Outcome of Mild and Moderate Preterm Newborns Admitted to NICU of Assiut University Children Hospital, Relation to Birth Weight

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Abstract: Prematurity and intrauterine growth restriction continues to be the major determinant of neonatal morbidity and mortality. The aim of this study was to assess morbidity and mortality of mild and moderate preterm newborns admitted to NICU of Assiut University Children Hospital, and to find out the effect of birth weight on these outcomes. Three hundreds and six preterm cases were included of which 194 were mild preterm (34-36 gestational weeks) and 112 were moderate preterm (32-33 gestational weeks). Cases with birth weight <10th percentile on growth charts were classified as small for gestational age (SGA). Cases were followed during the admission period for neonatal mortality and /or morbidity including respiratory distress (RD), need for mechanical ventilation, sepsis/meningitis, intraventricular hemorrhage (IVH), and necrotizing enterocolitis (NEC). The length of hospital stay was also recorded. Results showed that moderate preterm group had significantly higher susceptibility to RD and IVH, and higher need to mechanical ventilation than the mild preterm group. Furthermore, they showed higher rate of death and longer hospital stay than the mild preterm. There was a significant negative correlation between gestational age and length of hospital stay. According to birth weight it was noticed that SGA moderate preterm showed higher mortality rate and higher rate of IVH and sepsis/meningitis than the corresponding AGA group, while SGA mild preterm newborns had significantly lower rate of RD and higher rate of IVH and sepsis/meningitis than the corresponding AGA group. Both SGA subgroups had significantly longer hospital stay than the corresponding AGA groups. In conclusion, preterm infants especially SGA are at greater risk of neonatal morbidity and mortality. Management strategies and guidelines should be settled to prevent spontaneous preterm deliveries and to early diagnose and manage intrauterine growth restriction.

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1. Introduction:

Prematurity, defined as birth before 37 weeks gestation, is the major determinant of morbidity and mortality for newborns. Preterm births have increased 30% since 1981 and composed 12.5% of all births in some countries [(1)]. Preterm births account for 75% of perinatal mortality and more than half the long-term morbidity [(2)]. Kramer *et al.* [(3)] studied the contribution of mild (34-36 gestational weeks) and moderate (32-33 gestational weeks) preterm to infant mortality in United States and Canada. They found that, although the mortality rate of these groups was significantly lower than that of newborns whose gestational age < 32 weeks (severe preterm), yet these infants contribute substantially to over all infant and neonatal mortality. This is because these infants represent ~ 75% of total number of preterm infants and their deaths constitute much larger etiologic fraction of infant and neonatal mortality than do those who are more premature.

Evans *et al.* [(4)] found that, in addition to prematurity as the dominant risk factor of mortality, low birth weight for gestational age had a dose-response effect; the more growth restricted the infant, the greater the risk of mortality.

Advancement in the care of extremely preterm infants has led to a shift of focus away from the more mature preterm, who are being managed as near terms and treated as near normal [(5)]. The aim of this study was to assess morbidity and mortality of mild and moderate preterm newborns admitted to Neonatal Intensive Care Unit (NICU) of Assiut University Children Hospital, and to find out the effect of birth weight on these outcomes.

2. Patients and Methods

This study was conducted in the NICU of Assiut University Children Hospital in the period between January and December 2010. All admitted cases within the target gestational age range (32-36 weeks) were enrolled. Exclusion criteria included major congenital malformations, cases showed signs of intrauterine infection, and multiple births more than twin.

Prenatal data included maternal age, parity, socioeconomic state, consanguinity, medical diseases, prenatal medical care, and premature rupture of membrane. Mode of delivery, state of placenta, and multiple births were recorded. Gestational age was calculated in completed weeks from the first day of mother's last menstrual period or according to early gestational ultrasonographic report. According to the gestational age, the studied preterm cases were classified into mild preterm group (34-36 gestational weeks) and moderate preterm group (32-33 gestational weeks)(3). Birth weight and length was recorded. The birth weight was plotted against the National Center for Health Statistics charts(6) and patients had weights < 10^{th} percentile for their gestational age were classified as small for gestational age (SGA)(7). The ponderal index was calculated as follows {PI = weight (g)×100 / length $(cm)^3$}.

All cases were subjected to full physical examination and proper investigations according to their morbidity and managed accordingly. They followed up for the period of admission for neonatal mortality and /or morbidity including respiratory distress (RD), need for mechanical ventilation, sepsis/meningitis, intraventricular hemorrhage (IVH), and necrotizing enterocolitis (NEC). The length of hospital stay was recorded in completed days. The criteria for discharge from the NICU were fixed for all cases.

The study was approved by Ethical Committee of Assiut University. Collected data were coded, analyzed and computed using the Statistical Package for Social Science (SPSS) version 10. Chi-square test was used to assess differences between numerical values and student t-test was used to assess differences between continuous values. Correlations were assessed using Pearson coefficient. Differences were considered significant statistically when P< 0.05

3. Results

During the study period, 306 preterm newborns (32-36 weeks gestation) were eligible to the inclusion criteria; of which 194 were mild preterm (34-36 weeks) and 112 were moderate preterm (32-33 weeks). The demographic data and risk factors of the studied preterm newborns are shown in Table (1). In this study, the etiology of prematurity could not be precisely defined. However, depending on reviewing the maternal health record, 20.2% could be attributed to preterm premature rupture of membrane which followed by either induction of labor or cesarean delivery, 22.5% were due to medical indication (either maternal or fetal), and the remaining 57.3% were due to spontaneous preterm delivery. About 38% of the studied preterm cases were delivered by cesarean delivery of which 16% were elective cesarean delivery.

Table (2): shows the rate of adverse outcome of the studied preterm newborns according to gestational age. Moderate preterm group had significantly higher susceptibility to respiratory distress than the mild preterm group. Causes of respiratory distress included transient tachypnea of newborn, neonatal pneumonia, and respiratory distress syndrome. The majority of respiratory distress in the moderate preterm group was due to respiratory distress syndrome and lung immaturity (65/82; 79.2%), while the main cause in the mild preterm group was due to transient tachypnea of newborn (47/68; 69.1%).

Table (3): shows the rate of adverse outcome of the studied mild and moderate preterm newborns according to birth weight

Table (1): Demographic data and risk factors of the studied preterm newborns.

Demographic data & risk factors		Number (%)
Maternal factors	Mother <20 years	24 (7.8%)
	Primipara	53 (17.3%)
	Low socioeconomic	108 (35.3%)
	No antenatal care	94 (30.7%)
	Consanguinity	91 (29.7%)
	Maternal diseases	43 (14.0%)
	PROM	62 (20.2%)
	Cesarean section	117 (38.2%)
	Spontaneous preterm delivery	176 (57.3%)
Fetal factors	Sex (% male)	183 (59.8%)
	Multiple birth	115 (37.5%)
	Gestational age	
	32 – 33 weeks	112 (36.6%)
	34 – 36 weeks	194 (63.4%)
	Birth weight (mean ± SD)	1836.44 ± 421.20 g
	Small for gestational age	63 (20.5%)

Table (2): The rate of adverse outcome of the studied preterm newborns according to gestational age

	Mild preterm n = 194	Moderate preterm n = 112	P<
Respiratory distress	68 (35.5%)	82 (73.2%)	0.001
Mechanical ventilation	31 (15.9%)	59 (52.6%)	0.001
Sepsis/meningitis	47 (24.2%)	26 (23.2%)	NS
Necrotizing enterocolitis	4 (2.0%)	7 (6.2%)	NS
Intraventricular hemorrhage	27 (13.9%)	33 (29.4%)	0.05
Length of hospital stay	10.71 ± 5.2	14.34 ± 6.1	0.01
Death	24 (12.3%)	35 (31.2%)	0.01

Table (3): The rate of adverse outcome of the studied mild and moderate preterm newborns according to birth weight

	Mild preterm N= 194		Moderate preterm N= 112	
	SGA n=36	AGA N =158	SGA n=27	AGA n=85
Respiratory distress	9 (25.0%)	59 (37.3%)*	19 (70.3%)	63 (74.1%)
Mechanical ventilation	6 (16.6%)	25 (15.8%)	15 (55.5%)	44 (51.7%)
Sepsis/meningitis	12 (33.3%)	35 (22.1%)*	8 (29.6%)	18 (21.1%)*
Necrotizing enterocolitis#	1 (2.7%)	3 (1.8%)	2 (7.4%)	5 (5.8%)
Intraventricular hemorrhage	8 (22.2%)	19 (12.0%)*	12 (44.4%)	21 (24.7%)*
Length of hospital stay	12.28 ± 5.5	9.14 ± 4.9*	15.07 ± 7.1	13.61 ± 5.1*
Death	4 (11.1%)	20 (12.6%)	13 (48.1%)	22 (25.8%)*

SGA: small for gestational age AGA: appropriate for gestational age
Differences were calculated between SGA and AGA of each preterm group
* P < 0.05 ** P < 0.01
# Statistical difference could not be done due to small number of cases

4. Discussion

In this hospital based prospective descriptive study, we compared the adverse outcome of the admitted mild preterm (34-36 gestational weeks) versus the moderate preterm (32-33 gestational weeks) newborns. It was noticed that moderate preterm group had significantly higher susceptibility to respiratory distress, intraventricular hemorrhage and significantly higher need for mechanical ventilation than the mild preterm group (Table 2). Similar results were reported by Escobar *et al.*[8]. Furthermore, moderate preterm group showed higher rate of death than the mild preterm. Kramer *et al.*[3] found, in his population based study, that relative risk (RR) of infant mortality were higher among moderate preterm infants in USA (6.6) and Canada (15.2) than the mild preterm (RR were 2.9, and 4.5 , respectively).

In this study, the mean length of hospital stay was significantly higher in the moderate preterm group than the mild preterm group (Table 2). There was a significant negative correlation between gestational age and length of hospital stay (r = -0.047, P = 0.0217). Beside the more likely medical problems in the former group, further delay in discharge of these cases may be attributed to delayed establishment of breast feeding which is one criterion of discharge from our unit. It has been reported that feeding problems were the dominant reason for delay in discharge of preterm infants as immature infants are less able to achieve effective suckling and swallowing [9] . However, the larger number of cases in the mild preterm group makes the sum of admission days of this group was higher with subsequent higher cost of admission of these cases than that for the moderate preterm group. This is supported by similar findings reported by several investigators[9, 10]. Although in obstetric and pediatric practice, the mild preterm is considered functionally full term, this group of infants still pause neonatal medical problems.

It is noteworthy to mention that 16.2% of all studied cases were delivered by elective CS which was done between gestational ages 35- 36 weeks. In obstetric practice, 34 completed weeks of gestation began to be considered a maturation milestone, beyond which active interventions are rarely undertaken to prevent preterm birth (10) . Based on results reported by many investigators(9,11,12), late or mild preterm infants are at greater risks of neonatal morbidity and mortality than full term infants

Gestational age, however, is just one factor in newborn and infant morbidity and mortality; additional risk is associated with being small for gestational age. So we sub-classify each studied preterm group into SGA and AGA. Small for gestational age infants constituted 20.5% of the whole studied cases; 18.5% of the mild preterm group and 24.1% of the moderate preterm group. The association between growth restriction and prematurity has been reported(13,14). The explanation of this association may depend on the underlying condition; firstly growth restriction occurs and if the underlying pathology is severe premature labor supervenes (15) . The outcome of SGA preterm might differ than that of AGA preterm.

To study the effect of the birth weight on the adverse outcome of the preterm neonates, we compare the SGA group versus the corresponding AGA group of each gestational age group. It was noticed that the SGA moderate preterm group showed higher mortality rate than the corresponding AGA group, whereas, this finding was not found when we compared the SGA mild preterm group with the corresponding AGA group (Table 3). The SGA mild preterm group had significantly lower mean ponderal index than the moderate SGA preterm group (2.2 ± 0.41, 2.69 ± 0.26 $P< 0.05$). This means that the SGA mild preterm infants were of the asymmetric type (wasted: normal length and head circumference but with low weight for length) while those of the SGA moderate preterm group were of the symmetric type (stunted: symmetrical reduction in weight, length and head circumference). It has been hypothesized that symmetric SGA occurs early in gestation and is due to genetic and chromosomal abnormalities, while asymmetric SGA occurs late in pregnancy and is due to inadequate nutrition(7). This finding may denote that the growth restriction of moderate preterm are due to fetal causes rather than the prenatal malnutrition which may explain the high rate of their mortality.

Win *et al.*(16) found that there was a 3.6-fold greater risk of neonatal mortality in preterm SGA, when used neonatal growth standards, as compared with AGA infants. Piper *et al.*(17) showed that the neonatal mortality of infants with birth weight of less than the 10th percentile was higher than the AGA neonates at each gestational age up to 36 weeks.

Basso *et al.*(18) summarizes that neonatal mortality of SGA infants is not due to the growth restriction itself, but is due to some confounding factors causes the growth restriction and also causes the neonatal mortality. Such factors would include malformations, fetal or placental aneuploidy, infections or others.

Small for gestational age mild preterm infants had higher rates of intraventricular hemorrhage and sepsis/meningitis than the corresponding AGA group. Similarly, SGA moderate preterm infants had significantly higher rates of intra ventricular hemorrhage and sepsis/meningitis than the corresponding AGA group (Table 3). Simchen et al(19) found that SGA preterm infants had a higher mortality rate and high culture proven sepsis than the AGA preterm. Moreover, Win *et al.*(16) found that the neonatal morbidity including RDS, assisted ventilation, intraventricular hemorrhage were high among preterm SGA infants than the AGA group.

In this study it was noticed that SGA mild preterm infants had significantly lower respiratory distress than the AGA group. Whether the intrauterine growth restriction is protective from respiratory distress or not is still a point of conflict. Simchen *et al.*(19) found that growth restriction in the preterm neonate was not found to protect against neonatal outcomes associated with prematurity. They added that the presence of intrauterine growth restriction adversely affected survival independently of other variables. On the other hand, Sharma *et al.*(20) and Gortner *et al.*(21) observed a lower incidence of RDS in preterm infants with IUGR.

Furthermore, both SGA mild and moderate preterm groups had significantly longer hospital stay than the AGA groups. There was a significant negative correlation between birth weight and length of hospital stay ($r = - 0.036$, $P = 0.0341$). Rocha *et al.*(22) found that preterm SGA newborns had significantly longer hospital stay and greater need for NICU treatment than the AGA preterms.

A limitation of this study was that we did not include a full term group for comparison. We recommend further follow up of preterm infants throughout the first year of life to detect morbidity and mortality of this category of infants. Management strategies and guidelines should be settled to prevent spontaneous preterm deliveries and to early diagnose and manage intrauterine growth restriction. When considering elective preterm delivery for this high risk group of pregnancies, the increased risks in the neonatal period should be taken into account.

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