Clinical Profile of Neonatal Admissions at Prince Rashid bin Al-Hassan Hospital

Alaa Al Tawalbeh, MD, JB. Ahmad Sharadgah, MD, JB*. Mahera Malkawi, RN**. Kahrman Shawagfeh, RN**. Alaeddin Ali Saleh, MD, JB**

ABSTRACT

Objective: To determine the indications, clinical profile, and outcomes of neonatal admissions at Prince Rashid bin Al-Hassan Hospital.

Methods: Retrospective study of all neonates admitted to the neonatal intensive care unit (NICU) between January 1, 2016, and September 30, 2017. Collected data included gender, gestational age, birth weight, mode of delivery, clinical indication for admission, and discharge outcomes. All data was entered into a Microsoft Excel spreadsheet and analyzed using IBM (SPSS) Statistics version 26.

Results: A total of 2120 newborns were admitted to the NICU during the study period; 1551 (73.2%) were inborn and 569 (26.8%) out born. Of the 2120, 1117 (52.6%) were male and 1003 (47.3%) were female;1172 (55.3%) were term neonates and 948 (44.7%)preterm neonates; 55 were neonates with extreme low birth weight (ELBW), 153 were very low birth weight (VLBW), and 662 were low birth weight (LBW). Cesarean section delivery accounted for 60.6% of all admitted neonates. The most frequent clinical indications leading to admission were preterm and respiratory distress syndrome (43%), transient tachypnea of newborn(TTN) (16%), neonatal sepsis (15%), birth asphyxia (9.1%), and neonatal jaundice (7.2%). Early onset sepsis (EOS) and late onset sepsis (LOS) represented (56.4%) and (43.6%), respectively, of all proved cultures. *Staphylococcus aureus*, *Klebsiella* pneumoniae, and *Escherichia coli* were the most common isolated organisms leading to sepsis.Prematurity, neonatal respiratory distress syndrome (RDS), and neonatal sepsis were the most common risk factorsleading to death. The mortality rate was (7.5%) of all admitted newborns during our study period.

Conclusion: Prematurity, RDS, and neonatal sepsis were the significant clinical indicators leading to neonatal morbidity and mortality.The most common isolated organisms leading to neonatal sepsis were *Staphylococcus aureus* and *Klebsiella.*The majority of admitted neonates were term and latepreterm infants delivered by cesarean section.

Keywords: NICU admissions, Neonatal mortality, Neonatal outcomes, Early and Late onset sepsis.

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Introduction

The neonatal period is the most critical phase of life and is associated to risk for various diseases due to vulnerability during the period of physiological adjustment to adapt for life outside the uterus[1]. Survival rates of new borns highlight the development and quality of the healthcare system.

From the Departments of:
*Pediatric department.
** registered nurse.
Corresponding author: Dr. Ahmad Zaid Sharadgah MD,E-mail:studentahmad2@yahoo.com
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Overthe last two decades, developed countries have achieved a significant improvement in neonatal management, leading to increases survival rates of newborns as compared to those in developing countries, where both morbidity and mortality are higher[2].

Globally, UNICEF and the World Health Organization (WHO) estimated that about5.4 million deaths occurred in 2017 of children under 5 years. Significantly, the highest risk reportedly came in the first month of life, with2.5 million newborns dyingin the first month after birth, representing 47% of deaths at age below 5 years, compared to 29% and 25% of deaths occurring between 1 and 11 months and 1 and 4 years, respectively. The majority of newborn deaths occurred in developing and low-income countries with a mortality rate of 69 deaths per 1000 live births, in comparison witha lower mortality rate of 5.4 deaths per 1000 live births in developed countries[3].

Research points to various factors leading to neonatal mortality and morbidity. The most common causes of neonatal death include preterm birth, low birthweight, and congenital anomalies[4]. Infants withpreterm birth before 37 weeks and low birthweight are susceptible to serious medical complications associated withthe immune system, birth asphyxia, cardiovascular disorders, the gastrointestinal system, respiratory distress syndrome, and chronic lung disease[5, 6]. Furthermore, gestational age (GA) has been identified as a significant predictor of mortality and as extremely associated with chronic heart disease and respiratory problems[5]. Also, congenital anomalies lead to functional or structural disorders influencing mortality and morbidity rates of neonates. Commonly, heart defects, neural tube defects, and Down syndrome are the most severecongenital anomalies [7]. In addition, infections are among the major causes leading to neonatal death and are associated with 27% of neonatal deaths in developing and low-income countries, as compared with 4% of mortality in developed countries [6, 8]. However, most of the factors influencing neonatal mortality are potentially preventable and could be avoided by adequate neonatal care. Accordingly, the WHO has establishedsustainable development goals (SDGs) to beachieved by the year 2030[9]. These goals aim to reduce the neonatal mortality rate to less than 12 per 100 live newborns. Based on Jordan statistics data issued by UNICEF for2019, the infant mortality rate was 13 per 1000 live births, while neonatal mortality rate was 9 per 1000 live births [10].

Early diagnosis and proper management of neonatal intensive care units (NICUs) leads to improved survival rates and therapeutic outcomes with fewersevere morbidities[11]. Therefore, it is essential to study the admission rate and variability of preventable and treatable neonatal cases. This study aims to determine the indications, clinical profile and prevalence of the NICU admission rate at Prince Rashid bin Al-Hassan Hospital.

Methodology

A retrospective study was conducted at the NICU of Prince Rashid bin AL-Hassan Hospital from January 1, 2016, to September 30, 2017. Inborn and outborn admissions during the study period were included. Collected data included gender, birth weight, maternal age, gestational age, mode of delivery, respiratory support, sepsis, culture results, initial diagnosis, days of admission, discharged weight, and cause of deaths. All data was entered into Microsoft Excel and analyzed by IBM (SPSS) Statistics version 26.Analyzed data was presented as frequency distributions and percentages for categorical variables.Student's *t*-test and ANOVA were applied to examine the significance level for

continuous normally distributed variables. The normality of the distribution of data was tested using the Kolmogorov–Smirnov test.

Collected data was documented based on pretested variables; newborns were categorized based on gestation age into preterm neonates delivered before completed 37 weeks,whileterm neonates delivered at gestational age of 37 to 42 completed weeks[12]. Birth weight of neonates was categorized according to the WHO classification into low birth weight (LBW) less than 2500 grams, very low birth weight (VLBW) less than 1500 grams, and extreme low birth weight (ELBW) less than 1000 grams[13].

Respiratory Distress Syndrome (RDS) occurred when neonate's lung not completely developed and cannot provide enough oxygen. Diagnosis is based on oxygen level and chest X-ray findings of hyaline membrane or surfactant deficiency disease[14].

Transient Tachypnea of newborn (TTN) is a breathing disorder seen shortly after delivery, occurred by a delay in the clearance of fetal lung fluid after birth. Leading to tachypnea represented by faster breathing more than normal, ineffective gas exchange and associated with early RDS [15].Also, Birth asphyxia is defined based on WHO as the failure to initiate and sustain breathing at birth [16]. Meconium aspiration syndrome (MAS) is a clinical condition which characterized by respiratory complications occurred by meconium-stained amniotic fluid[17].Neonatal hyperbilirubinemia is a clinical condition when bilirubin increased above the normal level. Hyperbilirubinemia was diagnosed and managed according to AAP guidelines[18].

Cause of death was identified and recorded based on neonatal death report issued by pediatric specialist. Total number of deaths was used to calculate mortality rate.

Results

A total of 2120 neonates were admitted to the NICU during the study period. The demographic profile in **Table I** shows that 52.6% of admitted neonates were males and 47.3% were females. Inborn and outborn admitted neonates accounted for 73.2% and 26.8%, respectively. A total of 1930 (91%) neonates were admitted within the first 7days of birth. Preterm neonates accounted for 44.7%, while term neonates accounted for 55.3%. Delivery mode showed cesarean delivery associated with 1285 (60.6%) of total admitted cases.

Table I: Characteristic of Admitted Neonates (*n=2120)*

Parameters	Variables	Number	Percentage
Gender	Male	1117	52.6%
	Female	1003	47.3%
Place of Birth	Inborn	1551	73.2%
	Outborn	569	26.8%
Age at Admission	< 7 days	1930	91%
	> 7 days	190	9%

Gestational Age	Preterm	948	44.7%
	Term	1172	55.3%
Birth Weight	ELBW	55	2.6%
	VLBW	153	7.2%
	LBW	662	31.2%
	>2.5kg	1250	59%
Mode of Delivery	VD	835	39.4%
	CS	1285	60.6%

Abbreviations

ELBW: Extreme Low Birth Weight, VLBW: Very Low Birth Weight, LBW: Low Birth Weight
VD: Vaginal Delivery, CS: Caesarean section

Common morbidity-based admissions patterns in the NICU are summarized in **Table II** below. Preterm and respiratory distress syndrome (RDS) were the significant indicators leading to NICU admissions, accounting for 43% of total admissions cases. In addition to that, transient tachypnea of newborn (TTN) and suspected neonatal sepsis were associated to 16% and 15% of admissions, respectively. Birth asphyxia was reported among 193 neonates and accounted for 9.1%, while hyperbilirubinemia was observed among 153 neonates (7.2%).

Table II: Morbidity-based Admissions Profile(*n=2120)*

Cause	Admission	Percentage
Preterm/RDS	912	43%
TTN	339	16%
Neonatal Sepsis	318	15%
Birth Asphyxia	193	9.1%
Neonatal jaundice	153	7.2%
MAS	53	2.5%
Congenital Pneumonia(Infection)	38	1.8%
Post term	36	1.7%
Neural tube defects	21	1%
HIE	19	0.9%
Esophageal atresia	17	0.8%
Others	21	1%

Furthermore, the incident of neonatal sepsis was defined based on bacterial isolation from blood or cerebrospinal fluid (CSF) samples. Bacterial isolates causing neonatal sepsis are shown in **Table III**.

Table III: Isolated Pathogens from Proved Positive Cultures(*n=266)*

Bacterial Isolates	Number	Percentage
Staphylococcus aureus	95	35.55%
Klebsiella pneumoniae	78	29.2%
Escherichia coli	42	15.70%
Staphylococcus epidermidis	16	6.05%
Acinetobacter	11	4.19%
Enterobacter	8	3.02%
Pseudomonas	8	3.0%
Streptococcus sp	5	1.83%
MRSA	3	1.46%

Proved positive cultures were reported in 266 cases among our study. The most common microorganisms isolated were *Staphylococcus aureus* and *Klebsiella* pneumoniae, which significantly caused 35.5% and 29.2% of neonatal sepsis. Also, *Escherichia coli* associated with 15.7% of neonatal sepsis compared to *Staphylococcus epidermidis* 6%. In addition, *Acinetobacter*, *Enterobacter*, *Pseudomonas*,and *Streptococcus* were reported. Three samples were positive formethicillin-resistant *Staphylococcus aureus* (MRSA).
Furthermore, the distribution of culture positivity according to gender shows that 64% of positive cultures were associated to male neonates as compared to 36% for female neonates.

Table IV: Blood Culture Positivity-based Gender and Age(*n=266)*

Result	Male	Female	Total
Culture positive	171 (64%)	95(35.7%)	266 (12.5%)
Age <7 Days			
Gram-positive 38%		Gram-negative 62%	
Age >7 Days			
Gram-positive 39.65%		Gram-negative 60.34%	

Neonatal sepsis was classified based on onset symptoms. Early onset sepsis (EOS) within the first 7 days of life accounted for 56.4%, while late onset sepsis (LOS) after 7 days of birth was associated with (43.6%). **Table V** represents the isolated microorganisms in EOS and LOS.

Table V: The Distribution of Organisms in Early and Late-onset Sepsis

Organisms	Early onset (*n= 150*)	Late onset (*n= 116*)
Staphylococcus aureus	55 (36.66%)	40 (34.48%)
Klebsiella pneumoniae	43 (28.66%)	35 (30.17%)
Escherichia coli	31 (20.66%)	11 (9.48%)
Pseudomonas	5 (3.33%)	3 (2.58%)
Staphylococcus epidermidis (CoNS)	0 (0.0)	16 (13.79%)
Streptococcus sp	2 (1.33%)	3 (2.58%)
Acinetobacter	8 (5.33%)	3 (2.58%)
Enterobacter	6 (4.0%)	2 (1.72%)
MRSA	0 (0.0%)	3(2.58%)

The length of stay for NICU admissions is shown in **Table VI**. The majority of admissions (80%) stayed at the NICU for approximately1 week, while 36% of total admission cases were hospitalized for 3 days only. Only 5.5% of neonates were admitted for 24 hours.

Table VI: Distribution of Neonate's Hospitalization

Length of Stay	Total Number	Percentage
<24 Hours	117	5.5%
2–3 Days	775	36.6%
4–7 Days	827	39%
8–14 Days	170	8%
15–28 Days	212	10%
>28 Days	19	0.9%

In addition, discharge statistics showed that 1935 of total admitted neonates were discharged alive from the NICU, compared to 160 neonatal deaths and 25 cases that were transferred to a tertiary hospital. The obtained overall neonatal mortality rate (NMR) was 7.5%, as shown in **Table VII**.

Table VII: Outcomes of Discharged Neonates

Status Upon Discharge	No. of Neonates	Percentage
Live Neonates	1935	91.3%
Dead Neonates	160	7.5%
Transfer to Tertiary Hospital	25	1.2%

The distribution of risk factors causing death are presented in **Table VIII**. Prematurity and RDS were the significant risk factors leading to death and associated with 30% and 51%, respectively. Neonatal sepsis and congenital anomalies were reported to cause 14% and 3.2% of total deaths among our study.

Table VIII: Leading Factors of Neonatal Mortality

Cause of Death	No. of Deaths	Percentage
Respiratory distress	83	51.8%
Prematurity	49	30.6%
Sepsis	23	14.4%
Congenital anomalies	5	3.2%

Discussion

Among all neonatal admissionsduring the period of our study, the leading indicators for morbidity and mortality were prematurity and RDS. Along with TTN, neonatal sepsis, birth asphyxia, and hyperbilirubinemia were common causes of admissions. In addition, 60% of admitted neonates were delivered by cesarean section, significantly increasing the risk of respiratory problems.Approximately 50% of infants delivered by cesarean section required respiratory support compared to 12% of those withnormal deliveries[19, 20],highlighting the guidelines of the American College of Obstetrics and Gynecology (ACOG) that do not recommended elective delivery before gestation age of 39 weeks [21].

Furthermore, our findings are comparable to those of Sivasubramaniam et al.,who described the outcomesof Jordanian newborns admitted to a NICU at Al-Bashir Government Hospital, concluding that RDS and prematurity were the most common indicators for neonatal admissions (67%) and mortality (52%). Also, neonatal sepsis was reported in10%, jaundicein5%, and birth asphyxia in 4%[22].

In the current study, the obtained incident rate of proved neonatal sepsis was 12.5% within all neonatal admissions. Gram-negative bacteria were the main microbial isolates causing infection in both EOS and LOS, contributing 62% and 60% of all positive cultures, respectively. *Staphylococcus* aureus,*Klebsiella pneumoniae,*and *Escherichia coli* were the most common isolated pathogens. Furthermore, EOS was associated with 56.4% of neonatal sepsis, while LOS represented 43.6%. Median hospital stays for EOS and LOSwere reported as6.4 and 7.6 days. Moreover, the obtained incident and epidemiologic trend of neonatal sepsis is comparable with a 2015 study by Shehab El-Din et al., who reportedthe incident rates for LOS and EOS were45% and 55%, respectively.*Staphylococcus* aureus and *Klebsiella pneumoniae* were the predominant isolated pathogens causing EOS and LOS sepsis[23]. Also, Khasawneh et al. demonstrated in a 2020 study that streptococcus (GBS) and *Klebsiella pneumoniae* were the most common isolated microorganisms leading to EOS and LOS[24]. In addition, Al-Matary et al., in a 2019 study in King Fahad Medical City (KFMC), found that the risk of neonatal sepsis at EOS was 12% and at LOS was 88% among all positive cases. Streptococcus (33%) and E. *coli* (27%) were the most causative organisms for EOS,while *Staphylococcus* aureus (60%) and *Klebsiella pneumoniae* (17.5%) were the most frequent detectable pathogens at LOS [25]. However, inverse relationship was found between incidence rate of sepsis and gestational age and birth weight,putting premature neonates at higher risk of sepsis-associated mortality. Globally, sepsis-related mortality represented about30% in cases of EOS and ranged from 18% to 35% for LOS [26-28].

The status upon discharge represented the obtained mortality rate(7.5%) among all admitted neonatesduring the study period.Prematurity and RDS were the main causes leading to deaths (132/160); likewise, sepsis and congenital anomalies were associated with 23/160, 5/160 correspondingly.

On the other hand, Sivasubramaniam et al. in 2015 reported a higher mortality rate (8.7%) among admitted neonates at Al-Bashir Hospital. Similarly, the most frequent causesassociated with noenatal deaths were RDS (50%), prematurity (40%), and sepsis (9%)[22]. Also, Khasawneh et al.in 2020 demonstrated a lower neonatal mortality rate (3.5%) and reported the major cause for neonatal deaths was extreme prematurity (30/55) [11].

In parallel, Batieha et al. in 2016 found that neonatal mortality was 12% of all births in Jordan. Also, RDS was reported as the main cause of mortality and related to 53% of neonatal deaths, neonatal sepsis accounted for 16.2%, and birth asphyxia represented 10% of total neonates deaths [29]. Compatible results were obtained by Baghel et al. who reported in 2016 that 55% of neonatal

mortality occurred due to prematurity, RDS (38%), sepsis (11%), and congenital anomalies (2%) [30].
Furthermore, a retrospective cohort study at The University of Texas Southwestern Medical Center was performed by McIntire et al. who declared that respiratory distress syndrome (RDS), transient tachypnea of newborn (TTN), sepsis and hyperbilirubinemia were the most common causes leading neonatal morbidity. Also, neonatal death rate was found to be 4 deaths per 1000 lives, and associated with prematurity as leading cause of mortality [31].In addition, Reuter et al. declared that prematurity, respiratory complications including respiratory distress syndrome (RDS) and meconium aspiration syndrome (MAS) were the most common causes leading to neonatal admissions and associated with 29% and 15% respectively [32]. As well as, Edwards et al. studied the neonatal admissions rate in England and Wales at Cardiff University School of Medicine. Their findings demonstrated that the most common reason for admissions were associated with prematurity and respiratory distress. Also, they reported an inverse relationship between gestational age and incidence of respiratory distress[33].

During our study, the median length of hospitalization was 4 to 7 days, which is shorter than other reported hospitalization periodsof 2 to 8 days and 5.5 to 12.5 days[22, 24]. Significantly, the longer median length of stay at a NICU influences the economic burden for healthcare providers.The estimated cost of term neonate admissionto aNICU is approximately $2500,including respiratory support, medication, and nutrition[34]. However, a dramatic increase inNICU cost has beenreported for preterm, low birth weight, and congenital anomalies neonates[35, 36]. Inour study, the median gestational age (GA) was 37 weeks, median birth weight was 2.45 kg, and the median discharge weight was 2.63 kg. The mortality rate per live births was 160/15,024,leading to 9 deaths per 1000 live births, which is in line with the recommendation of the United Nation's Sustainable Development Goals (UN SDG3) to reduce perinatal and neonatal mortality rate to fewerthan 12 deaths per live births bythe end of 2030[37]. However, NICU admissions costs have not been fully described in government hospitals in Jordan, leading to difficulties related to adequate funding in developing countries fortreating severe prematurity complications for neonates (GA < 24 weeks).
In addition to that, Infectious Diseases Society of America (IDSA), the Pediatric Infectious Diseases Society (PIDS) and National Institute for Health and Care Excellence (NICE) have recommended preventable measures to reduce infection and to ensure better management of invasive procedures within NICU. Essentially, hand hygiene-based alcohol sanitizer before and after patient contact is effective and efficient against many microorganisms[38]. Also, many studies in developing countries have confirmed that maternal breast feeding contains secretory antibodies, phagocytes, lactoferrin and prebiotics which improve host defense and gastrointestinal function and associated with lower rate of neonatal sepsis and out breaks of infection [39, 40]. As well as proper management and safe procedure of Total Parenteral Nutrition (TPN) according to the guidelines of (IDSA), (PIDS) and (NICE) should be strictly followed by healthcare providers in NICU [41]. TPN with good medical practices including medications preparation and antibiotic stewardship have significantly improve the prevention and treatment of neonatal infections [42, 43]. Furthermore, continuous education and training for healthcare personnel regarding intravascular catheter use, proper procedures for the insertion, sterilization, and update infection control guidelines have been widely recommended [44].

Conclusion

Prematurity, RDS, TTN, and neonatal sepsis were the leading clinical indicators for NICU admissions and were responsible for 74% of the morbidity profile. On the other hand, prematurity, RDS, and sepsis were the most frequent causes of neonatal deaths, leading to a 7.5% neonatal mortality rate of all admitted neonates, and 9 deaths per 1000 live births meeting the target ofUN SDG3.

Ethics Approval

An Institutional Review Board (IRB) approval was obtained from the ethical committee at Royal Medical Services.

Patient data privacy and confidentiality are maintained as this study was conducted in compliance with the ethical standards per Helsinki declaration.

Limitation of study

The main limitation of our study is that a single-center study performed at NICU in Prince Rashid bin Al-Hassan Hospital leading to limited population. In addition, our study is retrospective over a relatively short period of time. Therefore, generalization of our findings and conclusion cannot be accurately describe and present the clinical profile of neonatal admissions for the whole Jordanian population.

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