Major Birth Defects at King Fahd Hofuf Hospital: Prevalence, Risk Factors and Outcome

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We analyzed the medical records of all live birth infants (LBs) born with major birth defects (MBDs) at King Fahd Hofuf Hospital (KFHH) during a three-year period. Our objectives were to determine defect prevalence rate, patterns, geographic differences, associated maternal and infant risk factors, and the contribution of the defects to mortality in our Neonatal Intensive Care Unit (NICU). Out of 30,159 infants born alive during the study period, 687 (2.27%) had one or more MBDs. Systems most commonly affected were the cardiac (20.8%), musculoskeletal (18.7%), and central nervous (18.3%) systems. We observed higher rates/1000 LBs of life-threatening CNS and cardiac defects and diaphragmatic hernia than rates reported from other countries. Rate of defects/1000 LBs increased from 0.79% in the birth-weight group =>4000 g to 15.2% in the birth-weight category <1500 g. Fifty-six infants with MBDs were born to diabetic mothers; diabetes was the only identified maternal disease associated with birth defects. Diabetic mothers and those of infants with chromosomal anomalies had higher means of age and parity than the control mothers (33.5 yrs (SD 5.2), 31.4 yrs (7.5), and 8.8 (3.8), 7.39 (3.8), for age and parity of diabetic and chromosomal anomalies respectively vs. 26.8 yrs (6.4) and 5.2 (3.7) in the controls, $P<0.01$). Out of the 687 infants, 254 (36.97%) died; and MBDs were the most common disease- specific cause of death in our NICU throughout the study period.

Ann Saudi Med 1995;15(4):

The impact of major or serious birth defects on the fetus and newborn infant is great, as they are now the leading cause of perinatal death, both in developed[1]and developing[2]countries including Saudi Arabia[3]. One basic approach toward understanding the nature of the problem in an infant with a congenital defect is to identify the possible risk factors. Therefore, studies that provide epidemio-logical data relevant to birth defects are needed. These data may have important implications for prevention, clinical care and etiologic research.

In this study, we present data on the prevalence, pattern and mortality of MBDs at King Fahd Hofuf Hospital (KFHH), Al Hasa area, during a

three-year period. Data were also analyzed to determine any infant or maternal factors associated with the defects and to study geographic differences in their incidence.

Subjects and Methods

KFHH is one of the big referral hospitals in Saudi Arabia with more than 9000 deliveries annually; approximately 10% and 30% of them are admitted to the NICU and observation area respectively. In this three-year retrospective study, we analyzed data from all live births (LBs) with major birth defects (MBDs) admitted to this hospital during the period from 1411H to 1413H.

MBDs were defined as those that affect the infant's survival or cause structural, cosmetic and/or functional handicaps that require surgical or medical care. The sources of the study were the infant and maternal medical files and the records of the NICU and Obstetric Department. The available data collected included identification, demographic, clinical and diagnostic information on the infants as well as information on the mothersí illness and pregnancy history. The following cases were excluded from analysis: stillbirths (SBs), premature infants (<37 weeks) with defects secondary to prematurity, e.g. patent ductus arteriosus and infants with acquired hydrocephalus associated with ventriculitis. Infants' conditions that were studied included sex, birth weight and gestational age. To determine the relationship between defects and birth weight, infants were divided into five weight groups (<1500 g, 1500 g to 1999 g, 2000 g to 2499 g, 2500 g to 3999 g, and =>4000 g), and we determined the weight-specific birth defect rates by dividing the number of infants with defects in each weight group by the total number of live births with the same weight group born during the study period. In addition, we calculated the rate ratios by dividing the rate of defects for infants in each weight category by that of infants weighing 2500 g to 3999 g. We also compared our rates of specific defects/1000 LBs with those reported from Libya[4] and the USA[5] to determine any geographic variation in incidence. Maternal factors that were analyzed included age, parity, previous abortion or stillbirth and maternal disease. The medical files of 1500 mothers who gave birth to healthy infants during the study period were randomly selected and served as controls for the study mothers.

TABLE 1. *Prevalence of major birth defects at King Fahad Hofuf Hospital (KFHH), 1411-1413H; comparison with rates from Libya[4] and USA[5]*. (PDF document)

Statistical Analysis

Statistical analysis was done with EPI-INFO version 5.01b.[6] Data were evaluated for significance with the Student's t-test, chi-square and Kruskal-Wallis test for nonhomogenous variances as well as the Cornfield 95% confidence limits (CI) around the birth defect rates. $P<0.05$ was considered statistically significant.

Results

Out of 30,159 infants born alive during the study period, 687 (2.27%) had one or more MBDs . Of these infants, 354 (51.5%) were female, 18 (2.6%) were non-Saudi, 10 (1.5%) were twins, 212 (30.9%) were preterm and 36 (5.2%) were outborn. The yearly prevalence of birth defects was almost the same during the three years. The most common system affected was the cardiac (20.8%) followed by the musculoskeletal (18.7%) and central nervous system (CNS) (18.3%). A total of 774 defects were detected in the 687 infants. The incidences of these specific birth defects are presented in Table 1 which also shows a comparison of our incidences with those reported from Libya[4]and the USA.[5] In our survey, we observed a higher incidence of cardiovascular defects, CNS defects and diaphragmatic hernia but a lower incidence of cutaneous and musculoskeletal defects, hypospadias and congenital hip dislocation. There was no significant difference in the overall distribution of defects regarding sex. Specific defects that occurred with higher frequency in males included cystic kidneys (10/10) and clubfoot (21/30). Female preponderance was noted in glaucoma (6/7), absent ears (6/7) and ichthyosis (3/4). Table 2 shows the rates of MBDs in different birth weight categories. The rate of defects/1000 LBs increased from 0.79% in the weight group =>4000 g to 15.2% in the weight group <1500 g.

TABLE 2.*Rates of major birth defects by birth weight; KFHH, 1411-1413H.* (PDF document)

The exact gestational age was recorded only for premature infants and was not recorded consistently for infants admitted for observation. Therefore, we could not study rates of defects according to gestational age or evaluate the effect of intrauterine growth retardation on the incidence of MBDs. However, the number of infants with defects in the gestational age groups <31 wk, 31-33 wk and 34-36 wk were 49, 34 and 129 infants respectively. There were only four postmature infants.

The means of mothers' ages in the study and control groups were 27.2 years (SD 6.9) and 26.8 years (SD 6.4) respectively with no significant

difference, even when mothers were divided into age categories. However, the mean age of diabetic mothers in the study group was significantly higher than that in the diabetics of the control group of 33.5 years (SD 5.2) vs 30.7 (SD 5.9), *P*= 0.010. The mean age of the mothers of infants with chromosomal anomalies was also higher than that of the controls of 31.4 years (SD 7.5) vs 26.8 years (SD 6.4), *P*= <0.01. We found an insignificant difference for parity and history of previous abortion between mothers in the two groups; mean (SD) 5.3 (3.7) vs 5.2 (3.7), *P*=0.56; 0.59 (1.1) vs 0.49 (1.0), *P*=0.27, for parity and abortion in the study and control groups respectively. However, when diabetic mothers were compared, there was a substantial difference for parity but not for abortion; mean (SD) 8.8 (3.8) vs 7.3 (3.7), *P*=0.035; 1.1 (1.5) vs 0.85(1.5), *P*=0.51 for parity and abortion in the diabetics of the study and control groups respectively. Means of parity and number of abortions in mothers of infants with chromosomal abnormality were significantly higher than in the controls; 7.39 (3.8) and 0.78 (1.1) for parity and abortion respectively, *P*<0.01 for both.

The percentage of diseased mothers in the control group was higher than that in the study group (17.2% vs 12.1%, *P*< 0.001), Figure 1. This was mainly due to a higher percentage of sickler (7.1%) and hypertensive mothers (3.5%) in the controls. The number of diabetics in the study group was significantly higher than that in the controls; 56 (8.2%) vs 49 (3.3%), *P*<0.05). All the study diabetics were insulin-dependent compared to only 10 (20.4%) in the control diabetics. The most frequently found defects among infants of diabetic mothers (IDMs) were CNS defects (14), hypertrophic cardiomyopathy associated with other defects (12), acyanotic heart defects (10), polydactyly (7), and cyanotic heart diseases (4).

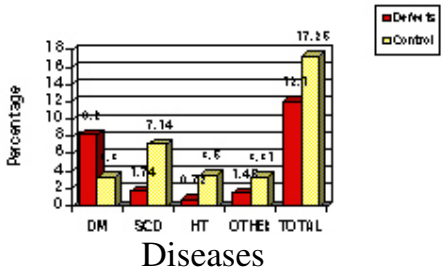

FIGURE 1. Comparison of maternal diseases. DM=diabetes mellitus; SCD=sickle cell disease; HT=hypertension.

Out of the 687 infants, 254 (36.97%) infants died. However, 17 and eight infants with severe cyanotic heart and renal anomalies respectively were transferred to other centers and their outcome was not recorded. Defects

with high mortality included miscellaneous (83.3%), cardiac (56.8%), CNS (51%), respiratory (50%) and intestinal (38.4%). Birth weight appeared to be a determining factor in increasing mortality. The percentage of infants who died for the weight groups <1500 g, 1500-1999 g, 2000-2499 g, 2500-3999 g, and =>4000 g were 80.4%, 50.0%, 48.9%, 25.4% and 30.8% respectively. Likewise, the percentage of infants who died in the gestational age categories <31 wk, 31-33 wk and 34-36 wk were 79.6%, 47.1% and 44.2% respectively. Seventeen (27.3%) of the IDMs died.

Major birth defects represented the most common cause of death in the NICU of KFHH during the study period (25.9%) followed by hyaline membrane disease (24.4%) and sepsis (23.5%), Figure 2. This contribution of birth defects to mortality almost remained unchanged throughout the three years of the study. The mean duration of NICU stay for all infants with birth defects was 12.44 days (SD 18.61). The longest duration was for IDMs with cardiomyopathy (36.2 days, SD 20.68) and infants with intestinal obstruction (36.11 days, SD 20.4) followed by hydrocephalic infants (31.25 days, SD 24.65).

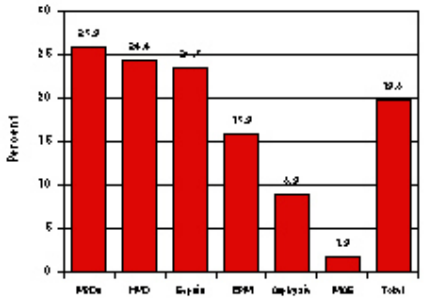

FIGURE 2. Cause-specific mortality rates, NICU, KFHH, 1411-1413H. MBDs=major birth defects; HMD=hyaline membrane disease; EPM=extreme prematurity; MAS=meconium aspiration syndrome.

Discussion

In the present study, only major and easily identified birth defects were included, the information was ascertained from different sources and a large number of infants born during the study period were admitted to the NICU and observation area and examined thoroughly. We believe, therefore, that there is a complete identification of the cases with major defects presenting at birth.

Our incidence rate (2.27%) of MBDs is relatively high considering that SBs were not included and that only defects manifesting at birth were studied. Furthermore, we observed a higher incidence of life-threatening malformations in our place than that reported from Libya and the USA (Table 1). In addition, a previous study[7] of an American population of both LBs and SBs found rates of 0.36, 0.15, 0.48 and 0.69/1000 infants for anencephaly, encephalocele, hydrocephalus and spina bifida respectively. This study and others[8] have observed a declining rate of these neural tube defects in their populations. We found approximately double these rates for the first three defects (Table 1) and there was no change in their incidence in the three years of the study. On the other hand, the lower incidence of some other defects in our study may be due to geographic differences, underdiagnosis or detection bias as an inherent limitation of a retrospective study. However, we undertook a one-month pilot study as a part of The Saudi Arabian Registry For Congenital Anomalies (SARCA) study and out of the 757 infants born in that month and screened carefully for birth defects, no single case of hip dislocation or coarctation was identified. Therefore, the possibility of detection bias in our study, although it cannot be excluded completely for asymptomatic defects, is unlikely for severe and obvious defects.

The high frequency of birth defects among LBW infants was reported before [5,9-10] and our data are consistent with these reports. We have also shown that the rate of birth defects increased greatly with decreased birth weight (Table 2). This finding has previously been shown by Mili and coworkers[5]and our results support their recommendations to study the complex etiology of LBW and to prevent risk factors for MBDs.

Older maternal age, grand multiparity and previous abortion have been described to be associated with higher frequency of some birth defects.[4,11] Further, changing maternal age and decreased parity were among the factors that led to the recent decline in the incidence of neural tube defects in different areas of the world.[12-13] However, with the exception of diabetic mothers and those of infants with chromosomal abnormalities, we found no significant differences in mothers' age, parity and history of abortion between the study and control mothers. This may be explained by the heterogeneous etiology of birth defects, small sample size of both groups, and/or the relatively high mean overall parity rate in our study groups. The increased age of diabetic mothers in the study group might be related to the higher chance of pre-existing diabetes in older diabetics and consequent increased frequency of malformations among their infants.

In spite of the dramatic fall of the stillbirth rate and overall perinatal mortality in IDMs over the past four decades, the incidence of congenital defects is virtually unchanged and their mortality is still high.[14] Maternal diabetes appeared to be an important contributor to the increased incidence of MBDs in our place; and our IDMs with birth anomalies suffered significant mortality and morbidity. Prospective studies are needed in the Al Hasa region to ascertain the incidence of birth defects in IDMs and to examine the relation between defects and risk factors in diabetic mothers.

Factors that may have contributed to the high mortality in our infants with MBDs include LBW and prematurity, sepsis, the seriousness of the defects themselves and /or a combination of all. However, we have shown that life-threatening malformations were more frequent in our place than in other areas; and our birth defect mortality rate was approximately five times that reported from Libya (37% vs. 7.5%).[4] Further, in areas where the sepsis rate is lower and the problems of prematurity were almost defeated, birth defects are now the most common cause of infant death.[1-3]We therefore believe that although sepsis and LBW were additional factors, the seriousness of the defects was a primary factor behind our excess mortality due to birth defects. In addition, with the use of surfactant and control of sepsis that started this year at KFHH, it is expected that mortality due to hyaline membrane disease and sepsis will be lower while that caused by MBDs will remain unchanged.

The results of this study indicate that every effort should be made to prevent the high incidence of birth defects among infants of the Al Hasa region and to reduce the excess mortality caused by these defects. This should include improving clinical care, intense etiologic research, and health education of the community. Based on the findings of this retrospective analysis, we plan to participate in the study of SARCA that aims at studying the epidemiology of birth anomalies in the Kingdom and establish a national registry for them.

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