Lower Mortality for Female-Female Twins than Male-Male and Male-Female Twins in Rural Senegal

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Twins have been registered prospectively for 12–22 years in 42 small villages in the Bandafassi area of Eastern Senegal. We studied 98 pairs of twins to test whether twins in opposite-sex pairs have higher postneonatal mortality than same-sex twins. Neonatal mortality for twins was 41.3%; mortality for infants and for children under age 5 years was 53.0% and 66.8%, respectively. Neonatal mortality was identical for same-sex and opposite-sex twin pairs, but much higher for boys than girls [relative risk = 1.8; 95% confidence interval (CI) = 1.2–2.6]. There was clustering of double neonatal deaths for all types of twins. In the postneonatal period, female-female twins had lower mortality than other twin types. Twins had higher postneonatal mortality as long as the co-twin was alive [mortality rate ratio (MR) = 2.6; 95% CI = 1.0–6.7]. Girls had excess mortality when the co-twin was of the opposite sex (MR = 4.3; 95% CI = 1.2–15.3), whereas there was no difference for boys. In conclusion, contact with a co-twin of the opposite sex increased child mortality for female twins. Our data are not sufficient to determine whether this difference is specific for girls or applies to boys as well. (Epidemiology 1995;6:419–422)

Keywords: neonatal mortality, opposite sex, postneonatal mortality, Senegal, sex, twins, cohort study.

Several studies of measles have found that transmission of measles from the opposite sex increases the severity of infection.[1–8] Hence, close contact with the opposite sex may be an important risk factor for severe disease and mortality. We have attempted to find other situations where the impact of contact with the same or the opposite sex could be assessed. In a retrospective study in Guinea-Bissau,[9] postneonatal mortality was found to be two times higher for opposite-sex than same-sex twins. Since this study was based on identification of twins in a general census of the population, it included only pairs in which at least one had survived. Although examination of the distribution of same-sex and opposite-sex pairs in different age groups did not indicate underreporting of same-sex pairs, a higher frequency of double deaths among same-sex twin pairs could have biased the observed tendency. We have therefore used data from 42 villages of the Bandafassi area in Eastern Senegal, monitored for 12–22 years,[2,10–12] to assess the impact on mortality of the sex composition of twin pairs. During the study period, 5,849 births were reported, of which there were 98 twin deliveries and 1 triplet delivery. Using this dataset, we have calculated neonatal and postneonatal mortality of twins and compared the risk of dying between opposite-sex and same-sex pairs. Neonatal mortality presumably is more related to genetic, pregnancy, and delivery-related problems. Postneonatal mortality, however, is likely to be due to infectious diseases, and transmission of infections from a co-twin may add to the burden of infections in the postneonatal period.

Subjects and Methods

Background

The Bandafassi study area is located in the Department of Kedougou in eastern Senegal, near the border between Senegal and Guinea.[10,11] The population is divided among three ethnic groups: Fula Bande, Niokholonko, and Bedik. Surveillance began in 1970 among the Niokholonko, who are part of the Mandenka cultural group; in 1975 among the Fula Bande, who are related to the Fula people of Guinea; and in 1980 among the Bedik, a small ethnic group with its own language, related to the Mande linguistic group. In 1992, the population of the study area numbered 8,398. The sociocultural system and demographic structure of this community has been described in detail elsewhere.[10,11]

Demographic Surveys

Once each year, usually between January and March, all villages were visited, the list of people present at the preceding visit was checked, and information was ob-

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TABLE 1. Peri/neonatal Mortality among Twins and Singletons, According to Sex and Time Period: Bandafassi, Senegal, 1970–1992

	Mortality (Deaths)*					
	MM	FF	M(F)	F(M)	Boys	Girls
1970–1985						
Twins	0.60 (25/42)	0.36 (5/14)	0.46 (10/22)	0.36 (8/22)	0.55 (35/64)	0.36 (13/36)
Singletons					0.12 (215/1,769)	0.09 (148/1,654)
1986–1992						
Twins	0.39 (10/26)	0.19 (7/36)	0.53 (8/15)	0.33 (5/15)	0.44 (18/41)	0.24 (12/51)
Singletons					0.11 (115/1,091)	0.09 (104/1,136)

* Information on sex is missing for two twin pairs of whom three individuals were stillborn.

tained on pregnancies, new births, marriages, migrations, deaths, and (lay) causes of death. Information was usually provided by the heads of compounds or by key informants in the village. Since pregnancies were registered every year, the likelihood that children were born and died without having been registered has been minimized. With the annual control of all persons registered in the area, deaths are not likely to have been missed in the study population.

Twin Births

Of the 98 twin deliveries, sex is missing for two twin pairs, of whom three individuals were stillborn. No other pair of twins was excluded from the analysis. All triplets died in the neonatal period.

Statistical Methods

We analyzed neonatal mortality, that is, within 1 month of birth, and postneonatal mortality, that is, from 1 month to 5 years of age, separately.[9] Since some stillborn children may have been registered as neonatal deaths, or *vice versa*, during the first years of surveillance, we have calculated a peri/neonatal mortality rate rather than separate stillbirth and neonatal mortality rates.

We have estimated cumulative mortality for each type of twin and period using Kaplan-Meier techniques. To assess the effect on postneonatal mortality of twin type, of time period, and of the other twin being alive, we used a multivariate Cox regression model[13] with age as the time scale. Since the focus is the impact of the sex of the co-twin on postneonatal mortality, we used only children from twin pairs in which both twins survived the neonatal period. Follow-up was censored at death, emigration, or 5 years of age, whichever came first. We controlled for the effect of time period using a binary covariate (from January 1, 1986, *vs* baseline before 1986). To examine the possible effect of sex and twin-type, we used female-female pairs as a default and defined two binary variables indicating status as male-male or female-male. To examine the effect of the co-twin being alive, we defined a time-dependent binary covariate indicating whether the co-twin was alive or dead. This approach allows for the dependence between survival times of children from the same twin pair and does not violate the assumptions in a standard Cox regression model. Effects are expressed as mortality rate ratios (MR) with 95% confidence intervals (CI).

Results

Peri/neonatal Mortality

The peri/neonatal mortality rate was 0.41 (81/196) compared with 0.10 (582/5,650) for singletons (Table 1). Peri/neonatal mortality was higher in male-male (MM) pairs [0.52 (35/68)] than in female-female (FF) pairs [0.24 (12/50)] [relative risk (RR) = 2.1; 95% CI = 1.2–3.7)], but not much greater than that for male-female (MF) pairs [0.43 (31/72)] (RR = 1.2; 95% CI = 0.9–1.8). There was no major difference in peri/neonatal mortality for boys in MF pairs [0.49 (18/37)] compared with MM pairs (RR = 1.0; 95% CI = 0.6–1.4). Mortality for females of MF twins [0.35 (13/37)] was 50% greater than that for females of FF twins (RR = 1.5; 95% CI = 0.8–2.8). Taken together, there was no difference in peri/neonatal mortality for same-sex [0.40 (47/118)] and MF pairs [0.42 (31/74)]. Twin boys, however, had substantially higher peri/neonatal mortality than twin girls (RR = 1.8; 95% CI = 1.2–2.6). Among singletons (Table 1), boys likewise had higher peri/neonatal mortality than girls (RR = 1.3; 95% CI = 1.1–1.5).

For all three types of twins, the number of double peri/neonatal deaths was larger than expected under the assumption of independence between deaths of co-twins,

TABLE 2. Distribution of Neonatal Deaths by Pairs, According to Twin Type: Bandafassi, Senegal, 1970–1992

	Number of Deaths per Pair			Number of Pairs
	0	1	2	
Children born 1970–1985				
Male-male	7	3	11	21
Female-female	4	1	2	7
Male-female*	11	4	7	22
Total	22	8	29	50
Children born 1986–1992				
Male-male	6	4	3	13
Female-female	14	1	3	18
Male-female†	5	7	3	15
Total	25	12	9	46

* F died in 1 pair; M died in 3 pairs.
† F died in 2 pairs; M died in 5 pairs.

TABLE 3. Age-Specific and Cumulative Mortality among Twins and Singletons, According to Sex and Time Period: Bandafassi, Senegal, 1970–1992

	Mortality (Deaths)						
	Same-Sex Twins		Opposite-Sex Twins			Singletons	
	MM	FF	M(F)	F(M)	Twins	M	F
1970–1985							
1–11 mo.	0.24 (4)	0.11 (1)	0.58 (7)	0.36 (5)	0.33 (17)	0.10 (156)	0.12 (181)
12–36 mo.	0.46 (6)	0.38 (3)		0.11 (1)	0.30 (10)	0.17 (228)	0.15 (192)
36–60 mo.	0.14 (1)		0.20 (1)	0.29 (2)	0.18 (4)	0.04 (49)	0.06 (62)
Infant	0.69	0.43	0.77	0.59	0.65	0.21	0.20
0–60 mo.	0.86	0.64	0.82	0.74	0.80	0.37	0.36
1986–1992							
1–11 mo.	0.20 (3)		0.33 (2)		0.09 (5)	0.06 (56)	0.06 (52)
12–36 mo.		0.04 (1)		0.29 (2)	0.07 (3)	0.11 (69)	0.08 (51)
36–60 mo.	0.17 (1)				0.05 (1)	0.04 (11)	0.05 (15)
Infant	0.51	0.19	0.69	0.33	0.39	0.16	0.14
0–60 mo.	0.59	0.23	0.69	0.52	0.46	0.28	0.25

irrespective of whether the expected number of double deaths was calculated from the mortality of twins or singletons (Table 2).

Postneonatal Mortality

Over the total period from 1970 to 1992, postneonatal mortality from 1 to 11 months of age was 0.20 among twins, yielding an infant mortality of 0.53. Childhood (1–4 years) mortality was 0.28. Hence, mortality under the age of 5 years for twins in these communities was 0.66. Postneonatal mortality from 1 to 59 months was 0.43 for twins, considerably higher than the mortality rate of 0.25 for singletons (Table 3). Cohorts born from 1986 onward showed a marked reduction in postneonatal mortality levels for both twins and singletons (Table 3), with little difference in postneonatal mortality for singletons and twins.

Postneonatal Mortality According to Type of Twin Pair

To assess the impact of the sex of the co-twin on postneonatal mortality, we limited the analysis to those

TABLE 4. Distribution of Postneonatal Deaths for Twin Pairs Surviving the Neonatal Period, According to Twin Type: Bandafassi, Senegal, 1970–1992

	Number of Deaths per Pair			Number of Pairs
	0	1	2	
Children born 1970–1985				
Male-male	0	3	4	7
Female-female	2	1	1	4
Male-female*	2	5	4	11
Total	4	9	9	22
Children born 1986–1992				
Male-male	3	2	1	6
Female-female	13	1	0	14
Male-female†	2	3	0	5
Total	18	6	1	25

* F died in 2 pairs; M died in 3 pairs.
† F died in 2 pairs; M died in 1 pairs.

47 pairs in which both survived the neonatal period (13 MM, 18 FF, and 16 MF pairs) (Table 4). In a Cox analysis adjusting for period and comparing mortality for type of twin pair, the risk of dying was considerably higher among male-male twins, boys in MF pairs, and girls in MF pairs compared with female-female twins (Table 5).

The risk of dying postneonatally was 2.6 times higher if the other twin was alive (MR = 2.6; 95% CI = 1.0–6.7) (Table 5). Adjusted for the survival status of the co-twin, girls in MF pairs had 4.3 times the mortality of girls in FF pairs (MR = 4.3; 95% CI = 1.2–15.3) (Table 5). Boys in MM pairs had 5.4 times higher (95% CI = 1.7–17.0) postneonatal mortality than girls in FF pairs.

Discussion

In European and Asian studies, same-sex twins have higher neonatal mortality than male-female pairs, presumably owing to frailty among monozygous twins.[14,15] In Eastern Senegal, there was little difference in peri/neonatal mortality for same-sex and opposite-sex twins. With an estimated ratio of 1:4, monozygous twins are likely to be a much smaller proportion of all twins in the present study than in Europe or Asia, where the expected ratio of monozygous to dizygous twins is 1:1.[16] The Bandafassi twinning rate of 1 per 58 births is normal for Africa, although considerably higher than in European and Asian populations.[16] With this high rate, it is unlikely that there has been an important underreporting of twins. The level of twinning in this study corresponds to what has been found in other areas of Senegal with more intensive follow-up.[16] Nonetheless, with the distribution of 21 MM twin pairs and 7 FF twin pairs in the period from 1970 to 1985 and the opposite tendency in the 1986–1992 period (13 MM pairs and 18 FF pairs), there may have been misreporting of sex among pairs where the twins died before receiving a name. Nevertheless, misclassification of sex has not affected the pairs in which both survived the neonatal period.

TABLE 5. Cox Regression Analysis of Ratios of Postneonatal Mortality Associated with Having a Living Co-twin, According to Twin Type; Only 47 Pairs in Which Both Survived the Neonatal Period Have Been Included: Bandafassi, Senegal, 1970–1992

	Ratio of Mortality (95% Confidence Interval)	
	Without Status of Co-twin	Including Status of Co-twin
M in MM pairs/F in FF pairs	4.6 (1.5–14.4)	5.4 (1.7–17.0)
M in MF/F in FF	4.0 (1.1–14.1)	4.6 (1.3–16.4)
F in MF/F in FF	3.5 (1.0–12.2)	4.3 (1.2–15.3)
Period*	0.4 (0.2–1.0)	0.4 (0.2–0.8)
Co-twin alive/co-twin dead		2.6 (1.0–6.7)

* Period: children born from January 1, 1986, and onward *vs* children born before.

The increased frailty among MM twins may partly explain why we did not find higher mortality among boys in MF pairs compared with MM twins. On the other hand, it may also be that a negative impact of the opposite sex is more pronounced for girls. In Bissau, mortality was more increased for singleton girls (OR = 7.5; 95% CI = 1.6–35.3) than for singleton boys (OR = 1.9; 95% CI = 0.8–6.5) with the nearest sibling of the opposite sex.[9] Our data were not sufficient to determine whether the higher mortality of opposite-sex than same-sex twins is specific for girls or applies to boys as well. We have observed in Senegal that measles vaccine has a particularly beneficial effect for girls.[17,18] Hence, it is possible that immunizations have played an important part in the much lower mortality among female than male twins, particularly after 1986.

There is no indication of preferential treatment of male or female twins. Hence, if close contact with the opposite sex is a risk factor in pairs in which both are alive, the risk is likely to be due to the impact of cross-sex transmission on infectious diseases. It appears likely that cross-sex transmission may be a problem in infections other than measles[1–8]; although other causes could generally not be assessed, exclusion of acute measles deaths did not matter for the relative risk between females in opposite-sex and same-sex twins (data not shown). Studies have not determined whether the impact of cross-sex transmission is due to differences in disease transmission patterns between the sexes or to interference with the immune system.[1–9] It is also possible that antigens contracted from the opposite sex may be more pathogenic than antigens from the same sex.[1,3] The possibility of sex-specific effects has been supported by recent observations that high-titer measles vaccines were associated with increased mortality for girls,[19] whereas low-titer measles vaccine reduced mortality more for girls than for boys.[17,18]

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