Neonatal mortality, risk factors and causes: a prospective population-based cohort study in urban Pakistan

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Objective To evaluate the prevalence, sex distribution and causes of neonatal mortality, as well as its risk factors, in an urban Pakistani population with access to obstetric and neonatal care.

Methods Study area women were enrolled at 20–26 weeks' gestation in a prospective population-based cohort study that was conducted from 2003 to 2005. Physical examinations, antenatal laboratory tests and anthropometric measures were performed, and gestational age was determined by ultrasound to confirm eligibility. Demographic and health data were also collected on pretested study forms by trained female research staff. The women and neonates were seen again within 48 hours postpartum and at day 28 after the birth. All neonatal deaths were reviewed using the Pattinson et al. system to assign obstetric and final causes of death; the circumstances of the death were determined by asking the mother or family and by reviewing hospital records. Frequencies and rates were calculated, and 95% confidence intervals were determined for mortality rates. Relative risks were calculated to evaluate the associations between potential risk factors and neonatal death. Logistic regression models were used to compute adjusted odds ratios.

Findings Birth outcomes were ascertained for 1280 (94%) of the 1369 women enrolled. The 28-day neonatal mortality rate was 47.3 per 1000 live births. Preterm birth, Caesarean section and intrapartum complications were associated with neonatal death. Some 45% of the deaths occurred within 48 hours and 73% within the first week. The primary obstetric causes of death were preterm labour (34%) and intrapartum asphyxia (21%). Final causes were classified as immaturity-related (26%), birth asphyxia or hypoxia (26%) and infection (23%). Neither delivery in a health facility nor by health professionals was associated with fewer neonatal deaths. The Caesarean section rate was 19%. Almost all (88%) neonates who died received treatment and 75% died in the hospital.

Conclusion In an urban population with good access to professional care, we found a high neonatal mortality rate, often due to preventable conditions. These results suggest that, to decrease neonatal mortality, improved health service quality is crucial.

Une traduction en français de ce résumé figure à la fin de l'article. *Al final del artículo se facilita una traducción al español.* الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

Of the estimated 130 million infants born each year worldwide,[1] 4 million die in the first 28 days of life. Three-quarters of neonatal deaths occur in the first week, and more than one-quarter occur in the first 24 hours.[1,2] Neonatal deaths account for 40% of deaths under the age of 5 years worldwide. Therefore, efforts to achieve the UN Millennium Development Goal 4 of reducing childhood mortality by two-thirds by 2015 are focused on reducing neonatal deaths in high-mortality countries.

Two-thirds of the world's neonatal deaths occur in just 10 countries, mostly in Asia. Pakistan is number three among these countries. With an estimated 298 000 neonatal deaths annually and a reported neonatal mortality rate of 49 per 1000 live births, Pakistan accounts for 7% of global neonatal deaths.[1–5] Infection (36%), preterm birth (28%) and birth asphyxia (23%) account for 87% of neonatal deaths worldwide.[1,2,6] Since causes of neonatal death vary by country and with the availability and quality of health care, understanding neonatal mortality in relation to these factors is crucial.[2,7–10] Data available on neonatal deaths in Pakistan come primarily from hospital studies, which have a selective referral bias, or from communities in which the cause of death is rarely recorded. Information on pregnancy complications and other events before delivery is limited.[4,5,11]

Given the paucity of reliable population-based information in Pakistan, this study was undertaken to examine the prevalence, sex distribution, timing and causes of neonatal death in a population-based pregnancy cohort in urban Pakistan. We hypothesized that the neonatal mortality rate in this urban population, with relatively good access to obstetric care and Caesarean section, would be substantially lower than that generally reported for Pakistan. This study therefore examines delivery outcomes in pregnant women with reasonably good access to professional health care who were enrolled at 20 to 26 weeks' gestation and followed with their infants to 28 days postpartum.

Methods

This prospective population-based study was conducted from September 2003 to August 2005 in four of 12 administrative units in the town of Latifabad, Hyderabad, Pakistan.

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Table 1. **Stillbirth and neonatal and perinatal mortality rates, by gender and in total, in a prospective study in an urban Pakistani population, 2003–2005**

Births and mortality rates	Births/ deaths	Males	Females	Total[a]
All births,[b] *n* (%)	1280	619 (51.5)	583 (49.5)	1280 (100)
Stillbirths,[c] rate per 1000 births (95% CI)	43	35.5 (20.7–50.4)	25.7 (15.4–38.7)	33.6 (23.6–43.6)
Early neonatal mortality, rate per 1000 live births (95% CI)	39	35.0 (19.5–50.4)	29.3 (14.7–43.9)	34.8 (24.1–45.5)
Late neonatal mortality, rate per 1000 live births (95% CI)	14	5.5 (0.0–11.8)	19.5 (7.5–31.5)	12.5 (6.0–19.0)
Neonatal mortality, rate per 1000 live births (95% CI)	53	40.5 (23.9–57.1)	48.8 (30.2–67.5)	47.3 (34.9–59.7)
Perinatal mortality, rate-1[d] (95% CI)	82	72.6 (51.2–94.0)	56.9 (37.1–76.7)	70.4 (55.7–85.1)
Perinatal mortality, rate-2[e] (95% CI)	96	77.9 (55.8–100.0)	75.9 (53.3–98.5)	82.5 (66.7–98.3)

CI, confidence interval.
[a] Gender not recorded for 78 births.
[b] Includes the 78 infants without gender data.
[c] The rate of stillbirths was calculated from the number of women with known birth outcomes ($n = 1280$), while neonatal and perinatal mortality rates were derived from the number whose outcomes were known at 28 days ($n = 1121$) plus stillbirths, where appropriate.
[d] Rate-1 is stillbirths plus mortality within 7 days per 1000 births.
[e] Rate-2 is stillbirths plus mortality within 28 days per 1000 births.

These four units covered an area with a low-to-middle income population of about 90 000 individuals, or about 9000 households. Permanent residents who planned to give birth in the catchment area were screened by lady health workers (LHWs) of the Pakistan Ministry of Health. These LHWs are female community residents who have had eight or more years of education and 15 months of government training. They provide basic maternal care, including child health services, and maintain logs of all pregnancies and birth outcomes among their assigned households. In the four study units, approximately 90 LHWs were trained in the research protocols, study recruitment, communication skills and confidentiality. Study nurses supervised the LHWs in the required fieldwork. We therefore believe that our study team was aware of nearly every pregnancy in the catchment area.

During their routine home visits, LHWs provided study information to pregnant women who were screened as eligible for the study. Women were eligible if they were aged 16 years or more, did not have a serious medical condition, planned to deliver in the catchment area and were at 20–26 weeks' gestation at enrolment. Women who indicated interest were scheduled for an appointment at the research clinic closest to their home. At the research clinic visit, gestational age was determined by ultrasound to confirm eligibility, and a physical examination and anthropometric measurements were performed. Various demographic and health data and routine antenatal laboratory test results were collected on pretested study forms by trained female research staff, which included two doctors, one dentist, two health visitors and one midwife. Prior to enrolment, all eligible women provided informed consent.

The LHWs tracked all enrolled women until delivery. Research staff also developed liaisons with public and private delivery facilities and home birth attendants to ensure complete birth reporting for the study. Once a delivery had been reported, a study physician and nurse visited the woman at home or at the health facility within 48 hours to collect maternal data on the delivery and birth outcome. A postnatal visit for data collection was made on about day 28.

Outcomes

Outcomes for all fetuses and neonates delivered after enrolment were clearly defined. A stillbirth was defined as any fetus born without a heartbeat, respiratory effort or movement, or any other sign of life. The stillbirth rate is the number of stillbirths per 1000 births. Neonatal death rates included all of the deaths of live-born infants on or before 28 days postpartum and the early neonatal death rate included all deaths of live-born infants occurring on or before 7 days of age. Both are expressed per 1000 live births. The perinatal death rate is the sum of neonatal deaths and stillbirths per 1000 births. In addition, a perinatal mortality-1 rate was defined as the sum of all stillbirths and neonatal deaths on or prior to day 7 (henceforth 7-day neonatal deaths) per 1000 births, and a perinatal mortality-2 rate as the sum of all stillbirths and deaths on or prior to day 28 (henceforth 28-day neonatal deaths) per 1000 births.

For all neonatal deaths and stillbirths, the study physician and nurse interviewed the mother about the circumstances leading to the event. Because most neonatal deaths occurred in hospitals, maternal reports were supplemented by a review of hospital records by the study physician. Finally, the completed study forms on mothers who experienced a neonatal death were reviewed jointly by a neonatologist (*SS*) and the primary author (*IJ*) using the Pattinson et al.[12] adaptation of the Aberdeen classification[13] for developing countries. Details of stillbirths in our study community and the overall methodology have been reported previously.[14]

The Pattinson et al. adaptation of the Aberdeen classification was used because it identifies the potential for both preventing and reducing avoidable fetal and neonatal mortality.[12] The primary obstetric cause of neonatal death was defined in the classification as the obstetric antecedent factor or event that initiated the process or sequence of events leading to the death of the neonate. The classification system is non-hierarchical and allows for the identification of the following obstetric causes of neonatal death: preterm labour (< 37 weeks) or premature rupture

of membranes, antepartum haemorrhage, intrapartum asphyxia, infection, intrauterine growth retardation including postmaturity, hypertension, fetal abnormality, maternal disease, trauma and unexplained intrauterine death. For the classification of the primary obstetric cause of death, intrapartum asphyxia included prolonged labour, meconium aspiration and umbilical cord compression or accident. Fetal abnormalities included chromosomal and somatic abnormalities. A single obstetric cause was assigned to each neonatal death.

In addition, the final cause of a neonatal death was also assigned according to the event that caused the death, as follows: immaturity-related, birth asphyxia or hypoxia, infection, congenital abnormality, trauma, other or unknown. In this classification, immaturity-related deaths included those due to extreme multiorgan immaturity (only in infants born less than 28 weeks' gestation) and hyaline membrane disease or clinical respiratory distress in the absence of any other detectable cause. Death due to birth asphyxia was recorded when a normally formed term baby was unable to initiate and sustain respiration at birth or had a low Apgar score or clinical signs of hypoxia or meconium aspiration. Congenital abnormalities included chromosomal and somatic malformations.

The study was undertaken under the auspices of the Global Network for Women's and Children's Health Research. The study was reviewed and approved by the Aga Khan University Ethical and Review Committee in Pakistan and institutional review boards at the University of Alabama at Birmingham and Research Triangle International in the United States of America.

Sample size

For this study, we had sufficient resources to study approximately 1300 pregnant women and their neonates. Since we were evaluating many different risk factors and the sample size was fixed, the following calculation was performed to determine the likelihood that a specific risk factor would have a significant association with neonatal mortality: with an expected neonatal mortality rate of 50 per 1000 live births, the expected 95% confidence interval associated with a sample size of 1300 births is ±12 neonatal deaths per 1000 live births.

Table 2. **Demographic and clinical characteristics of the mothers of infants who died within 28 days postpartum or who survived, in a prospective study in an urban Pakistani population, 2003–2005**

Characteristic	Neonatal death within 28 days No. (%)[a]	Surviving infant No. (%)[a]	RR (95% CI)
Maternal age (*n* = 1116)			
< 20 years	3 (5.9)	57 (5.4)	1.2 (0.4–3.8)
20–35 years (reference)	39 (76.5)	910 (85.5)	1.0 (NA)
> 35 years	9 (17.7)	98 (9.2)	1.5 (1.0–4.1)
Maternal schooling (*n* = 1116)			
None	20 (39.2)	355 (33.3)	2.1 (0.7–6.1)
≤ 5 years	12 (23.5)	188 (17.7)	1.4 (0.4–5.1)
6–10 years	14 (27.5)	334 (31.4)	1.7 (0.5–5.1)
> 10 years (reference)	5 (9.8)	188 (17.7)	1.0 (NA)
Husband employed (*n* = 1113)			
Yes (reference)	46 (92.0)	1028 (96.7)	1.0 (NA)
No	4 (8.0)	35 (3.3)	2.4 (0.9–6.3)
Previous perinatal loss (*n* = 905)			
Yes	12 (29.3)	192 (2.2)	1.4 (0.7–2.7)
No (reference)	29 (70.7)	672 (77.8)	1.0 (NA)
Maternal weight at study enrolment (*n* = 1116)			
< 50 kg	20 (39.2)	335 (31.5)	1.4 (0.8–2.4)
≥ 50 kg (reference)	31 (60.8)	730 (68.5)	1.0 (NA)
Maternal height (*n* = 1116)			
< 145 cm	6 (11.8)	75 (7.0)	1.7 (0.7–3.9)
≥ 145 cm (reference)	45 (88.2)	990 (93.0)	1.0 (NA)
Haemoglobin level at study enrolment (*n* = 1114)			
< 8 g/dl	3 (5.9)	35 (3.3)	1.6 (0.5–5.0)
8–11 g/dl (reference)	48 (94.1)	942 (88.6)	1.0 (NA)
≥ 11 g/dl	0 (0.0)	86 (8.1)	0.0 (NA)
Maternal genital infection (*n* = 1116)			
Yes	0 (0.0)	42 (3.9)	0.0 (NA)
No (reference)	51 (100)	1023 (96.1)	1.0 (NA)
Antenatal care visits (*n* = 1116)			
None	1 (2.0)	42 (3.9)	0.5 (0.1–3.8)
1–4	15 (29.4)	253 (23.8)	1.3 (0.7–2.3)
> 4 (reference)	35 (68.6)	770 (72.3)	1.0 (NA)

CI, confidence interval; RR, relative risk; NA, not applicable.
[a] Denominators for demographic and clinical characteristics may differ due to non-response.

Data management and analysis

All data were entered centrally. Data audits, including inter- and intra-form consistency checks, were performed at data entry, and additional audits were performed by the data centre (i.e. Research Triangle International, NC, USA). Data were analysed using SAS version 9.1.3. (SAS Institute Inc., NC, USA). For the descriptive analysis, frequencies, percentages and rates were calculated, and 95% confidence intervals (CIs) were determined for mortality rates. Relative risks (RRs) and 95% CIs were calculated to evaluate

the associations between potential risk factors and neonatal death. In addition, logistic regression models were used to compute adjusted odds ratios (AORs) and their associated 95% CIs.

Results

Between September 2003 and August 2005, LHWs identified 2205 pregnant women from the study area, 25% of whom were not eligible for study enrolment. Of the 1659 eligible, 17% either refused to participate (6%) or failed to appear at the research clinic (11%). Thus, 83% of those eligible, or 1369 women, were enrolled at 20–26 weeks' gestation. Birth outcome data were obtained for 1280 (94%) of the enrolled women and 28-day follow-up data, for 1121 women. The demographic characteristics of the women whose neonatal outcomes were known at 28 days were not significantly different from those who were lost to follow-up or who refused to participate ($P > 0.05$ for age, educational level, marital status, maternal height and maternal weight).

Rates were as follows: stillbirth, 33.6 per 1000 births (95% CI: 23.6–43.6); early neonatal mortality, 34.8 per 1000 live births (95% CI: 24.1–45.5); 28-day neonatal mortality, 47.3 per 1000 live births (95% CI: 34.9–59.7); perinatal mortality-1 (i.e. stillbirths plus all early neonatal deaths), 70.4 per 1000 births (95% CI: 55.7–85.1); and perinatal mortality-2 (i.e. stillbirths plus all neonatal deaths), 82.5 per 1000 births (95% CI: 66.7–98.3) (Table 1). Of the 53 neonatal deaths, 39 (75%) occurred in the first 7 days. Although the difference was not statistically significant, early neonatal and perinatal mortality-1 rates were slightly higher among males than females (35.0 versus 29.3 per 1000 live births, $P = 0.60$; and 72.6 versus 56.9 per 1000 births, $P = 0.29$, respectively). However, the 28-day neonatal mortality rate was slightly lower among males than females (40.5 versus 48.8 per 1000 live births; $P = 0.51$), as shown in Table 1. The reason for this difference was that the late neonatal mortality rate (i.e. for deaths from days 8 to 28) was significantly lower for males than females (5.5 versus 19.5 per 1000 live births, $P = 0.05$).

Table 2 compares the characteristics of mothers whose infants died within the 28 days following delivery with those of mothers whose infants

Table 3. **Clinical and delivery variables for infants who died within 28 days postpartum and for those who survived in prospective study of neonatal mortality in an urban Pakistani population, 2003–2005**

Variables	Death within 28 days (*n* = 53) No. (%)[a]	Surviving infant (*n* = 1066) No. (%)[a]	RR (95% CI)
Gestational age at birth (*n* = 1119)			
< 37 weeks	31 (58.5)	189 (17.7)	5.8 (3.4–9.7)
≥ 37 weeks (reference)	22 (41.5)	877 (82.3)	1.0 (NA)
Birth weight (*n* = 1021)			
< 2000 g	6 (26.1)	55 (5.5)	5.6 (2.3–13.6)
≥ 2000 g (reference)	17 (73.9)	943 (94.5)	1.0 (NA)
Gender (*n* = 1055)			
Male	22 (46.8)	521 (51.7)	0.8 (0.5–1.5)
Female (reference)	25 (53.2)	487 (48.3)	1.0 (NA)
Place of delivery (*n* = 1121)			
Home	10 (18.9)	218 (20.3)	0.9 (0.5–1.8)
Hospital or other health-care facility (reference)	43 (81.1)	850 (79.6)	1.0 (NA)
Birth attendant (*n* = 1111)			
Traditional birth attendant or other	6 (11.5)	175 (16.5)	0.6 (0.3–1.4)
Nurse, midwife or equivalent	9 (17.3)	256 (24.2)	0.6 (0.3–1.2)
Doctor (reference)	37 (71.2)	628 (59.3)	1.0 (NA)
Mode of delivery (*n* = 1068)			
Vaginal (reference)	30 (63.8)	830 (81.3)	1.0 (NA)
Caesarean section	17 (36.2)	191 (18.7)	2.3 (1.3–4.2)
Preterm rupture of membranes (*n* = 1116)			
< 12 hours (reference)	46 (90.2)	1000 (93.9)	1.0 (NA)
12–24 hours	5 (9.8)	65 (6.1)	1.6 (0.7–4.0)
Colour of amniotic fluid (*n* = 995)			
Clear (reference)	28 (63.6)	793 (83.4)	1.0 (NA)
Meconium-stained	12 (27.3)	116 (12.2)	2.7 (1.4–5.3)
Other	4 (9.1)	42 (4.4)	2.5 (0.9–7.0)
Amniotic fluid odour (*n* = 975)			
Foul-smelling	9 (23.8)	76 (7.8)	3.1 (1.5–6.2)
Not foul-smelling (reference)	32 (76.2)	858 (92.2)	1.0 (NA)
Prolonged labour (*n* = 1066)			
Yes	4 (8.5)	137 (13.4)	0.6 (0.2–1.7)
No (reference)	43 (91.5)	882 (86.6)	1.0 (NA)
Vaginal bleeding (*n* = 1019)			
Excessive	6 (13.3)	59 (6.0)	2.3 (1.0–5.1)
Normal (reference)	39 (86.7)	915 (94.0)	1.0 (NA)
Antepartum fever with chills (*n* = 1056)			
Yes	7 (15.6)	90 (8.9)	1.9 (0.9–4.1)
No (reference)	38 (84.4)	921 (91.0)	1.0 (NA)

CI, confidence interval; NA, not applicable; RR, relative risk.

[a] Denominators for demographic and clinical characteristics may differ due to non-response.

survived. On univariate analysis, no maternal characteristic was found to be significantly associated with neonatal death. Regression analysis confirmed the absence of a significant association in this population.

Table 3 shows a comparison of the delivery and clinical characteristics of infants who died in the 28 days following delivery and those who survived. Factors found to be significantly associated with neonatal death in the univariate analysis include gestational age < 37 weeks (RR, 5.8; 95% CI: 3.4–9.7), birth weight < 2000 g (RR, 5.6; 95% CI: 2.3–13.6), Caesarean section (RR, 2.3; 95% CI: 1.3–4.2), meconium-stained fluid (RR, 2.7; 95% CI: 1.4–5.3), foul-smelling amniotic fluid (RR, 3.1; 95% CI: 1.5–6.2) and excessive vaginal bleeding (more than blood-stained mucus) during labour (RR, 2.3; 95% CI: 1.0–5.1). Neither gender, premature rupture of membranes, prolonged labour nor maternal fever was significantly associated with neonatal mortality. When these factors (excluding birth weight because of its collinearity with gestational age) were evaluated together using regression analysis, gestational age < 37 weeks (AOR, 5.0; 95% CI: 2.5–9.9) and Caesarean section (AOR, 2.3; 95% CI: 1.1–4.7) were the only factors that remained significant predictors of neonatal mortality. These results suggest that the other factors found to be significant in the univariate analysis may have been acting through their relationship to gestational age or birth weight or to the mode of delivery. In a subsequent univariate analysis of delivery risk factors in which gestational age, birth weight and mode of delivery were excluded, significant relationships were found between neonatal mortality and foul-smelling amniotic fluid (AOR, 2.1; 95% CI: 1.0–5.4) and excessive vaginal bleeding (AOR, 1.6; 95% CI: 1.0–4.5).

Table 4 presents details of the medical care received by infants who died in the 28 days following delivery and their mothers both at birth and before neonatal death. Of the 53 neonatal deaths, 45% occurred in the first 48 hours and 73% within 7 days. Eighty per cent of infants who died were born in a hospital or maternity clinic, and 69% were delivered by a doctor (data not shown). Thirty-five per cent of all neonatal deaths and 55% of those that occurred within 48 hours followed delivery by Caesarean section. Seventy-five per cent of all neonatal deaths and 91% of deaths within 48 hours occurred in the hospital. Of the 45 infants who died within 28 days and who received medical treatment, 87% were treated in a hospital and 13% in a clinic.

Table 4. **Medical care received by infants who died within 28 days postpartum and their mothers, both at delivery and before neonatal death, in prospective study in an urban Pakistani population, 2003–2005**

Medical care	Deaths			
	All No. (%)[a]	Within 48 hours No. (%)[a]	Within 3–7 days No. (%)[a]	Within 8–28 days No. (%)[a]
Neonatal death	53 (100)	24 (45.3)	15 (28.3)	14 (26.4)
Mode of delivery (*n* = 51)				
Vaginal	33 (64.7)	10 (45.5)	12 (80.0)	11 (78.6)
Caesarean section	18 (35.3)	12 (54.5)	3 (20.0)	3 (21.4)
Place of death (*n* = 51)				
Home	13 (25.5)	2 (9.1)	5 (33.3)	6 (42.9)
Hospital	38 (74.5)	20 (90.9)	10 (66.7)	8 (57.1)
Treatment before death (*n* = 51)				
Yes	45 (88.2)	20 (90.9)	13 (86.7)	12 (85.7)
No	6 (11.8)	2 (9.1)	2 (13.3)	2 (14.3)
Place of treatment (*n* = 45)				
Clinic	6 (13.3)	1 (5.0)	2 (15.4)	3 (25.0)
Hospital	39 (86.7)	19 (95.0)	11 (84.6)	9 (75.0)

[a] Denominators for demographic and clinical characteristics may differ due to non-response.

Table 5 presents the primary obstetric and final causes of neonatal death as determined using the Pattinson et al. classification. The obstetric factors associated with neonatal death were: preterm labour (34%), intrapartum asphyxia (21%), antepartum haemorrhage (9%), infection (4%), congenital abnormality (4%) and intrauterine growth retardation (2%). No obstetric cause was found in 19% of cases.

Almost 75% of neonatal deaths were attributed to three final causes: immaturity-related (26%), birth asphyxia or hypoxia (26%) and infection (23%). Congenital abnormality accounted for 8%. Almost all deaths classified as due to immaturity or asphyxia occurred during the first week of life. There were no deaths classified as infection-related (i.e. involving sepsis, pneumonia or meningitis) in the first 48 hours. Although low birth weight was not considered as an independent cause of death, in 54% of neonatal deaths the infant weighed < 2500 g at birth, with 87% of these low-birthweight infants being preterm.

Discussion

To address UN Millennium Development Goal 4 on reducing childhood mortality, there is a need for better population-based data on the rates and causes of neonatal death. Our prospective population-based study provided a rare opportunity to obtain reliable information on the rate, timing and direct cause of neonatal death. Because pregnant women from a defined population were enrolled at 20 to 26 weeks' gestation and followed with their infants to 28 days postpartum, data on antepartum history, delivery and events before neonatal death, in addition to maternal interview data, were available, so we could determine the causes of death quite reliably. Our study therefore provides information on neonatal mortality in a population with relatively good access to professional maternity and neonatal care.

The high 28-day neonatal mortality rate of 47 per 1000 live births and the high 7-day perinatal mortality rate of 70 per 1000 births observed in our study are striking, since they represent outcomes in an urban cohort in which a high proportion of births took place in a health facility assisted by skilled attendants, and a high proportion of sick neonates were cared for in the formal health-care system. Since reported neonatal mortality rates for all of Pakistan

are in the range of 45–50 per 1000 live births, our hypothesis that the neonatal mortality rate in this urban population would be substantially lower than that reported for the rest of Pakistan proved incorrect. We believe there are two reasons for this finding. First, we suspect that, because of underreporting, actual Pakistani neonatal mortality rates may be higher than reported and, second, that, despite the seemingly appropriate quantity of care provided for women in the study, the quality may have been suboptimal.

Recently there has been a growing demand for perinatal mortality data to be disaggregated by gender, geographic location and socioeconomic status, to enable programmes to improve resource allocation and monitoring.[8] Our study reports gender-specific neonatal mortality rates in a defined urban population. The gender differential in early and late neonatal mortality is worth noting. Proportionately, there were more male deaths in the early neonatal period, a finding consistent with the well described biological survival advantage of girls in the neonatal period. In contrast, there were more female deaths in the late neonatal period. Reduced care-seeking for girls compared with boys has been reported in several settings, especially in south Asia.[15,16]

The most common primary obstetric causes of neonatal death were preterm delivery in 34%, intrapartum asphyxia in 21% and antepartum haemorrhage in 9%. The relative importance of these causes is reflected in the distribution of the final causes of neonatal death: immaturity-related in 26%, birth asphyxia or hypoxia in 26% and infection in 23%. These results are consistent with WHO reports on the causes of neonatal death in developing countries and also with other reports from Pakistan.[2,4,5] Furthermore, our finding that infection, including sepsis, pneumonia and meningitis, is an important contributor to neonatal deaths that occur after 3 days postpartum among hospital-born neonates is consistent with recent studies from developing countries and emphasizes the importance of monitoring delivery and hospital-acquired infection.[17]

It could be argued that the high neonatal mortality seen in this population may be due to selective recruitment of high-risk women into the study. However, women were enrolled into the study by LHWs during routine home visits, and a substantial majority of all eligible women were enrolled. Study nurses cross-checked enrolment and LHW delivery logs to ensure that women enrolled prenatally and those for whom we had delivery results were the same women. In addition, the baseline characteristics of the study population are typical for the area. We therefore believe that the risk of biased reporting of neonatal mortality for this population is small.

We were surprised by the high Caesarean section rate of 19% in this community. However, in comparison with rural areas of Pakistan, where home birth and a very low Caesarean section rate are the norm, there is now a growing trend in urban areas towards hospital birth and associated Caesarean delivery.[18,19] We therefore believe that the high Caesarean section rate seen in this urban population is closer to the norm than is commonly realized. The UN recommends a Caesarean section rate of 5–15% to optimally minimize maternal and neonatal mortality rates.[4,20] This recommendation presumes that these Caesarean sections are performed in a timely manner on appropriate women. Evidence from other areas of Pakistan suggests that this may not be the case.[21]

Recent reports from developing countries have shown improvements in perinatal and neonatal outcomes with increased coverage by health services and skilled birth attendants.[2,8,22] However, our findings suggest that women experienced avoidable antenatal and obstetric complications despite good availability of antenatal care, a high rate of births in a health facility with skilled birth attendants, and a "high" Caesarean section rate. Intrapartum events such as heavy vaginal bleeding and the presence of foul-smelling amniotic fluid were significant risk factors for early neonatal death. Deaths associated with these factors may be modifiable through effective antenatal and intrapartum care. Furthermore, while the majority of sick neonates received some formal health care before death, we suspect that higher quality neonatal

Table 5. **Primary obstetric and final causes of neonatal deaths that occurred within 28 days postpartum in prospective study in an urban Pakistani population, according to the time of death, 2003–2005**

Cause of death	Deaths (n = 53)			
	Within 48 hours No.	Within 3–7 days No.	Within 8–28 days No.	All No. (%)
Primary obstetric cause of death				
Preterm labour or premature rupture of membranes	10	5	3	18 (34)
Intrapartum asphyxia	8	3	0	11 (21)
Antepartum haemorrhage	2	3	0	5 (9)
Infection	1	0	1	2 (4)
Congenital abnormality	1	0	1	2 (4)
Intrauterine growth retardation	0	1	0	1 (2)
Rhesus incompatibility	0	0	1	1 (2)
No obstetric cause	0	2	8	10 (19)
Cause undetermined due to insufficient information	2	1	0	3 (5)
Final cause of death				
Immaturity-related	11	2	1	14 (26)
Birth asphyxia or hypoxia	8	6	0	14 (26)
Infection (involving sepsis, pneumonia or meningitis)	0	5	7	12 (23)
Congenital abnormality	2	0	2	4 (8)
Other	1	2	2	5 (9)
Cause undetermined due to insufficient information	2	0	2	4 (8)
Total	**24**	**15**	**14**	**53 (100)**

care would also result in reduced mortality in these cases.

Without improved quality, increased health-care coverage is unlikely to substantially improve perinatal and neonatal outcomes.[2,8,22,23] Recent reports from Pakistan and other low-resource settings indicate that substandard care, inadequate training, low staff competence and a lack of resources, including equipment and medication, are all factors that contribute to neonatal deaths.[23,24] Since the quantity of care in this study's setting was relatively high for a developing country, it is likely that the quality of care will need to be improved if the neonatal mortality rate is to be substantially reduced. We therefore speculate that improvements in health-system performance and ongoing clinical audits[25] could reduce the high rates of adverse perinatal outcomes in a population such as ours with a high level of health-care coverage. ■

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Résumé

La mortalité néonatale, ses facteurs de risque et ses causes : étude de cohorte prospective en population dans une zone rurale du Pakistan

Objectif Evaluer la prévalence, la distribution par sexes et les causes de la mortalité néonatale, ainsi que ses facteurs de risque, dans une population pakistanaise urbaine, ayant accès aux soins obstétricaux et néonatals.

Méthodes Des femmes de la zone étudiée ont été recrutées à 20-26 semaines de grossesse pour participer à une étude de cohorte prospective en population, réalisée de 2003 à 2005. Des examens physiques, des examens de laboratoires anténatals et des mesures anthropométriques ont été pratiqués et l'âge gestationnel a été déterminé par échographie pour confirmer l'admissibilité dans l'étude. Des données démographiques et sanitaires ont également été recueillies au moyen de formulaires d'étude préalablement testés, par des membres féminins du personnel de recherche formés à cet effet. Les mères et les nouveau-nés ont été revus dans les 48 heures suivant l'accouchement et le 28e jour après la naissance. Tous les décès néonatals ont été analysés à l'aide du système de Pattinson et al. pour leur affecter des causes obstétricales et finales ; leurs circonstances ont été déterminées en interrogeant la mère ou la famille et en examinant les dossiers hospitaliers. On a calculé, les fréquences et les taux de mortalité, ainsi que les intervalles de confiance à 95 % associés à ces derniers. On a également déterminé les risques relatifs pour évaluer les associations entre les facteurs de risque éventuels et les décès néonatals. On a fait appel à des modèles de régression logistique pour calculer les odds ratios ajustés.

Résultats On a déterminé l'issue de l'accouchement pour 1280 (94 %) des 1369 femmes participant à l'étude. Le taux de mortalité néonatale à 28 jours était de 47,3 pour 1000 naissances vivantes. Il existait une association entre les naissances avant terme, les accouchements par césarienne et les complications intrapartum, d'une part, et les décès néonatals, d'autre part. Près de 45 % des décès sont intervenus dans les 48 heures et 73 % dans la première semaine après l'accouchement. Les principales causes obstétricales de décès étaient le travail avant terme (34 %) et l'asphyxie intrapartum (21 %). Comme causes finales de décès, on relevait, dans l'ordre, les causes liées à l'immaturité (26 %), l'asphyxie ou l'hypoxie pendant l'accouchement (26 %) et les infections (23 %). Ni le fait d'accoucher dans un établissement de soins, ni la réalisation de l'accouchement par un professionnel de santé, n'étaient associés à une baisse du nombre de décès néonatals. Le taux d'accouchement par césarienne était de 19 %. Presque tous les nouveau-nés décédés (88 %) avaient reçu un traitement et 75 % d'entre eux étaient morts à l'hôpital.

Conclusion Dans une population urbaine disposant d'un accès satisfaisant aux soins de santé, nous avons relevé un taux de mortalité néonatale élevé, souvent dû à des affections évitables. Ces résultats laissent à penser qu'il est essentiel d'améliorer la qualité des services de santé pour faire baisser la mortalité néonatale.

Resumen

Mortalidad neonatal, factores de riesgo y causas: estudio de cohortes prospectivo basado en la población en el Pakistán urbano

Objetivo Evaluar la prevalencia, la distribución por sexos y las causas de la mortalidad neonatal, así como los factores de riesgo asociados, en una población urbana del Pakistán con acceso a atención obstétrica y neonatal.

Métodos Entre 2003 y 2005 se realizó un estudio de cohortes prospectivo basado en la población con embarazadas que se encontraban entre la 20 y la 26 semana de gestación. Se sometió a las mujeres a exploración física, pruebas de laboratorio prenatales y mediciones antropométricas y se determinó la edad gestacional mediante ecografía para confirmar la elegibilidad. Personal investigador femenino reunió también datos demográficos y sanitarios mediante formularios que se habían ensayado previamente. Las mujeres y los recién nacidos fueron examinados de nuevo en el término de 48 horas tras el parto y a los 28 días del nacimiento. Todas las defunciones neonatales fueron analizadas mediante el sistema ideado por Pattinson y col. para asignar las causas obstétricas y finales de la defunción; las circunstancias de la muerte se determinaron interrogando a la madre u otros familiares y examinando las historias clínicas. Se calcularon las frecuencias y las tasas, y se determinaron los intervalos de confianza del 95% de las tasas de mortalidad. Se calcularon los riesgos relativos para evaluar la relación entre los factores de

riesgo potenciales y la mortalidad neonatal, y el cálculo de las razones de posibilidades ajustadas se hizo mediante regresión logística.

Resultados Se determinaron los resultados obstétricos de 1280 (94%) de las 1369 mujeres participantes. La tasa de mortalidad neonatal a los 28 días fue de 47,3 por 1000 nacidos vivos. Los nacimientos prematuros, las cesáreas y las complicaciones durante el parto se asociaron a mortalidad neonatal. Un 45% de las defunciones se produjeron en el término de las primeras 48 horas, y el 73% durante la primera semana. Las principales causas obstétricas de defunción fueron el parto prematuro (34%) y la asfixia intraparto (21%). Las causas finales se clasificaron como relacionadas con la inmadurez (26%), con situaciones de asfixia o hipoxia en el parto (26%) y con infecciones (23%). El hecho de dar a luz en un centro de salud o con la asistencia de profesionales sanitarios no se asoció a un menor número de muertes neonatales. La tasa de cesáreas fue del 19%. Casi todos (88%) los recién nacidos que fallecieron habían recibido tratamiento, y el 75% murieron en el hospital.

Conclusión En una población urbana con buen acceso a atención profesional, observamos una tasa de mortalidad neonatal elevada, debida con frecuencia a problemas prevenibles. Estos resultados llevan a pensar que la mejora de la calidad de los servicios de salud es fundamental para reducir la mortalidad neonatal.

ملخص

وفيات الولدان، عوامل الاختطار والمسببات: دراسة أترابية مجتمعية استباقية في منطقة حضرية في باكستان

الغرض: تقييم معدلات وفيات الولدان، وتوزعها بحسب الجنس، وأسبابها، وعوامل الاختطار، وذلك في مجتمع حضري باكستاني تتوفر له إمكانية الحصول على الرعاية التوليدية ورعاية الولدان.

الطريقة: تم في دراسة أترابية مجتمعية استباقية، أجريت بين عامَيْ 2003 و2005، تسجيل الحوامل اللاتي تراوح العمر الحملي لديهن بين الأسبوع العشرين والأسبوع السادس والعشرين، وذلك في المنطقة التي جرى فيها البحث. وقد خضعن للفحوص البدنية، والمختبرية الخاصة بالرعاية السابقة للولادة، إلى جانب قياسات أنثروبومترية. وحُدِّد العمر الحملي باستخدام الموجات فوق الصوتية لتأكيد الأهلية للاشتراك في الدراسة. وجمعت موظفات مدرّبات على الأعمال البحثية، بيانات ديموغرافية وصحية على نماذج مسبقة الاختبار خاصة بالدراسة. وفحصت النسوة والولدان مرة أخرى وذلك في غضون 48 ساعة من الولادة، وفي اليوم الثامن والعشرين بعد الولادة. وروجعت جميع حالات وفيات الولدان وفق نظام ((باتينسون وآخرون)) لتحديد الأسباب التوليدية والنهائية للوفاة. وحددت ظروف الوفاة من خلال سؤال الأم والعائلة، وكذلك من خلال مراجعة سجلات المستشفى. وتم حساب التواتر والمعدلات، وحددت فواصل الثقة بنسبة 95% لمعدلات الوفيات. وتم أيضاً حساب المخاطر النسبية لتقييم الارتباط بين عوامل الاختطار المحتملة وبين وفاة الوليد. واستخدمت نماذج التحوف اللوجستي لحساب نسب الأرجحية المصححة.

الموجودات: تم التحقُّق من الحصائل الولادية لـ 1280 (94%) من بين 1369 امرأة مسجلة في الدراسة. وبلغ معدل وفيات الولدان خلال الـ 28 يوماً الأولى بعد الولادة 47.3 لكل 1000 مولود حي. وكان هناك ارتباط بين الولادة المبتسرة، والولادة القيصرية، وحدوث مضاعفات أثناء الوضع، وبين وفيات الولدان. وتبين أن نحو 45% من الوفيات قد وقعت خلال 48 ساعة من الولادة، و73% منها وقعت خلال الأسبوع الأول. وكانت الولادة المبتسرة (34%)، والاختناق أثناء الوضع (21%) من بين الأسباب التوليدية الأولية للوفاة. وصنّفت الأسباب ذات الصلة بعدم اكتمال النمو (26%)، والاختناق أو نقص التأكسج أثناء الولادة (26%)، والإصابة بعدوى (23%) كأسباب نهائية. ولم يكن هناك ارتباط بين حدوث الولادة في مرفق صحي أو على يد مهنيِّين صحيِّين، وبين قلة عدد الوفيات. وبلغ معدل الولادة القيصرية 19%، وكان جميع الولدان المتوفين تقريباً (88%) قد تلقّوا معالجة، كما توفي 75% منهم في المستشفى.

الاستنتاج: وجد الباحثون ارتفاعاً في معدلات وفيات الولدان لأسباب يمكن في العادة توقيها، وذلك في مجتمع حضري يحصل سكانه بشكل جيد على رعاية صحية مهنية. وتشير هذه النتائج إلى أن تحسين جودة الخدمات الصحية يُعد أمراً حاسماً لتقليل وفيات الولدان.

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