

## A COMPARISON OF MORBIDITY AND MORTALITY AMONG EARLY, MODERATE AND EXTREME PREMATURE INFANTS REPORTING IN GILGIT

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### ABSTRACT

**Objective:** To compare the morbidity and mortality among early, moderate and extreme premature infants reporting in Gilgit.

**Study Design:** Comparative cross sectional study.

**Place and Duration of Study:** Neonatal intensive care unit, Combined Military Hospital, Gilgit, from Jun 2017 to Jun 2018.

**Methodology:** Patients who had completed antenatal visits in Gynae dept and delivered premature babies were recruited in this study. Premature babies from 34 to 37 weeks of gestation are termed as late preterm, 32 to <34 weeks as moderate preterm, with 28 to <32 weeks as very preterm and extreme premature if they are <28 weeks of gestation. The variables which were included in our study were antenatal checkups, period of gestation, weight of baby, period of hospital stay, mode of delivery of oxygen and outcome in terms of being discharged or expired.

**Results:** Number of patients was 101 in this study. Males were 59 (58.4%) and females were 42 (41.6%). Mean weight of study population was  $1.81 \pm 1.67$  kg. Oxygen was given via nasal prongs to 63 (62.4%) patients, via continuous positive airway pressure to 15 (14.9%) patients, via head box to 18 (17.8%) patients and via mechanical ventilation to 5 (5%) patients. 83 (82.2%) babies survived and discharged and 18 (17.8%) expired during hospital stay.

**Conclusion:** Our study concluded that lesser the gestational age, greater is the morbidity and mortality of the preterm babies.

**Keywords:** Continuous positive airway pressure, Low birth weight, Mechanical ventilation, Preterm, period of gestation.

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### INTRODUCTION

Pre term birth is defined as any birth before 37 completed weeks of gestation calculated from first day of last menstrual cycle. Accurate calculation of gestational age is some time difficult, especially in low income countries where most of the mothers have no access to medical facilities. In comparison birth weight is easy to calculate<sup>1</sup>. Preterm babies can be further classified on the basis of weight and gestational age. Low birth weight is defined as babies with birth weight of less than 2500 grams. Babies with birth weight of less than 1500 grams are termed as very low birth

weight and extremely low birth weight babies are those with birth of less than 1000 grams. However, birth weight does not truly predict pre term mortality and morbidity. Gestational age is a true predictor of pre term mortality and morbidity. Babies with gestation age of 34 to <37 weeks are termed as late pre term, 32 to <34 weeks as moderate pre term, with 28 to <32 weeks as very pre term and extreme pre term if gestational age is less than 28 weeks<sup>2</sup>.

Pre term births are about 11% of the all births worldwide. Statistics published in 2018 stated that approximately 15 million babies are born pre term every year. In most of the countries this figure is on rise. Pre term births and its complications are not only the leading cause of neonatal mortality, but also now considered as

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the principal cause of childhood mortality up to the age 5 years<sup>3</sup>. The under 5 mortality, worldwide, during MDG 4 (Millennium Development Goals) decreased by more than 50%. Impressive decrease was observed in diseases like measles and malaria. Highest contribution of less than 5 mortality was from Africa and southern Asia. About 6 million children died under the age of 5 years in 2015. Neonatal deaths accounted for about 45% of the under 5 mortality. About 1 million children under 5 years of age died of pre term complications, making it the topmost cause of under 5 mortality<sup>4</sup>. Besides mortality, pre term birth is also a significant cause of morbidity in neonatal period and beyond. Most of the neonatal intensive care unit admissions are due to pre term babies. In different parts of Pakistan, the reported admission due to pre term births and its complications is about 23 to 48%<sup>5,6</sup>.

The care and needs of pre term babies vary greatly from that of term babies. They present with different types of problems. The common complications encounter in pre term babies are respiratory distress syndrome, intraventricular hemorrhages, necrotizing enterocolitis, hypothermia, hypoglycemia and neurological problems. These babies frequently need oxygen for respiratory distress which may result in retinopathy of pre maturity and bronchopulmonary dysplasia. Establishment of feeding is very difficult in these patients, most of the time requiring total parenteral nutrition<sup>7</sup>. However, with good neonatal care the mortality from pre term complications may be reduced. A lot of efforts have been carried out to stop pre mature labor and to prevent mortality and morbidity from complications of pre maturity. Some of these interventions have successful result but some not. For halting pre mature labor, pessaries, anti-biotics or beta 2 agonists are used with variable success. Antenatal steroids are given to the mother for fetal lung maturity. Neurodevelopmental outcome of pre term babies may be improved by giving magnesium sulfate antenatally to mother. Likewise, prophylactic probiotics may reduce the incidence of necrotizing enterocolitis in pre term babies<sup>1,8</sup>.

The rationale of our study was to conduct a study in Gilgit as premature births is a major public health problem and since it is a major cause of mortality in NICU setup. By timely addressing the risks factors of preterm morbidity and mortality we would be able to improve survival of these babies.

## METHODOLOGY

This cross sectional study was carried out at NICU of Combined Military Hospital Gilgit. The period was from June 2017 to June 2018. Sample size was calculated by using World Health Organization sample size calculator with 95% confidence interval, anticipated population proportion is 23-48% given in already published data and absolute precision required was 10%. Sample size was calculated to be 101. Sampling technique used was non probability consecutive sampling. All preterm babies delivered in hospital were included in the study. Term and post term babies, neonates with congenital anomalies and babies of non-consenting parents were excluded from the study.

Pre term baby was defined as a baby born before 37 completed weeks of gestation from first day of last menstrual period. They were further categorized into babies with gestational age <37 weeks to 32 weeks (moderate to late pre term), <32 to 28 weeks (early pre term) and less than 28 weeks (extreme pre term). Birth weight of the babies was categorized as weight more than or equal to 2500, 1500 to 2499 (low birth weight), 1000 to 1499 (very low birth weight) and less than 1000 grams (extreme low birth weight). In addition to intravenous antibiotics, supportive therapy in the form of oxygen support, fresh frozen plasma or red cell concentrate was given. Antenatal check was marked as booked if mother had more than 3 antenatal visits and unbooked if mother had not any regular antenatal visits. Outcome was regarded as discharged if baby was sent home in satisfactory condition and expired if baby died during stay in NICU. Hospital stay for each baby was considered in number of days. Appropriate radiological and laboratory

investigations were carried out to diagnose different diseases and complications of pre maturity.

Data was collected on a specially designed Proforma. Approval was taken from hospitals ethical and research committee. After explaining the purpose and benefits of the study to parents, informed consent was taken from parents of patients. Detailed history was obtained including

**Table-I: Descriptive statistics of study population.**

Parameters	Frequency (%)
<b>Weight group (kg)</b>	
>2.5	1 (1%)
1.5-2.5	71 (70.3%)
1-1.5	27 (26.7%)
<1	2 (2%)
<b>Gestational Age (Weeks)</b>	
32-36.6	70 (69.3%)
28-32	25 (24.8%)
<28	6 (5.9%)
<b>Therapy other than Antibiotics</b>	
Oxygen	89 (88.9%)
Fresh frozen plasma	9 (8.1%)
Red cells concentrates	3 (3%)
<b>Mode of Delivery of Oxygen</b>	
Nasal Prongs	63 (62.4%)
Continuous Positive Airway Pressure	15 (14.9%)
Head Box	18 (17.8)
Mechanical Ventilator	5 (5%)
<b>Gender</b>	
Male	59 (58.4%)
Female	42 (41.6%)
<b>Outcome</b>	
Discharged	83 (82.2%)
Expired	18 (17.8%)
<b>Booking Status</b>	
Booked	75 (74.3%)
Un booked	26 (25.7%)

Weight (kg) = 1.8 ± 1.67, Period of stay (days) = 7.40 ± 6.04

antenatal checkup. Exclusion criteria were strictly followed to avoid bias in the study and for controlling confounders. All cultural, social and traditional values were kept in mind.

The data was entered in SPSS-20. Qualitative variables like gender, birth weight group, gestational age, therapy other than antibiotics, mode of delivery of oxygen, booking status and outcome were measured as frequencies and

percentages. Continuous vari-ables like weight and hospital stay in days were measured by mean and standard deviation. Post stratification chi-square test was applied. A *p*-value ≤0.05 was taken significant.

**RESULTS**

Total number of patients in this study was 101. Male babies were 59 (58.4%) and females

**Table-II: Comparison between both groups.**

Parameters	Discharged (82.2%)	Expired (17.8%)	<i>p</i> -value
<b>Weight group (Kg)</b>			
>2.5	1	-	0.64
1.5-2.5	59 (83%)	12 (16.9%)	
1-1.5	22 (81.4%)	5 (18.5%)	
<1	1 (50%)	1 (50%)	
<b>Gestational Age (Weeks)</b>			
32-36.6	61 (87.1%)	9 (12.8%)	<0.001
28-32	21 (84%)	4 (16%)	
<28	1 (14.2%)	6 (85.7%)	
<b>Therapy other than Antibiotics</b>			
Oxygen	78 (87.6%)	11 (12.3%)	<0.001
Fresh frozen plasma	3 (33.3%)	6 (66.6%)	
Red cells concentrates	2 (66.6%)	1 (33.3%)	
<b>Mode of Delivery of Oxygen</b>			
Nasal Prongs	52 (82.5%)	11 (17.4%)	<0.001
Continuous Positive Airway Pressure	15 (100%)	-	
Head Box	16 (88.8%)	2 (11.1%)	
Mechanical Ventilator	-	5 (100%)	
<b>Gender</b>			
Male	49 (83%)	10 (16.9%)	0.786
Female	34 (80.9%)	8 (19%)	
<b>Booking Status</b>			
Booked	64 (85.3%)	11 (14.6%)	0.159
Un booked	19 (73%)	7 (26.9%)	

were 42 (41.5%). Mean weight (kg) of study population was 1.8 ± 1.67. Mean duration of hospital stay (days) was 7.40 ± 6.04. Regarding therapy 89 patients were given oxygen, 9 were transfused FFP and 3 were transfused RCC. Oxygen was delivered via nasal prongs to 63 patients, via head box to 18 patients, via CPAP to 15 patients and 5 patients were placed on mecha-

nical ventilation. Regarding outcome, 83 (82.2%) babies were discharged in satisfactory condition while 18 (17.8%) expired during hospital stay. 75 (74.2%) mothers had regular antenatal checkup while 26 (25.7%) did not have regular antenatal checkup as given in table-I. Stratifications was done in respect to different parameters and post stratification chi square test was applied as given in table-II.

## DISCUSSION

Among different studies done in a neonatal intensive care setup, the variables which were associated with a better outcome included female sex, exposure to antenatal corticosteroid therapy, singleton birth, and increased birth weight (per 100-g increment). Oxygen is the most common drug used in NICU. Premature babies admitted to neonatal intensive care unit (NICU) require oxygen therapy in different forms. The different modes by which oxygen may be delivered include noninvasive means like nasal flow, by head box, continuous positive pressure, face mask and invasive means like mechanical ventilation. However, oxygen is a two edge sword. It also has adverse effects if given in higher concentration than required like bronchopulmonary dysplasia and retinopathy of prematurity<sup>9</sup>. Among the patients in our study too, oxygen was the most common drug used: 88.9% patients required oxygen. Oxygen was delivered via nasal prongs to 63 patients, via head box to 18 patients, via CPAP to 15 patients and 5 patients were placed on mechanical ventilation. Pre term babies may require blood products in the form of red cell concentrate, platelets transfusion and fresh frozen plasma. Pre term babies may become anemic because of anemia of prematurity or due to frequent blood sampling. However, most of the pre term transfusions are top up transfusion. Although there are set recommendations for pre term platelets transfusion, most of the platelets transfusions are prophylactic. Likewise, most of the fresh frozen plasma transfusions to pre term are also prophylactic. A study done in 2016 in Italy and UK stated almost 63% and 42% of the fresh frozen plasma transfusions are prophy-

lactic<sup>10</sup>. However, in our study cohort the blood product transfusions trend was a bit low. Nine babies were transfused with fresh frozen plasma and 3 were transfused with red cell concentrates.

Pre term babies stay longer in hospital than term babies. The mean duration of preterm babies in our hospital was  $7.40 \pm 6.04$  days. This is some what comparable to other studies carried out in Peshawar and Karachi where the duration of stay of preterm babies ranged from 4 to 11 days<sup>11,12</sup>. The duration of hospital stay is much shorter in our study cohort as compared to some other studies. In a Nigerian study conducted in 2018, the mean duration of hospital stay for preterm babies was 17 days where 40% of the babies were very low birth weight and 13% were extreme low birth weight. In our study, only 2 babies were with extreme low birth weight and babies with very low birth weight were 27%. Similarly, in their study the gestational age ranged from 21 to 36 weeks, whereas in our study it ranged from 26 to 36 weeks<sup>13</sup>. In the literature it has been mentioned that more preterm male expire as compared to female pre termers. This female survival advantage is observed throughout life span: from in utero to adulthood<sup>14</sup>. However, this theory did not hold true for our study as 10 out of 59 male expired as compared to females of which 8 of 42 expired. No baby with more than 2500 grams expired in our study. Seventeen percent of babies in weight range of 1500 to 2499 grams 18% of the pre termers in weight range of 1000 to 1499 gram and 50% of the babies with weight less than 1000 grams expired in our study. Similar trend was observed in a study conducted in Peshawar where also mortality increased with decreasing birth weight. In that study 10% of the pre termers with weight more than 2.5 kg, 24% of the babies in weight range of 1.5 to 2.5 kg, 40% of neonates with weight between 1 to <1.5 kg and 70% of the babies with weight less than 1 kg expired<sup>11</sup>.

A Chinese study reported that most preterm babies are male as compared to female. The male patients in their study were about 60%. Our study also had male predominance with 58.4%

preterm babies being male<sup>15</sup>. Another study from Karachi revealed male to be 57% and female 43%<sup>12</sup>. Similar to our study they also divided birth weights into 4 categories. The mean birth weight in their study was  $1.88 \pm 0.5$  kg whereas in our study it was  $1.81 \pm 1.67$  kg. about 16% of the admitted neonates were with weight more than 2.5 kg, about 52% were in weight group 2.5 to 1.5 kg, 26% in weight group 1 to 1.5 kg and the remaining 6% were with weight less than 1kg<sup>12</sup>. In our study neonates with weight more than 2500 grams were 1%, neonates with age 1500 to 2500 grams were 70.3%, with weight 1000 to 1500 grams were 26.7% and with weight less than 1000 grams were 2%. The preterm mortality in their study was 14% which is somewhat comparable to our study: 17.8% babies expired in our study. The most important and statistically significant risk factor of preterm mortality observed in our study was gestational age. With increasing gestational age the preterm mortality decreased. This finding is in accordance with the published literature. A European study, carried out in multiple countries, also established the fact that gestational age is the principle predictor of preterm mortality<sup>16</sup> the same correlation of gestational age and preterm mortality has been proven in other studies too<sup>17,18</sup>.

## CONCLUSION

The most important risk factor for preterm mortality in our study was gestational age. Preterm mortality increased significantly with decreasing gestational age. However, the likelihood of a favorable outcome with intensive care can be better estimated by consideration of three other factors in addition to gestational age: male gender, birth weight and antenatal checkup.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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