Epidemiological aspects of prematurity in the Eastern region of Saudi Arabia

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ABSTRACT

الأهداف: تقييم الخصائص الوبائية ومعدل النجاة لدى الأطفال الخدّج الذين تم تشخيصهم بالمستشفى التعليمي بالمنطقة الشرقية بالمملكة العربية السعودية.

الطريقة: تمت الدراسة عن طريق استقصاء بحثي استعادي لملفات الأطفال الخدّج المنوّمين بمستشفى الملك فهد الجامعي بمدينة الخبر بالمملكة العربية السعودية، والبالغ عددهم 476 خديج، في الفترة من يونيو 2008م إلى يونيو 2013م، لتحليل وتقييم الخصائص الديموغرافية، وزن الولادة ومعدلات نجاة الأطفال الخدّج.

النتائج: تم تسجيل 476 خديج مع انتشار إجمالي قدره 7.5%. كما كشف التحليل الوصفي عن نسبة 55% من الذكور ضمن إجمالي عدد الحالات. بلغت نسبة الخداجة الحادة 9%، والخداجة المتوسطة 20%. وفقا لوزن الولادة: بلغت نسبة الخدج ذي الوزن الحاد 11%. كما أن 157 (32%) من إجمالي عدد الحالات كانت لرضع صغار لعمر الحمل. تم تسريح 58% من إجمالي المواليد الخدج ذي الوزن الحاد من وحدة العناية المركزة لحديثي الولادة. كان العدد الإجمالي للوفيات 7.6%. وفيما يتعلق بجنس الجنين، كان معدل وفيات الذكور الخدج 53%. كما تراوحت نسبة التسريح من العناية بحسب عمر الحمل ما بين 30% إلى 97.6%.

الخاتمة: أظهرت النتائج أن الخصائص الوبائية للخداجة بمستشفى جامعي بالمنطقة الشرقية بالمملكة العربية السعودية تتشابه إلى حد كبير مع مختلف الدراسات الدولية المنشورة بالمجلات العلمية حول العالم.

Objectives: To assess the epidemiological characteristics of prematurity and survival rate in preterm infants diagnosed at a university hospital in the Eastern province of Saudi Arabia.

Methods: A retrospective study was carried out of 476 preterm infants who were admitted with the diagnosis of prematurity to King Fahd Hospital of the University, Al-Khobar, Saudi Arabia, between June 2008 and 2013. Demographics, birth weight, and neonatal survival rate were analyzed.

Results: Four hundred and seventy-six preterm infants were admitted with a total prevalence of 7.5%. Descriptive analysis revealed 55% were males. Extremely preterm infants (<28 weeks' gestation) comprised 9% and very preterm infants (28 to <32 weeks' gestation) comprised 20%. Extremely low-birth-weight (ELBW) infants (<1000 g) comprised 11%. One hundred and fifty-seven (32%) infants were small for gestational age. Out of the total number of ELBW infants, 58% of them were discharged. The overall mortality was 7.6%. The mortality rate of male infants was 53%. The survival to discharge according to gestational age ranged from 30-97.6%.

Conclusion: The estimated prevalence of preterm births in a university hospital in eastern province of Saudi Arabia, is consistent with various studies from different parts of the world.

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Prematurity has been, and still is, one of the major causes of neonatal morbidity and mortality in intensive care units (ICUs) worldwide. It is considered the second leading cause of neonatal mortality after congenital anomalies, and a major determinant of neonatal and infant morbidity.[1] Preterm birth affects almost 11.1% of all pregnancies worldwide.[2] Preterm infants are at higher risk for acquiring complications that result from either anatomic or functional immaturity. A common finding on mortality and morbidity for very low birth weight infants is that the risk of developing

complications decreases with increasing gestational age and birth weight.[3] The survival of very low birth weight infants has improved significantly with the development of antenatal and neonatal intensive care during the last 2 decades. Among all early neonatal deaths (deaths within the first 7 days of life) that are not related to congenital malformations, 28% are due to preterm birth.[4] Prematurity accounts for most admissions to ICUs in the immediate newborn period. As ICU costs are high, quantifying the prevalence and short-term complications of prematurity is crucially important to allow for rational planning, allocation of most frequent etiologies, and proper management. In 2005, a study[5] estimated that the costs to the USA alone in terms of medical and educational expenditure and lost productivity associated with preterm birth were more than US$ 26.2 billion.

Although there are international published studies targeting this entity, current available studies on the incidence of prematurity from Saudi Arabia are scant. Almost all published studies from this region have not been recent and have been plagued with problems of small sample size or the lack of distinct focus on preterm infants.[6-12] The few reliable quantitative figures of prematurity in Saudi Arabia emphasize the importance of such study. The aim of this study is to determine the prevalence of prematurity, retrospectively in the preterm infants who were admitted in the Eastern Province of Saudi Arabia.

Methods. The medical records of preterm infants admitted to the Neonatal Intensive Care Unit (NICU) with a diagnosis of prematurity at the King Fahd Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia between June 2008 and June 2013 were reviewed retrospectively. The following variables were reviewed from their files: gestational age, gender, nationality, birth weight, mortality, and length of neonatal stay in the NICU.

The study followed the World Health Organization (WHO) definition of preterm birth as its only inclusion criteria, which is defined by any birth before 37 completed weeks of gestation, or fewer than 259 days since the first day of the woman's last menstrual period (LMP).[13] Gestational age (GA) was determined upon the first day of LMP. Preterm infants born at gestational age of 23 weeks or less, or infants with birth weight less than 400g were excluded from the study (n=8).

After obtaining ethical approval from the Institutional Review Board (IRB) of the University of Dammam, data for the study were obtained from the hospital records and exported to MS Excel for data manipulation and cleaning. The final data was exported using the Statistical Packages for Social Sciences (IBM Corp., Armonk, NY, USA) for analysis.

A search strategy was used to find prior related studies. A systematic literature search was applied to PubMed (from 2010 to present). We used a combination of controlled vocabulary and key words; prematurity, preterm births, and prematurity in Saudi Arabia. The results of the search were then reviewed by the research team. References from included studies were hand-searched to identify any additional relevant studies.

For the purpose of this study, prematurity was subdivided on the basis of gestational age into: extremely preterm (<28 weeks), very preterm (28 to <32 weeks), and moderate or late preterm (32 to <37 completed weeks of gestation).[13] This is in line with best practice guidelines on the subject. Birthweight classification was based on the classification defined by the Centers for Disease Control[14] as extremely low-birth-weight (ELBW) with birth weight <1000g, very low-birth-weight (VLBW) with birth weight ranging between 1000-1499g, low-birth-weight (LBW) with birth weight ranging between 1500-2499g, normal birth weight (NBW) with birth weight ranging between 2500-3999g, and high birth weight (HBW) with birth weight equals to or more than 4000g. Mortality was defined by death as a result of prematurity and/or at least one of its short-term complications during the hospitalization period. Small for gestational age was defined as birth weight below the 10th percentile for age.[15]

For statistical analysis, a simple descriptive analysis was used to measure the study variables. Bar charts and tables were used to summarize the study figures and results. Comparison was made between the characteristics of preterm infants based on both gestational age and birth weight. Livebirth numbers were included to determine the study's rate of preterm births. For continuous variables, distributions were compared graphically and statistically.

Results. Over the study period, the number of live births delivered at the hospital was 6455. Based on

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the retrospective review of the medical reports, a total of 484 preterm infants were admitted to the NICU during this period. Eight patients were excluded from the study due to either being born at a gestational age of 23 weeks or less, or with birth weight less than 400 g. After these exclusions, the number of patients selected for the study was 476. Thirty-one infants (6.5%) were referred to our hospital from other regional hospitals. The total prevalence of preterm births was 7.5%, with 6455 live births. The distribution and rate of preterm births per year are shown in **Figure 1**. The preterm infants' demographic data descriptive analysis revealed that 263 of them were males (55%), and 213 of them were females (45%). The prematurity and birth weight classifications of the study population are shown in **Table 1**.

One hundred and fifty seven (32%) of our study population were small for gestational age (SGA), whereas 5 (10.9%) extreme preterm infants were SGA. The mean gestational age was 32 weeks and 4 days, whereas mean gestational age of ELBW infants was 26 weeks and 3 days with a range of 24-31 weeks. The mean birth weight of the total study population of preterm infants was 1827.6g, whereas the mean birth weight of ELBW infants was 727.83g with a range of 430g to 980g. Out of the total number of ELBW infants, 58.5% (n=31) of them were discharged from the NICU with a mean length of stay of 85.25 days and a range between 57-188 days. Out of the discharged ELBW, 45.2% (n=14) were males. The lowest birth weight of the discharged ELBW preterm infants was 580g. The overall mortality was 7.6%. The mortality rate of male preterm infants was 53%, compared with 47.2% females.

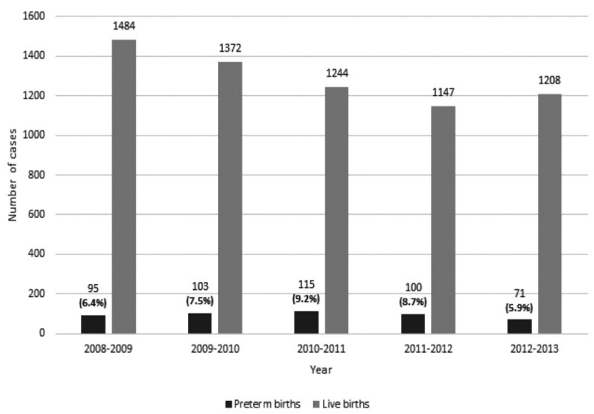

Figure 1 - The distribution of prematurity case per year admitted to the Neonatal Intensive Care Unit (NICU) with diagnosis of prematurity at the King Fahd Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia.

Infants with birth weights <1000g, the mortality rate was 41.5%, whereas 3.3% of infants with birth weights >1000g died prior to discharge. Furthermore, 52.7% of the mortalities occurred in infants with birth weights <800g. The survival rate per birth weight is shown in **Table 2**.

In regard to the gestational age, the survival rate per gestational age is shown in **Table 3**. The survival to discharge according to gestational age was ranging from 30-97.6%.

Discussion. More than one in 10 of babies born in 2010 were premature, making an estimated 14.9 million preterm infants (11.1%) of all pregnancies worldwide, of which more than 1 million died as a result of their prematurity. Most preterm births (84%, 12.5 million) occur after 32 completed weeks of gestation.[2] This data

Table 1 - Classification of the study population according to gestational age and birth weight.

Variables	n	(%)
According to gestational age		
Extremely preterm (<28 weeks)	44	(9.2)
Very preterm (28 to <32 weeks)	96	(20.2)
Late preterm (32 to <37 weeks)	336	(70.6)
According to birth weight (grams)		
Less than 1000 (ELBW)	53	(11.1)
1000 to 1499 (VLBW)	100	(21.0)
1500 to 2499 (LBW)	258	(54.2)
2500 to 3999 (NBW)	64	(13.5)
Equals to or more than 4000 (HBW)	1	(0.2)
Total	**476**	**(100)**

ELBW - extremely low-birth-weight, VLBW - very low-birth-weight, LBW - low-birth-weight, NBW - normal birth weight, HBW - high birth weight

Table 2 - Survival by birth weight classification, with scaled survival rates among ELBW infants with 200 g increments.

Birth weight (grams)	Survival rate n (%)	
400g to 999g (ELBW)	31/53	(58.5)
400g to 599g	2/13	(15.4)
600g to 799g	16/24	(66.7)
800g to 999g	13/16	(81.3)
1000 to 1499 grams (VLBW)	92/100	(92.0)
1500 to 2499 grams (LBW)	253/258	(98.1)
2500 to 3999 grams (NBW)	63/64	(98.4)
More than 3999 grams (HBW)	1/1	(100)
Total	**440/476**	**(92.4)**

ELBW - extremely low-birth-weight, VLBW - very low-birth-weight, LBW - low-birth-weight, NBW - normal birth weight, HBW - high birth weight

Table 3 - Survival by gestational age, with scaled survival rates among extremely preterm infants.

Gestational age (weeks)	Survival rate n (%)	
Extremely preterm (<28 weeks)	23/44	(52.2)
24 weeks' gestation	3/10	(30.0)
25 weeks' gestation	3/8	(37.5)
26 weeks' gestation	4/7	(57.1)
27 weeks' gestation	13/19	(68.4)
Very preterm (28 to <32 weeks)	89/96	(92.7)
Late preterm (32 to <37 weeks)	328/336	(97.6)
Total	**440/476**	**(92.4)**

Table 4 - Survival to discharge by birthweight in 100 grams increments.

Birth weight	King Fahd Hospital of the University Data Survival rate of infants (%)		NICHD Neonatal Research Network data* Mean survival rate (%)
401g to 500g	0/3	(0.0)	16
501g to 600g	2/11	(18.0)	36
601g to 700g	8/12	(66.6)	61
701g to 800g	8/10	(80.0)	79
801g to 900g	5/8	(62.0)	88
901g to 1000g	9/11	(81.0)	92
1001g to 1100g	8/12	(66.0)	92
1101g to 1200g	20/21	(95.0)	94
1201g to 1300g	20/20	(100)	96
1301g to 1400g	17/18	(94.0)	96
1401g to 1500g	27/27	(100)	98

*Survival to discharge by birthweight in 100g increments among infants born in National Institute of Child Health and Human Development (NICHD) Neonatal Research Network centers between Jan. 1, 1997, and Dec. 31, 2002, with center variability.[22]

represents a fundamental challenge for over-financed health, training, and social service sectors globally. Prematurity is now the second-leading cause of death in children under 5 years, and the single most important cause of death in the critical first month of life.[16] As an indicator in the area of maternal and perinatal health, preterm births reflects the distinct discrepancies between different nations with regard to perinatal health, neonatal mortality rates, and survival rates.

In our study, 55.25% of the preterm infants were males, which is consistent with most other studies,[17] and the cause of male predominance is not yet completely explained, but it could be related to the fetal sex hormone effects that influences the labor-inducing deliveries.[18] As our study is focusing on the descriptive data of overall prematurity and LBW infants, there is no local studies to compare our finding with. We found the estimated prevalence of prematurity in this study was approximately 7.5% during the study period between 2009 and 2013. However, when comparing our data of preterm births to the data of the 10 countries with the highest numbers of preterm births according to worldwide estimates of preterm birth rates in the year 2010 for some selected countries, we found that our estimate of preterm births rate in 2010 (7.5%) is far lower than the high rates of the preterm births of those countries except for China (7.1%), which is listed as the second based on the number of preterm births, and that is due to the high number of livebirths as compared with our study.[2]

Our study trend of distribution of preterm infants by gestational age is higher than the international scale; with extremely preterm infants of 9.2% versus 5.2%, very preterm infants of 20.1% versus 10.4%.[2] This could be explained by the fact that our hospital is a referral center for high risk cases and pregnancies, with 6.5% of our study population being outside referrals after delivery, and out of which most were below 32 weeks' gestation. In addition, there is a good percentage of antenatal high risk pregnancies referrals as well.

One hundred and fifty seven (32%) of our study population were SGA, this finding was higher than the international trends of preterm-SGA for the top 10 low-income and middle-income countries with the highest numbers of SGA infants born in 2010 as found by Lee et al[19] (ranging between 22.3% and 16%), and this difference can be explained as a result of being a referral hospital for high-risk pregnancies with 7.6% of our preterm-SGA being referred cases. In one study, Al-Alaiyan et al[20] stated that Saudi VLBW infants are more likely to be born as small for gestational age (SGA), which might represent a genetic factor, poor maternal nutrition, or suboptimal antenatal care and follow-up. In comparison with our findings, among the total number of preterm-SGA, 26.7% were VLBW infants, whereas in another local study concerning exclusively VLBW preterm infants it was 30.2%.[21] At an international level, based on perinatal information for VLBW infants born in the National Institute of Child Health and Human Development (NICHD) Neonatal Research Network between January 1997 and December 2002, the prevalence of preterm-SGA was 21%.[22]

Our results revealed that 92.4% of our population survived to discharge during the study period. Of the total number of ELBW infants, 58.5% of them were

discharged from the NICU with a mean length of stay of 85.25 days, and 45% were male infants. With reference to gender, we found that the mortality rate was 52.7% in male preterm infants compared with 47.2% in female preterm infants. This finding of female predominance in countering the survival to discharge estimates in ELBW infants are supporting the well-established consensus adopted by Neonatal Research Network (NRN) of The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).[23] Also, we found that the lowest birth weight of the discharged ELBW preterm infants was 580 g. In infants with birth weights below 1000 g, mortality was 41.5%, whereas 3.3% of infants with birth weights more than 1000 g died prior to discharge. Furthermore, 52.7% of the mortalities occurred in infants with birth weights below 800g.

One of the strengths of this study is that we emphasized the survival rate of our population by 2 methods based on gestational age and birth weight. Based on birth weights, preterm infants <1000 g were divided into 3 groups; those weighing 400-599g had a survival rate of 15.3%, those weighing 600-799g had a survival rate 66.6% and finally preterm infants weighing 800-999g had a survival rate of 81%, almost 4 times improvement in chance of survival compared to those less than 600g.

National Institute of Child Health and Human Development Neonatal Research Network study that was undertaken to document the mortality and morbidity of infants weighing from 501-1500 g at birth, according to gestational age, birth weight, and gender, during 2 periods (1995-1996 and 1997-2002), we compared our results with those of the NICHD and found an almost similar survival rate of preterm infants by birthweight except at birthweight of 401-500 g,[22] and this is might be due to the difference between the 2 study population sizes. This comparison is shown in **Table 4**.

We found a continuous increasing trend of survival among preterm infants as shown in **Table 2**, and this is due to the marked development of antenatal and neonatal intensive care concepts regarding the implementation of strict policies and procedures, infection control measures, and evolution of applied medical practices during the last 2 decades. Also, the survival rate by gestational age varies among different groups of the population. The survival rate of preterm infants with gestational age of 24 weeks was 30%, with a major difference equalling 38% when compared to the survival rate of preterm infants with gestational age of 27 weeks (68%). A significant improvement in survival rate by gestational age was seen in preterm infants of 28 weeks' gestation with a survival rate of 90%. The survival to discharge ranged from 30-98.4% based on gestational age. When we compared our findings of survival per gestational age to those of 3 regional hospitals in the Kingdom, we found them comparable with their results.[20]

The limitations of our study include the relative small number of infants enrolled. Secondly, being a referral center for high-risk cases may demonstrate slightly exaggerated figures in regards to our rates of prematurity and preterm-SGA, though we tried to emphasize our results for both groups in a separable manner. Finally, this study represents data of a single center; thus our results cannot be generalized to all preterm infants in Saudi Arabia.

In conclusion, findings of this study have estimated the prevalence of preterm births in a university hospital in the eastern province of Saudi Arabia, and compare the epidemiological characteristics of prematurity with various international studies from different parts of the world. Wide retrospective and prospective studies at a national level are needed to determine the accurate prevalence and survival rates of prematurity in Saudi Arabia.

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Statistics

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