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Stillbirths in an Urban Community in Pakistan

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Abstract

Objective—To determine stillbirth risk factors and gestational age at delivery in a prospective developing country birth cohort.

Study Design—1369 Pakistani women were prospectively enrolled at 20 - 26 weeks, the gestational age determined by ultrasound, and risk factors and pregnancy outcomes assessed.

Results—The stillbirth rate was 33.6/1000 births despite 96% of women receiving prenatal care, 83% attended by skilled providers in hospital and a 20% cesarean section rate. 51% of stillbirths occurred $\geq$ 37 weeks and 19% from 34–36 weeks. Only 4% had congenital anomalies. Hemoglobin $<$ 8 g/dL, vaginal bleeding and preeclampsia were associated with increased stillbirth risk.

Conclusions—In this developing country with reasonable technical resources defined by hospital delivery and a high cesarean section rate, stillbirth rates were much higher than US rates. That most of the stillbirths were term, did not have congenital anomalies and the demise appeared to be recent, suggests that many Pakistani stillbirths may be preventable with higher quality obstetric care.

Keywords

stillbirth; obstetrical care; developing countries

Introduction

Stillbirth is one of the most common adverse outcomes of pregnancy. Each year, 3.3 million stillbirths are reported, with 97% occurring in developing countries[1]. Because registries are available in only four percent of the developing world and under-reporting is a common problem[2], it is likely that an additional 1-2 million stillbirths occur, but are not reported.

Stillbirth rates vary by geographic region and socioeconomic status. Rates of 5 per 1000 or less are seen in the U.S. and most developed countries while stillbirth rates in the range of 30 to 40/1000 births are common in the least developed countries[3]. South Asia has the world's largest numerical stillbirth burden with rates ranging from 25 to 40/1000 births. Within

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Pakistan, reported stillbirth rates vary from 36 per 1000 to 70 or more per 1000 in some rural areas[2,4-8]. In contrast, the World Health Organization (WHO) reports a Pakistani stillbirth rate of 22 per 1000 births[9]. One reason for the discrepancy among reports is that the lower limit of the gestational age or birthweight varies widely. Many developed countries use 20 weeks as the lower gestational age cutoff for stillbirth, but some developed countries such as Sweden still use 28 weeks as the lower cutoff. In developing countries, the most commonly used cutoffs are 28 weeks or 1000 grams[3,10,11].

Stillbirths occurring in the peripartum period are generally normal in appearance, and are often called *fresh* stillbirths. When the skin is not intact, or “*macerated*,” it implies death >24 hours before delivery[2]. In developed countries, intrapartum stillbirths comprise less than 10% of all stillbirths, while in many developing countries, higher proportions of the stillbirths are thought to occur intrapartum[2]. The occurrence of an intrapartum stillbirth in a developed country is considered the result of inadequate care[12]. Intrapartum stillbirths in developing countries may represent inadequate access to essential obstetric care and inadequate care[13].

Other factors associated with the high stillbirth rates in developing countries are infection, including congenitally-acquired infections such as syphilis, Gram negative sepsis, malaria, birth injury, hypertensive disease, especially when associated with poor management of preeclampsia/eclampsia, poor nutritional status, previous stillbirth, congenital anomalies, and sickle cell disease [3]. Because most of the research has been hospital-based rather than population-based, much is still unknown about the prevalence and etiology of stillbirth in developing countries. Thus, our goal in this study was to determine the stillbirth rate, the risk factors for stillbirth, and gestational age at delivery in a well-defined, prospective urban developing country stillbirth cohort.

Methods

The study was reviewed and approved by the Aga Khan University Ethical and Review Committee and the Institutional Review Boards at the University of Alabama and RTI International in the US. All women provided informed consent prior to participating in the study. The study was conducted in the town of Latifabad, one of the four urban sub-divisions of the district of Hyderabad in the province of Sindh in southern Pakistan. Latifabad has a population of 700,000, predominantly *Mohajirs* (the descendants of Urdu-speaking Muslims that migrated from India in 1947). Although the population of urban Sindh has the highest per capita income in Pakistan, at least 14% of the residents of towns such as Latifabad live below the poverty line. Latifabad is divided into 12 units; women from four low to middle socioeconomic units were recruited to the study. The total population in the four units was 90,000 people.

This was a community-based, prospective cohort study of 1369 pregnant women who were enrolled in the second trimester (20-26 weeks of gestation) and followed through six weeks postpartum. Pregnant women who were permanent residents and who planned to deliver in the defined catchment area were potential study participants. The women were recruited from September 2003 to August 2005. We worked in cooperation with the Ministry of Health's National Programme for Family Planning and Primary Health Care. This program provides basic maternal child health services through home visitation by a cadre of Lady Health Workers (LHWs). The LHWs are drawn from the area they serve and have completed a minimum of eight years of school education. They receive 15 months of training in basic maternal and child health services and counseling, including antenatal and new born care, nutritional counseling, and treatment of minor ailments and appropriate referral. We provided them an orientation on the study objectives and protocols and training on study recruitment, communication skills and maintaining confidentiality and privacy in research. Each LHW covers a population of

approximately 100 households. One of the LHWs' basic functions is to identify and register all pregnant women within their catchment population. All pregnant women in the catchment areas were identified by the LHWs who made an initial assessment of the eligibility of the woman for inclusion in the study. Eligibility requirements included pregnant women who were permanent residents of and planned to deliver in the catchment area, returned to the clinic after the initial LHW home visit, and were between 20 and 26 weeks gestation.

At the home visit, the LHW screened potential participants for eligibility, provided women with a brief study orientation, and scheduled an appointment for the pregnant women to visit the research clinic. At the research clinic, gestational age at enrollment was determined using the last menstrual period and confirmed by an ultrasound conducted by a study physician, informed consent was obtained, and the required data were collected on pre-tested study forms by research staff trained to carry out the study protocol. Demographic data were also collected prospectively using pre-tested questionnaires. A clinical examination was performed by study physicians. Study staff collected additional study data during home visits one-week after enrollment, one month before the estimated date of delivery, within 48 hours after delivery, and at 28 days after delivery.

The LHWs tracked all enrolled women until the pregnancy was completed and the pregnancy outcome recorded by the study staff. The study team developed a liaison with all the public and private delivery facilities and the local home birth attendants in order to capture all birth outcomes in the study cohort. Once a delivery was reported to the study clinic either by the LHW, the hospital staff or by the woman/family, the research medical officer and a study nurse visited the woman at her home or at the health facility within 48 hours of delivery to collect the maternal delivery and postnatal data and to confirm the birth outcome.

A stillbirth was defined as an infant born after enrollment in which no sign of life (breathing, crying, heartbeat) was evident. Whether the infant was macerated or not was determined. For all reported stillbirths, a physician trained in general research methodology and specifically in data collection related to this study, visited the home and collected information from the family about the circumstances related to the event, and treatment provided. For the deliveries that occurred in a hospital, this information was supplemented and verified by the hospital records. Finally, the records of all stillbirths were reviewed by a neonatologist (SS) and the primary author (IJ).

The primary obstetric cause of stillbirth was assigned jointly using the Pattinson et al[14] adaptation of the Aberdeen Classification[15] for developing countries. The primary cause of death is defined as the obstetric antecedent factor or event that initiated the process or sequence of events leading to the death of the fetus. The classification system is non-hierarchical and allows for the identification of the following primary causes, using set criteria and definitions: intrapartum asphyxia, spontaneous preterm labor, antepartum hemorrhage, intrapartum infections, intrauterine growth retardation (including post maturity), hypertension, fetal abnormality, maternal disease, trauma and unexplained intrauterine death[14]. A single cause is assigned to each stillbirth.

Data Management and Analysis

All data were entered centrally; data edits, including inter and intra-form consistency checks, were performed at entry with additional edits performed by an independent data center. The data were analyzed using SAS- version 9.0. Descriptive analyses were performed, Chi-square and Fisher's exact test were completed, and relative risks and 95% confidence intervals were calculated for the prospectively identified variables associated with stillbirth.

Results

From September 2003 to August 2005, 2205 pregnant women were registered by the LHWs in the study area (Figure 1). Eighty-five percent (n=1879) met the pre-screening criteria (resident of the area and less than 26 weeks gestation) and were referred to the clinic for further screening. Of the 1606 who attended the clinic, 1369 (85%) pregnant women were confirmed to be between 20 and 26 weeks of gestation, were willing to participate and enrolled in the study. Birth outcomes and follow-up were ascertained for 1280 (94%) of the women enrolled in the study. Among the reasons for non-ascertainment of outcome were delivery outside the area and loss to follow-up (5%) and refusal of subsequent visits (1%).

There were 43 stillbirths; the overall stillbirth rate was 33.6 per 1000 births. Table 1 lists the demographic and maternal risk factors in the study population. The majority of women enrolled were Urdu speaking (81%), with Punjabi, Pushto and Sindhi ethnicities representing the majority of the remaining population. One third of the population had a household monthly income of < 600 rupees (\$10 US) and another third had a household income of between 600 and 1000 rupees per month. About half lived with an extended family while the other half lived within a nuclear family arrangement. Eighty-five percent of the women enrolled were between 20 and 35 years old, with only 10% older than 35 years. Nearly a third of the population had no formal education and only 18% had >10 years of formal education. Nearly three-fourths of the women had a birth interval of > 24 months; 23% had experienced at least one pregnancy loss; 20% were primagravidas and 25% were $\geq$ gravida 5. These characteristics were not significant risk factors for stillbirth, although there was a trend toward a previous pregnancy loss and high parity being risk factors for stillbirth.

Table 2 describes the characteristics of labor, delivery and birth in the overall population and among the stillbirths (n= 43). Nineteen percent of liveborn deliveries were preterm (< 37 weeks gestation) vs. 49% for stillbirths (RR 3.9, 2.2-6.9). Fifty one percent of all stillbirths were term and 19% were late preterm (34-36 weeks) and thus potentially salvageable. Of those with available data, 96% had no evidence of gross congenital anomalies and 73% were fresh, suggesting a peripartum demise. Sixty percent of the stillbirths were male compared to 51% of the live births ($p = 0.3250$).

Of the prenatal risk factors examined at 20 - 26 weeks gestation, about 92% of enrolled women were anemic with hemoglobin concentrations ≤ 11 gm/dl; of these, 89 % had hemoglobin levels between 8 and 11 gm/dl. While values between 8 and 11 were not associated with an increased risk for stillbirth, hemoglobin levels < 8 gm/dl were a significant risk factor for stillbirth (RR 3.8, 1.6-9.2). Labor and delivery characteristics associated with stillbirth included foul-smelling amniotic fluid (RR 4.6, 2.1-9.8), cloudy or meconium-stained fluid (RR 12.1, 5.6-25.8 and 4.2, 1.8-9.7 respectively) and excessive bleeding during delivery (RR 5.5, 2.7-11.2). However, neither prolonged labor (11% of stillbirths and 13% of live births), nor maternal fever (6% of stillbirths and 9% of live births) were significantly associated with an increased risk of stillbirth.

Access to medical care was similar for women with stillbirths and live births (Table 3). Ninety-five percent of all women received at least one prenatal care visit; 72% of the live births received more than 4 visits compared to 69% of women with a stillbirth, ($p = NS$). Seventy nine percent of live births compared to 84% of stillbirths, ($p = NS$) were conducted at a hospital, clinic or health center with the remaining 20% conducted in a home setting; 60% of live birth deliveries were attended by a physician, 22% by a nurse or equivalent provider, 11% by a traditional birth attendant and 5% by a family member. Seventy one percent of stillbirth deliveries were conducted by physician. Overall, 20% of all deliveries and 14% of stillbirths were performed by cesarean section.

The stillbirths in this study were commonly associated with antepartum hemorrhage (23%), intrapartum asphyxia (23%) and spontaneous preterm labor (18%), followed by maternal disease (8%). (Table 4) Seven intrauterine fetal deaths (18%) were classified as unexplained as these occurred at term, were without a congenital anomaly, were mostly macerated and no cause could be determined. Almost 90% of antepartum hemorrhages were associated with a clinical abruption. Elevated blood pressure (140/90) on admission was recorded for 56% of the women with a history of antepartum hemorrhage. These cases are classified as abruption with hypertension and not as hypertensive disorders in accordance with the classification system we employed. While 9 of the 43 fetal deaths were noted to have foul smelling amniotic fluid, each of these cases had factors other than infection that were thought more likely to be causal. Among women delivering with maternal disease who had a stillbirth, two had diabetes and one maternal jaundice, cause and type unknown.

Comment

This study had a number of strengths and weaknesses. The strengths include the recruitment of women from a specific geographic area, the prospective nature of the study, the high follow-up rate, ultrasound determination of gestational age, the determination of the outcomes regardless of whether the delivery occurred at home or in the hospital, and the attempt to identify specific causes of death. Among the weaknesses, the relatively small number of stillbirths and the absence of autopsies stand out.

The most striking finding of this study was the high rate of stillbirth (33.6 per 1000 deliveries) in a community where the majority of women were delivered at a hospital facility by a doctor or midwife, with an overall 20% cesarean section rate. Moreover more than half of the stillbirths in this population were term and another 19% were late preterm (34-36 wks). There were few congenital anomalies (4%) among the stillbirths and most were without maceration, indicating that many of the stillbirths occurred in the peripartum period and thus were potentially salvageable during the time of labor and delivery [2]. Lawn et al note that appropriate cesarean section should prevent many of the fetuses with these characteristics from dying during labor, and further suggest that many of these deaths could be avoided with improved obstetric care and more rapid response to obstetric complications [2]. Thus, the findings from this study suggest that despite giving birth in a health facility and having cesarean section rates even higher than recommended for many developing countries, women may not have received appropriate obstetric care [16]. Our study reinforces findings from other recently published studies that report a failure of Pakistani health facilities to offer essential and comprehensive obstetric care; deficiencies in staff competence have also been reported [17,18]. We therefore speculate that upgrading health system performance will reduce the high stillbirth rates and other adverse pregnancy outcomes even in populations with adequate access to maternity care.

In the U.S. and other developed countries, most of the stillbirths occur antenatally and are frequently macerated. In this study, most stillbirths were fresh, indicating that most fetal deaths occurred close to delivery. A recent population based study in rural areas of Pakistan, where the stillbirth rate was 47/1000 births, reported that 75% were fresh, results similar to this study [19]. Based on these and other data [20], it appears that there are major differences in the timing of stillbirths between developed and developing countries, with a far greater percentage of stillbirths in developing countries occurring in the peripartum period.

In the US, 50% of the stillbirths occur at less than 28 weeks (approximately 1000g) and nearly 80% are preterm [21]. The gestational age distribution of stillbirths in most developing countries is unknown, in part because gestational age is not routinely assessed. However, in this study, all the gestational ages were assessed by mid-trimester ultrasound. That 51% were term and another 19% were late preterm suggests that the gestational age pattern in Pakistan

is different from that found in developed countries with a far greater likelihood that a stillbirth, when it occurs, will occur at or close to term. Nevertheless, even with a high proportion of stillbirths at or near term, in this study, preterm birth was significantly associated with stillbirth.

In developed countries, even with an autopsy and histologic evaluation of the placenta, the cause of many stillbirths remains unknown [22]. In this study, these evaluations were unavailable and the cause of death was determined based on questions asked of the delivery attendant, family members and the mother, and if available, a review of the medical record. Therefore our results likely will only approximate causes assigned using more sophisticated methods. Nevertheless, in these stillbirths, it appears that severe antenatal anemia is a relatively potent risk factor, while the constellation of asphyxia, hypertension, antepartum hemorrhage and abruption also contributed to the risk for stillbirth. The frequent observation in the stillbirths of foul smelling amniotic fluid suggests that intramniotic infection plays an important role as well.

In Hyderabad, Pakistan, stillbirths are a common adverse pregnancy outcome occurring in more than 3% of births. The risk factors appear similar to those seen in other geographic areas. Because so few stillbirths had congenital anomalies and most were term or near term and fresh, this study suggests that the majority of those stillbirths should be preventable with better obstetric care. Since the *quantity* of care in this setting is relatively high for a developing country, with provision of prenatal care, skilled birth attendance, and a high rate of cesarean section seen in both the overall and stillbirth population, it is likely that the *quality* of care would need to be improved for the stillbirth rate to be substantially reduced. For example, the interventions used in many developed countries to identify women at risk for stillbirth, including fundal height measurements and third trimester ultrasound to search for fetal growth retardation, routine screening for diabetes, and fetal kick counts and non stress testing to identify fetuses at risk of dying, are rarely used in Pakistan and were not in routine use in Hyderabad during the course of this study.

In developed countries, a perinatal death review in which each death is examined for etiology and preventability is often the first step undertaken in order to develop appropriate interventions to reduce adverse outcomes. Because it appears that the medical resources are available to achieve a lower stillbirth rate in Hyderabad than we observed, we recommend the initiation of an ongoing perinatal death review in order to better define the causes of stillbirth, to determine which stillbirths may be preventable, and to direct interventions and resources to improve perinatal outcomes. If undertaken, it is likely that such a review would find a general lack of appropriate monitoring for women most at risk for stillbirth, e.g. those with growth retardation, hypertension, diabetes, and hemorrhage, and failure to perform appropriately timed cesarean sections for those at high risk of fetal death.

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Figure 1.
Enrollment Flow Chart

Table 1**Demographic and Maternal Risk Factors***

	Live births n (%)	Stillbirths n (%)	Relative risk (95% CI)	p-value
Total Enrolled	1,237	43		
Maternal age (years)				0.2415
< 20	69 (6)	1 (2)	0.5 (0.1,3.3)	
20- 34	1,045 (85)	34 (81)	1.0	
≥ 35	117 (10)	7 (17)	1.8 (0.8,4.0)	
Household monthly income (Rupees; 60 = \$1 US)				0.4998
<i>Per capita</i>				
Low (< 600 Rs)	215 (32)	4 (20)	0.5 (0.2,1.8)	
Middle (600 to 1000 Rs)	250 (38)	9 (45)	1.0 (0.4,2.7)	
Upper (> 1000 Rs)	197 (30)	7 (35)	1.0	
Maternal education (years)				0.7298
No education	412 (34)	15 (36)	1.0 (0.4,2.3)	
1-5	214 (17)	9 (21)	1.1 (0.4,2.9)	
6-10	390 (32)	10 (24)	0.7 (0.3,1.7)	
> 10	215 (18)	8 (19)	1.0	
Ethnicity				0.7914
Urdu	998 (81)	36 (86)	1.0	
Other (Punjabi, Pushto, Sindhi)	233 (19)	6 (14)	0.7 (0.3,1.7)	
Family structure				0.0855
Extended	635 (52)	16 (38)	0.6 (0.3,1.1)	
Nuclear-only	596 (48)	26 (62)	1.0	
Birth interval (months)				0.0797
< 12	6 (1)	0 (0.0)	-----	
12 - 24	205 (27)	1 (5)	0.1 (0.0,1.1)	
≥ 24	553 (72)	19 (95)	1.0	
Gravida				0.0506
Primigravida	221 (18)	9 (21)	1.0	
1 - 2	388 (31)	7 (17)	0.5 (0.2, 1.2)	
3 - 4	322 (26)	9 (21)	0.7 (0.3,1.7)	
≥ 5	299 (24)	17 (41)	1.4 (0.6, 3.0)	
Pregnancy loss				0.0572
At least one previous loss	222 (22)	12 (36)	1.9 (1.0,3.9)	
No previous loss	775 (78)	21 (64)	1.0	

* Totals for each category may be less due to missing values. Percentages may not add up to 100% due to rounding.

Table 2

Labor and delivery	Live births* n (%)	Stillbirths n (%)	Relative risk (95% CI)	p-value
Gender				0.3250
Male	597 (51)	22 (60)	1.4 (0.7,2.6)	
Female	568 (49)	15 (41)	1.0	
Gestational age at birth				<0.0001
Preterm	232 (19)	21 (49)	3.9 (2.2,6.9)	
Term	1,003 (81)	22 (51)	1.0	
Multiple gestation				0.2482
Singleton	1,175 (99)	30 (97)	0.3 (0.0,1.8)	
Twin	10 (1)	1 (3)	1.0	
Gross congenital abnormality				0.3506
Yes	120 (11)	1 (4)	0.3 (0.0,2.3)	
No	1,000 (89)	27 (96)	1.0	
Signs of maceration				----
Fresh	NA	22 (63)	----	----
Macerated		8 (23)		
Don't know		5 (14)		
Hemoglobin (g/dl)				0.0281
< 8	39 (3)	5 (12)	3.8 (1.6, 9.2)	
8-11	1,096 (89)	34 (81)	1.0	
> 11	94 (8)	3 (7)	1.0 (0.3, 3.1)	
Length of labor**				1.0000
Prolonged	157 (13)	4 (11)	0.8 (0.3,2.4)	
Normal	1,024 (87)	31 (89)	1.0	
Smell of amniotic fluid				<0.0001
Foul	94 (9)	9 (27)	4.6 (2.1,9.8)	
Not foul	971 (89)	19 (58)	1.0	
Don't know	30 (3)	5 (15)	7.4 (2.9,18.8)	
Color of amniotic fluid				<0.0001
Clear	899 (82)	13 (39)	1.0	
Meconium-stained	141 (13)	9 (27)	4.2 (1.8,9.7)	
Other unclear	53 (5)	11 (33)	12.1 (5.6,25.8)	
Fever in labor				0.7758
Presence of fever	105 (9)	2 (6)	0.6 (0.2,2.6)	
No fever	1,042 (91)	32 (94)	1.0	
Not known	2 (<1)	0 (0)		
Vaginal bleeding***				<0.0001
Excessive bleeding	71 (6)	10 (29)	5.5 (2.7,11.2)	
Normal bleeding	1,053 (93)	24 (69)	1.0	
Not known	8 (1)	1 (3)		

* Totals for each category may be less due to missing values. Percentages may not add up to 100% due to rounding.

** Labor was defined as prolonged if it was > 12 hrs for primiparas or > 8 hours for multiparas

*** Vaginal bleeding was defined as excessive based on clinical opinion of birth attendant.

Table 3

Medical care: Stillbirths and Live Births

	Live births * n (%)	Stillbirths n (%)	Relative risk (95% CI)	p-value
Place of delivery				0.7932
Hospital	978 (79)	36 (84)	1.0	
Health Center	11 (1)	0	----	
Home/other	248 (20)	7 (16)	0.8 (0.3, 1.7)	
Birth Attendant				0.5077
Doctor	737 (60)	30 (71)	1.0	
Nurse/Midwife	278 (23)	5 (12)	0.5 (0.2, 1.2)	
LHW	9 (1)	0 (0.0)	----	
TBA	130 (11)	5 (12)	0.9 (0.4, 2.4)	
Other	72 (6)	2 (5)	0.7 (0.2, 2.8)	
Mode of delivery				0.3768
Vaginal	941 (80)	30 (86)	1.5 (0.6, 3.9)	
C-section	242 (20)	5 (14)	1.0	
Antenatal care received				0.6929
No antenatal care	51 (4)	2 (5)	1.2 (0.3, 4.6)	
At least one visit	1,180 (96)	40 (95)	1.0	
Prenatal Care Visits				0.7396
None	51 (4)	2 (5)	1.2 (0.3, 4.9)	
1-2	121 (10)	6 (14)	1.5 (0.6, 3.5)	
3-4	172 (14)	5 (12)	0.9 (0.4, 2.3)	
>4	887 (72)	29 (69)	1.0	

* Totals for each category may be less due to missing values. Percentages may not add up to 100% due to rounding.

Table 4**Obstetric Factors Associated with Stillbirth**

Factors	n (%)
Antepartum hemorrhage	9 (23%)
• Clinical signs of abruption with hypertension	5 (56%)
• Clinical signs of abruption without hypertension	3 (33%)
• Antepartum hemorrhage of unknown origin	1 (11%)
Spontaneous preterm labor	7 (18%)
Intrapartum asphyxia	9 (23%)
Maternal disease	3 (8%)
Post maturity	1 (3%)
Fetal abnormality	1 (3%)
Trauma	1 (3%)
Infections	1 (3%)
Unexplained	7 (18%)
• Fresh	3 (43%)
• Macerated	4 (57%)
Total	39 (100%)*

* insufficient information available on 4 cases