term neonate with at least one of the following conditions: death within the seven days of life, Multiple convulsions, Cardiopulmonary resuscitation any time before discharge, Apnea corrected by oxygen or by resuscitation, Need for intubation at birth, Hyperbilirubinemia bilirubin >250µmol/L (needing phototherapy or exchange transfusion), Hypotonia, Severe thrombocytopenia with or without the bleeding disorder, Stupor, obtundation or Coma, Abnormal respiratory rate persisting for two days or longer, Need for blood transfusion and Abnormal heart rate.

We found that the proportion of neonatal severe morbidity at term was 47.5%. This finding was higher than that of other studies on severe morbidity. A study done in Atlanta had a proportion of 2.5% (Shapiro-Mendoza et al., 2008). A study in the Netherlands found a proportion of 17.1%.[11] A recent study was done in Washington 5% -18%.[12] The proportions were lower compared to our study due to similar reasons as could be due to differences in study settings. They are high-level neonatal units with fewer referrals and fewer admissions than our setting. The low proportion of severe neonatal morbidity in developed countries may also be due to the availability of equipment and expertise. Only some studies on the severe morbidity of term neonates are available in developing countries to compare with ours. A study in Northern Tanzania examined neonatal admission to ICU risk factors.[13] The proportion of neonates admitted was 15%. However, the methodology was different; although diagnostic criteria were admission to the neonatal intensive care unit, it was a disease-specific study, and term neonates were not dealt with separately as in our study.

Urinary tract infection was independently associated with severe early neonatal morbidity of neonates admitted at the MNH neonatal care unit. These neonates were about 16 times at higher risk of severe early neonatal morbidity. This outcome was also like a study done in the UK by Murphy et al.[18] and another study by Osorno et al.[19] even though these are related to poor outcomes among the neonates and not severe morbidity. This could be due to differences in the study setting and the methodology used. Another study done in Israel showed that Maternal UTI is independently associated with preterm delivery, pre-eclampsia, intra-uterine growth restriction (IUGR), and cesarean deliveries (CD). Nevertheless, it was not associated with increased perinatal mortality rates compared with women without UTI.[20]

Many other studies associated UTI with adverse pregnancy and neonatal outcomes, including low birth weight, premature rupture of membranes, intrauterine growth restriction, and even death.[21-23] The mechanism of UTIs causing PROM was believed to be the release of metalloproteinases by macrophages via cytokines, which similarly degrade the membranes as collagenases and phospholipase are issued from bacteria.[21] Maternal UTI was also associated with neonatal sepsis.[24] This study also observed that neonates born with a birth weight below 2500 grams were independently associated with severe early neonatal morbidity. These infants were classified as having low birth weight.[25] Another observation also strengthens this in a setting in Nigeria that showed birth weight was a significant predictor of neonatal mortality.[26, 27] Similar findings were in a setting in Canada where morbidity and mortality were found to increase among term neonates who were born with a birth weight below the 3rd percentile of their gestation age. The study further showed low birth weight related

to a lower five-minute Apgar score, high incidence of seizures in the first 24 hours of life, increased risks of need for intubation at the delivery room, increased risk for neonatal sepsis, and mortality.[21]

Conclusion

The proportion of early neonatal morbidity at term among all admissions at Muhimbili National Hospital neonatal unit was high (538/2104) x1000, which equals 255.7 per 1000 neonates. The proportion of babies with severe morbidity among those with early neonatal morbidity at term was 47.5%. This study revealed that the severity of illness in the early neonatal period is independently associated with maternal urinary tract infection during pregnancy and low birth weight of term neonates. That attention to the term neonate is equally essential to the preterm/Low Birth weight neonate.

Limitation and Mitigations

Due to a lack of resources in our setting, the MAIN tool had to be modified. So, we used the Modified MAIN tool. This needs to be validated. This tool cannot be compared with the MAIN tool since it differs by 20 items. We have only used this Modified MAIN tool for research purposes, and its clinical application will require extensive studies for validation. Discrimination of neonates to severe morbidity was done by creating a composite of neonatal morbidity obtained from modified MAIN tool items where the presence of 1 or more items was diagnostic.

Intrapartum predictor assessment for mothers who delivered their baby outside MNH may be limited since some were not referred with their partograph and had poorly filled or no referral letter. However, this was controlled by including items in the questionnaire, which captured the information needed.

Recommendations

Severe early neonatal morbidity of a term neonate with no congenital anomaly had a very high incidence at MNH. This high morbidity warrants further investigation. Longer-term outcomes, including growth and development, were not done, and there is a need for this to be done.

More resources, both human resources and types of equipment such as CPAP, should be invested in the district hospitals to avoid transfers. The Modified MAIN tool needs to be further validated in low-resource settings. In that context, comparing the performance (sensitivity, specificity, negative and positive predictive value) of the modified tool used in this study to the original MAIN tool is needed. It can only be done in centres where both can be compared.

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Authors' contributions

FA was involved in the conceptualisation and design of the study, data collection, interpretation, and information feedback. IMS was involved in data entry, cleaning, and analysis. The PM was involved in logistics, conceptualisation, design of the study, data collecting tool, analysis, interpretation, flow arrangement of the work, and revising. KM was involved in the working plan, data analysis, interpretation, and critique work revising on the neonate's part and participated in manuscript writing.

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