Pattern of neonatal and postneonatal deaths over a decade (1995-2004) at a Military Hospital in Saudi Arabia

Muhammad A. Majeed-Saidan, DCH, FRCP, Fawaz T. Kashlan, MD, Atyah A. Al-Zahrani, MBBS, Faisal Y. Ezzedeen, MD, Amer N. Ammari, MBBS, Msc.

ABSTRACT

الأهداف: التعرف على أسباب الوفاة المباشرة عند الأطفال بعد الولادة في قسم العناية المركزة لرعاية الخدج، خلال عشرة سنوات.

الطريقة: جُمعت المعلومات حول جميع الأطفال الذين توفوا في قسم العناية المركزة لرعاية الخدج خلال عشرة سنوات وذلك في المستشفى العسكري بالرياض – المملكة العربية السعودية، في الفترة من يناير 1995م وحتى نهاية ديسمبر 2004م، بطريقة مستقبلية. بُحث في ملف كل طفل تم ادخالة إلى قسم العناية المركزة لرعاية الخدج. تمت مراجعة حالة كل طفل بعد الوفاة مع اثنين على الأقل من الأطباء المتخصصين في الأطفال الخدج، وحُدد السبب المباشر للوفاة. صُنفت أسباب الوفاة حسب تقسيمات ويكلزورث المعدلة لأسباب الوفاة حول الولادة.

النتائج: خلال فترة الدراسة وُلد 79871 طفلاً حياً. كان هناك 526 حالة وفاة، من بينهم 446 (84.2%) تمت ولادتهم في المستشفى العسكري، و80 طفلاً (15.8%) ولدوا خارج المستشفى العسكري. من الأطفال اللذين ولدوا في المستشفى العسكري 251 توفوا بين اليوم الأول و السادس، و 103 توفوا بين7–27 يوماً، و 92 توفوا بعد عمر27 يوماً. التشوهات الخلقية المميتة كانت أحد أسباب الوفاة في (36%) من الأطفال، بينما الولادات المبتسرة ومضاعفاتها كانت سبباً في وفاة (42%) منهم، والاختناق الولادي في (5%)، وأمراض مختلفة في (17%) من الحالات.

خاتمة: الولادات المبتسرة ومضاعفاتها تبعتها التشوهات الخلقية المميتة كانتا السبب الرئيسي للوفيات في هذه الدراسة.

Objective: To describe and monitor the causes of neonatal and postneonatal deaths in the Neonatal Intensive Care Unit (NICU) over a 10-year-period.

Methods: This is a descriptive study of all infants who died in the NICU from January 1995 until December 2004 at Riyadh Military Hospital, Riyadh, Kingdom of Saudi Arabia. Data were collected prospectively on all infants admitted to NICU. The cause of death for each infant was discussed and determined by at least 2 consultant neonatologists. Deaths were classified according to the modified Wigglesworth's classification of perinatal death.

Results: During the study period, there were 79871 live births and 526 deaths, in which 446 (84.2%) were inborn deaths and 80 (15.8%) were outborn. Of the inborn deaths, 251 infants died between 1-6 days, 103 died between 7-27 days, and 92 died after 27 days. Lethal malformations led to death in 36%, prematurity and its complications in 42%, hypoxic ischemic encephalopathy in 5%, while other specific diagnoses, combined, led to death in 17% of the cases.

Conclusion: Prematurity and its complications followed by congenital malformations were the leading causes of death.

Saudi Med J 2008; Vol. 29 (6): 879-883

From the Neonatal Intensive Care Unit, Department of Pediatrics, Riyadh Military Hospital, Riyadh, Kingdom of Saudi Arabia.

Received 2nd October 2007. Accepted 14th April 2008.

Address correspondence and reprint request to: Dr. Muhammad A. Majeed-Saidan, W932, Riyadh Military Hospital, PO Box 7897, Riyadh 11159, Kingdom of Saudi Arabia. Tel. +966 (1) 4777714 Ext. 25834. Fax. +966 (1) 2919165. E-mail: msaidan@rmh.med.sa

Maternal and neonatal mortality and morbidity have declined in most countries over the last several decades. With the improvement and sophistication in the perinatal and neonatal care over the last 2 decades, extremely low birth weight babies (<1000 grams) are contributing significantly to the perinatal and neonatal mortality rates. Neonatal mortality rate (NMR) and infant mortality rate (IMR) are considered important indicators of health provision. Declining NMR and IMR are used as a measure of improvement in obstetrical, perinatal, and neonatal care.[1] Late fetal death (stillbirth) and early neonatal death are combined into one category described as perinatal mortality, and accordingly the perinatal mortality rate can be calculated. There has been an increasing dissatisfaction with the use of the perinatal mortality rate to assess the quality of perinatal and neonatal care in a population.

The main cause of neonatal death is now more related to prematurity instead of to asphyxia as it used to be in the first half of the twentieth century when these rates were described.[2] As stated by Keeling et al[3] in their paper on classification of perinatal death "The aim of death classification is to derive strategies to understand the reason for, and ultimately prevent, perinatal mortality." Wiggleswoth, in his original report,[4] assigned the causes of perinatal death into 5 groups to which most perinatal deaths can be provisionally classified when autopsy is not carried out or not available. These groups are: 1. Still birth, 2. Congenital malformation, 3. Prematurity and its complications, 4. Asphyxia, 5. Specific conditions. In the Kingdom of Saudi Arabia (KSA), consistently published data regarding post-neonatal mortality rate (PNMR), NMR, still birth rate (SBR), and the actual causes of death are sparse although the Ministry of Health collects neonatal data from various hospitals in the kingdom. The aim of this report is to present data collected prospectively on the causes of neonatal and postneonatal deaths for infants admitted to the Neonatal Intensive Care Unit (NICU) of Riyadh Military Hospital, KSA over a 10-year-period.

Methods. This is a descriptive study of all infants who died in the NICU from January 1995 until December 2004. Data were collected prospectively on all infants admitted to NICU of Riyadh Military Hospital which is the largest Military Hospital in the Kingdom with just over 1000 beds. It is a tertiary center with all the medical and surgical subspecialties available. The Price Sultan Cardiac Centre is within the hospital compound. It serves the Saudi army personnel and their families. The Saudi army recruits from all over the kingdom, and its personnel represent a good cross section of the Saudi society. Live born infants admitted to NICU and then died before discharge were included. All outborn infants admitted to NICU including those who died were excluded. Early neonatal death (END) is defined as death that occurs up to a completed 6 days following birth, while early neonatal mortality rate (ENMR) is defined as the END per 1000 live births. Late neonatal death (LND) is defined as death between 7 and 27 days, while late neonatal mortality rate (LNMR) is defined as the LND per 1000 live births. Neonatal mortality is defined as death between 0 and 27 days of life, while NMR is defined as the death occurring between 0-27 days per 1000 live birth. Post neonatal death (PND) is death after 27 days of life until the age of one year, while post neonatal death rate (PNDR) is defined as death after 27 days of life until one year of age per 1000 live birth.[5] Corrected neonatal mortality rate (cNMR), is the NMR calculated after exclusion of babies with lethal malformations. Following the death of each baby, the consultant in charge prepares a detailed death summary and fills out a computer data sheet. All deaths during any given month will be discussed by all the consultants in the unit. Two aspects of care are discussed in depth; the first one is the most likely immediate cause of the death and the second is whether any part of the care could have been optimized as part of our internal audit to improve the quality of care. The causes of death are then classified by one of us according to the modified Wigglesworth's classifications[3] initially for the END group, then for all the deaths. The modified Wigglesworth classification for perinatal death, in brief, with the number of infants in each group is presented in **Table 1**. A monthly mortality meeting between the obstetricians, the perinatologists, and the neonatologists are held to discuss all aspects of the perinatal and neonatal care. This is followed by parental counseling as clinically indicated or referral to other subspecialties. The total number of deliveries and the number of still births, as reported in the Department of Obstetric and Gyn ecology annual reports and the paper by Mesleh et al[6] were used. Infants with multiple dysmorphic features were evaluated by the consultant geneticist, and other subspecialists were consulted as indicated. Chromosomal studies, medical photographs, various imaging studies, metabolic screen and DNA banking were requested for most of the cases. Malformations were considered lethal if they are well-recognized entities or a combination of multiple malformations for which it was difficult to sustain life. The decision to limit the care in infants with lethal malformation and those with extreme prematurity with severe complication (severe intraventricular hemorrhage with cerebral involvement, disseminated intravascular coagulopathy, and prolonged severe hypoxia) was taken by at least 3 consultant neonatologists, in addition to consultants with other subspecialties, as needed, after parental agreement. Premature birth was defined as birth before the completion of 37 weeks of gestation. In our NICU, our policy is to provide resuscitation to all infants born with birth weight above 500 grams unless the infant is found to have lethal or multiple congenital anomalies on prenatal ultrasonography or at birth. Infants born with birth weight less than 500 grams were resuscitated only if prenatal ultrasound had shown significant intrauterine growth restriction or after comprehensive prenatal parental counseling in other specific situations. Cases of hypoxic ischemic encephalopathy (HIE) were classified according to Sarnat and Sarnat staging.[7] All cases diagnosed as HIE and found to have inborn errors of metabolism (IEM) or lethal congenital malformations were excluded from this group. Babies with IEM were diagnosed on the basis of Tandem mass spectrometry and urine gas chromatography/mass spectrometry in addition to

other tests, according to the individual case. Autopsy is not allowed in the Kingdom of Saudi Arabia except for legal reasons. Biopsies from various organs, as part of the investigations, are allowed and were performed with parental approval for some cases. Specific diagnostic tests, not available in our hospital, were sent to other centers inside or outside the Kingdom.

Epi info 2000, statistical software for the Centers for disease control and prevention was used for data entry and analysis. Chi square test and descriptive statistics were used to analyze the data.

Results. During the study period, there were 79871 live births and 526 deaths. Four hundred and forty-six (84.2%) were inborn and 80 (15.8%) were outborn. Of the inborn infants, there were 269 (60.4%) males and 177 (39.6%) females with a male/female ratio of 1.5/1. Early neonatal death occurred in 251 (56.3%), LND in 103 (23.1%) while 92 (20.6%) were PND. The causes of death during the early neonatal period and for all the inborn deaths, according to the modified Wigglesworth's classification, are shown in **Figure 1**. In group 2 (death due to lethal malformation), the immediate causes of death are shown in **Table 2**. The most common chromosomal anomalies were trisomy 18 in 12 infants (41.4%), trisomy 13 in 11 infants (37.9%), while other rare lethal chromosomal malformations were diagnosed in 6 infants (20.7%). There were 9 infants (5.7%) born with multiple dysmorphic features but did not have a definite diagnosis made in spite of extensive investigations. In group 3 (death due to prematurity and its complications), 187 infants died during the 10 years' period. There were 128 males (68.4%) and 59 females (31.6%) with a male/female ratio of 2/1. The number of deaths according to gestation is shown in **Figure 2**. One hundred and six infants (56.7%) were less than 26 weeks, 76 (71.7%) of them died during the first 6 days of life (END). According to the birth weight criteria, out of 187 infants, there were 18 infants (9.6%) with a birth weight below 500 grams, 99 infants

Table 1 - The modified Wigglesworth's[3] classification of perinatal death and the number of babies in each subgroup (N=446).

Group	Description	No. of babies (%)
1	Still birth	NA
2	Lethal malformations	161 (36)
3	Prematurity and it's complications	187 (42)
4	Birth asphyxia	22 (5)
5	Specific diagnosis	76 (17)

NA - not applicable

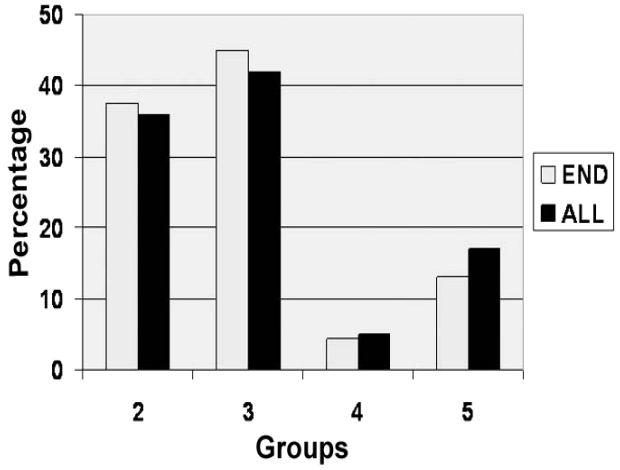

Figure 1 - Distribution of deaths according to the modified Wigglesworth's classification for early neonatal death END and the whole group.

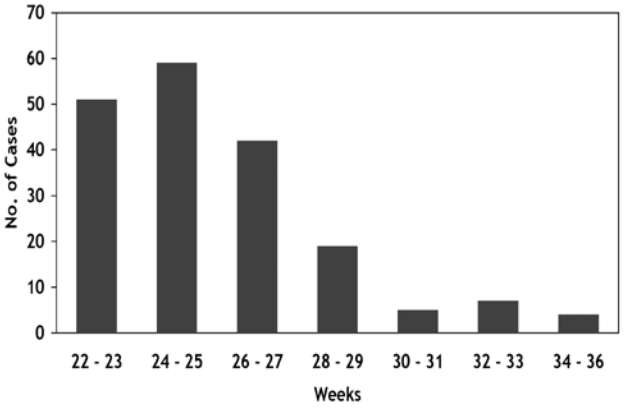

Figure 2 - Death due to prematurity and its complications by gestation (weeks).

Table 2 - The causes of death in group 2 (N=161).

Cause of death*	No. of babies	(%)
Renal agenesis / bilateral MCDK†	30	(18.6)
Chromosomal anomalies	29	(18)
Specific syndromes	28	(17.4)
CNS/ Neuromuscular disorders	28	(17.4)
CVS malformations	16	(9.9)
Inborn errors of metabolism	11	(6.9)
Multiple dysmorphic features	9	(5.6)
Lung hypoplasia	5	(3.1)
Others	5	(3.1)
Total	**161**	**100**

*The cause of death as decided upon at the mortality review
†MCDK - multicystic dysplastic kidneys,
CNS - central nervous system , CVS - cardio-vascular system

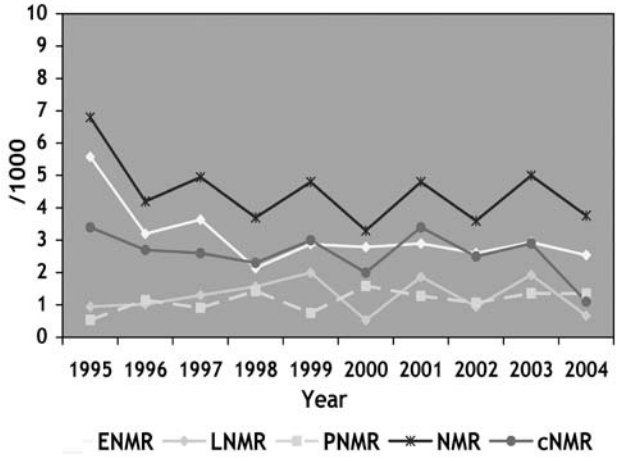

Figure 3 - Mortality rates during the 10 year period. Early neonatal mortality rate (ENMR), late neonatal mortality rate (LNMR), post-neonatal mortality rate (PNMR), neonatal mortality rate (NMR), and Corrected neonatal mortality rate (cNMR).

Table 3 - The immediate causes of death in group 5 (N=76).

Cause of death*	No. of babies	(%)
Diaphragmatic hernia	19	(25)
Pulmonary Hypoplasia	5	(6.6)
CVS malformations	7	(9.2)
Group B Streptococcus septicemia	4	(5.2)
Specific syndrome	11	(14.6)
Inborn errors of metabolism	3	(3.9)
Hydrops fetalis	5	(6.6)
Neonatal tumors	4	(5.2)
CNS malformations	6	(7.9)
Others	12	(15.8)
Total	**76**	**(100)**

*The cause of death as decided upon at the mortality review
CNS - central nervous system , CVS - chorionic villus sampling

(52.9%), with a birth weight between 500-749 grams, 41 infants (21.9%) with a birth weight between 750-999 grams and 29 infants (15.5%) were at or above 1000 grams. Twenty-two infants died of HIE (group 4), 15 term, and 7 pre-term infants. The male/female ratio in this group was 2/1. Over the same period there were 79871 live births, this gave a ratio of one death due to HIE for every 3500 deliveries. Deaths due to specific diagnoses (group 5) are shown in **Table 3**. Twenty-four babies died as of respiratory failure, 19 of them (79%) were due to diaphragmatic hernia and its complications. Specific syndromes included; DiGeorge (2), epidermolysis bullosa (2) and one for each of the following syndromes: retinoic acid embryopathy, 3C syndrome, Dandy-Walker variant, thanotophoric dwarfism, and arthrogryposis multiplex congenita. The ENMR, LNMR, PNMR, NMR, and the cNMR, for the study period, are shown in **Figure 3**.

Discussion. There are 2 main reasons for carrying out comparisons of neonatal outcomes: as an indicator of maternal and neonatal health care in a population allowing inter-regional and international comparisons, and to monitor the quality of perinatal and neonatal care provision. In addition, it provides information for the performance management of perinatal and neonatal services. In this study, we report on the causes of neonatal and postneonatal deaths from prospectively collected data in a single institution from the Kingdom of Saudi Arabia.

Our neonatal and postneonatal mortality rate can be compared only to similar studies reporting on mortality rate for infants admitted to NICU and died before discharge. Such studies from KSA are scarce and are different in their methodology. Since the establishment of our NICU, it was our policy to classify neonatal and postneonatal deaths according to Wigglesworth's classification. Although it was primarily developed for classifying deaths during the perinatal period, we have used it to classify deaths during the early neonatal period and for the entire inborn deaths. **Figure 1** Shows that there was no significant difference between the percentages of death among the 2 groups. This may indicate that the modified Wigglesworth's classification could be used for all the neonatal deaths, before hospital discharge, and up to one year of age. The use of the modified Wigglesworth classification for LND and PND needs further validation as previously shown by Keeling et al.[3]

Thirty-six percent of deaths were due to lethal malformations. This could be due, in part, to a high degree of consanguineous marriages (54.3%) in the Riyadh region.[8] This percentage of lethal malformation is higher than the 30.8% reported by Bassuni[9] from the southern region of Saudi Arabia. The major difference between the 2 reports is in the way data were collected; in Bassuni's report, all babies were outborn while in our report all deaths were inborn. This could mean that some babies with clearly lethal conditions, like bilateral renal agenesis and trisomy 13 or 18, died at their birth hospitals.

Mansouri[10] in a 5-year-review reported a perinatal mortality of 23% due to prematurity and its complications in contrast to our report of 42%. Neither birth weight nor gestational age was mentioned in Mansouri's paper. In our report 18 infants died with birth weight less than 500 grams, representing 4% of the total inborn deaths, and 9.6% of deaths due

to prematurity and it is complications, whereas 99 infants died with birth weight between 500-750 grams, representing 22% of the total inborn deaths, and 53% of deaths due to prematurity, and it is complications. In a report by Serenius et al,[11] 31.6% of neonatal deaths were due to prematurity. Their report included only 15 babies less than 1500 grams with a mean gestational age of 28.8 weeks. In the END group of our study, prematurity and its complications accounted for 45% of deaths, 99 of the 113 babies (87.6%) who died from prematurity and its complications were less than 28 weeks of gestation.

Serenius et al,[11] choose a multiple 6-hour sample periods over a year (1979-1980). The difference in the method of data collection and the fact that smaller and smaller babies are being resuscitated and receiving intensive care could explain the difference in mortality rates in this group. Serenius reported END due to birth asphyxia in 8 babies (0.54% or 5.4 death/1000 live births) compared to 11 (0.014% or 0.14/1000 live births) in our study. This difference could be due to the major improvement in perinatal care in the Kingdom with a perinatal mortality rate decreased by 50% over the same time period from nearly 40/1000 live births to just over 15/1000 live births in most of the major institutions.[12]

In a previous report by Mesleh et al[6] from our institution, only babies who died during the first week of life were included. This gave a lower NMR and cNMR. The PNMR in our institution has reduced from 25.8/1000 live births in 1979 to 10.2/1000 live births in 2004.[6] This is due to improvement in obstetrical, perinatal, and neonatal care.[12] Some cases with congenital malformations and inborn errors of metabolism were included in group 5 (death due to specific diagnoses) as their initial diseases were considered non lethal and they died from other reasons, such as fulminating sepsis or respiratory failure after prolonged ventilation.

We choose to report our PNMR, ENMR, LNMR, NMR, and cNMR (**Figure 3**) without comparing it with others. This is that most reports from within the same country fail to report details of birth weight and gestation for the various subgroups. Birth weight and gestation could affect the previous rates as well as perinatal mortality rates, clearly demonstrated by Wigglesworth.[2,4] The higher incidence of lethal malformations contributing to a higher still birth rate, perinatal mortality rates and NMR makes it difficult to compare to other parts of the world as reported by Mesleh,[6] Bassuni,[9] and the current study. In spite of the recent advances in biochemical testing, various imaging modalities and sophisticated chromosomal analysis, the unavailability of postmortem examination remains a limiting factor for this study

In summary, in KSA, a "data base" needs to be established for all the major institutions and for the country as a whole with clearly defined numerators to avoid confusion in reporting. This will be useful to monitor the improvement in health care within institutions and in the country as a whole.

References

1. Bucciarelli RL. Neonatology in the United State: Scope and Organization. In: MacDonald MG, Seshia MMK, Mullet MD, editors. Avery's Neonatology Pathophysiology & Management of the Newborn. 6th ed. Philadelphia (PA): Lippincot Williams & Wilkins; 2005. p. 24-39.
2. Kramer MS, Liu S, Luo Z, Yuan H, Platt RW, Joseph KS. Analysis of perinatal mortality and its components: Time for a change? ***Am J Epidemiol*** 2002; 156: 493-497.
3. Keeling JW, MacGillivray I, Golding J, Wigglesworth J, Berry J, Dunn PM. Classification of perinatal death. ***Arch Dis Child*** 1989; 64: 1345-1351.
4. Wigglesworth JS. Monitoring perinatal mortality a pathophysiological approach. ***Lancet*** 1980; 2: 684-686.
5. Macfarlen A, Johnson A, Mugford M. Epidemiology. In: Roberton NRC, editor. Textbook of Neonatology. 2nd ed. London: Churchill Livingstone; 1992. p. 3-27.
6. Mesleh RA, Kurdi AM, Sabagh TO, Algwiser AA. Changing trends in perinatal deaths at the Armed Forces Hospital, Riyadh, Saudi Arabia. ***J Obstet Gynaecol*** 2001; 21: 49-55.
7. Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress A clinical and Electroencephalographic Study. ***Arch Neurol*** 1976; 33: 696-705.
8. Saedi-Wong S, Al-Farayh AR. Effects of consanguineous matings on anthropometric measurement of Saudi newborn infants. ***Fam Pract*** 1989; 6: 217-220.
9. Bassuni W, Abbag F, Asindi A, AL Barki A, Al-Binali AM. Neonatal deaths in the Asir region of Saudi Arabia: Experience in a referral neonatal intensive care unit. ***Ann Saudi Med*** 1977; 17: 522-526.
10. Mansouri H. Perinatal mortality at King Abdulaziz university hospital Jeddah, Saudi Arabia. ***Saudi Med J*** 1996; 17: 176-179.
11. Serenius F, Swailem AR, Edressee AW, Ohlsson A. Causes of perinatal death at a Saudi maternity hospital. ***Acta Paediatr Scand Suppl*** 1988; 346: 70-79.
12. Hashim TJ, Anokute CC. Imbalances in perinatal mortality in health regions of Saudi Arabia. ***Saudi Med J*** 1994; 15: 376-379.