Causes of Fetal and Neonatal Mortality By Race in a Selected U.S. Population

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Abstract: In a large prospective study (1959-1966), the perinatal mortality rate for U.S. Whites was 34 deaths per 1000 total births, for Blacks 51/1000, for Puerto Ricans 41/1000, and for Orientals 23/1000. A number of disorders were responsible for these differences. Premature rupture of the fetal membranes occurred 92 per cent more often in Blacks than in Whites, marked placental growth retardation 56 per cent more often, amniotic fluid infections 45 per cent more often, and major congenital malformations 15 per cent more often. Most other disorders were less common in Blacks than in Whites. Stratifying the data by selected factors, such as prepregnancy body weight and antenatal medical care, eliminated or greatly reduced almost all of these interracial differences. The only major unexplained differences remaining were an excess of amniotic fluid infections and major congenital malformations in Blacks, and an excess of abruptio placentae and large placental infarcts in Whites. (*Am J Public Health* 69:857-861, 1979.)

Perinatal mortality rates are substantially greater in the United States than in many other economically advanced nations.[1] Much of the excess U.S. mortality is centered in nonwhites.[2] To identify the disorders responsible for U.S. racial differences, autopsy and placental data must be integrated with detailed clinical information about pregnancy, labor, delivery, and the neonatal period. Such integrated analyses are undertaken on only a small portion of fetal and neonatal deaths in the U.S.[3, 4] Between 1959-1966, the data needed for such integrated analyses were collected on nearly 60,000 pregnancies in a study sponsored by the U.S. Public Health Service.[5, 6] Whites, Blacks and Puerto Ricans were represented in sufficient numbers to permit intergroup comparisons of the frequencies and death rates of common placental and fetal disorders. Information was also adequate to identify many of the environmental and constitutional factors associated with placental and fetal disease differences between the races.

Material and Methods

The Collaborative Perinatal Project of the National Institute of Neurological and Communicative Disorders and Stroke prospectively recorded events of gestation, labor, delivery, and the neonatal period in patients at 12 medical school affiliated hospitals in different regions of the United States.[5, 6] Autopsies were performed on 1,435 fetal and neonatal deaths that occurred between 20 weeks of gestation and 28 days after birth, the age frame included in the present study. Our analyses included 26,329 White, 27,912 Black, 3,814 Puerto Rican, and 241 Oriental infants on whom needed clinical data were available. Race or Puerto Rican designation was established by mothers' self-identifications.

I reviewed the clinical and postmortem material, including microscopic sections, from the fetal and neonatal deaths in the study to standardize the recognition and recording of specific disorders. Four specially trained technicians reviewed microscopic sections from the placentas to standardize the recognition and recording of abnormalities in that organ. I checked the non-routine abnormalities.

Cases may appear in more than one diagnostic category in the case counts of the disorders if more than one diagnosis was made on the infant and placenta. Primary and secondary diagnoses were assigned to each fatal case. The primary diagnosis was intended to identify the disorder that initiated the course to death. For example, hemorrhage may have caused preterm delivery and a neonatal death but both were attributed to placenta previa if placenta previa caused the hemorrhage. Primary diagnoses were used to identify the cause of a fatality so fatal cases appear only once as a fatality and the perinatal mortality rates for each diagnostic category are mutually exclusive (Table 1).

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TABLE 1—Frequencies, Case Fatality and Perinatal Mortality Rates for Common Fetal and Neonatal Disorders by Ethnic Group

	Whites	Blacks	Orientals	Puerto Ricans
Amniotic Fluid Infection				
Cases per 1000 births (Number of cases)	101.1(1404)	146.2(2159)[d]	104.6(16)	96.6(250)
Deaths per 100 cases (Number of deaths)	2.6(36)	5.2(113)[d]	6.3(1)	3.6(9)
Perinatal mortality rate	2.6	7.8[d]	6.5	3.5
Premature Rupture Membranes				
Cases per 1000 births	169.6(4465)	325.4(9082)[d]	124.5(30)	306.0(1167)[d]
Deaths per 100 cases	1.5(68)	1.4(131)	3.3(1)	0.8(9)
Perinatal mortality rate	2.6	4.7[d]	4.1	2.4
Large Placental Infarcts				
Cases per 1000 births	40.6(937)	23.9(509)[d]	31.8(7)	40.9(134)
Deaths per 100 cases	6.0(56)	15.3(78)[d]	0	11.9(16)[a]
Perinatal mortality rate	2.4	3.7[b]	0	4.9[b]
Major Congenital Anomalies				
Cases per 1000 births	40.0(895)	46.1(1075)[c]	29.1(6)	29.7(90)[c]
Deaths per 100 cases	16.2(145)	13.1(141)	0	28.9(26)[b]
Perinatal mortality rate	6.5	6.1	0	8.6
Abruptio Placentae				
Cases per 1000 births	24.1(603)	19.1(488)[d]	21.4(5)	7.7(27)[d]
Deaths per 100 cases	15.3(92)	24.4(119)[c]	0	44.4(12)[c]
Perinatal mortality rate	3.7	4.7	0	3.4
Hydramnios				
Cases per 1000 births	24.2(612)	14.2(365)[d]	12.7(3)	4.5(16)[d]
Deaths per 100 cases	0.8(5)	2.5(9)	0	6.3(1)
Perinatal mortality rate	0.2	0.4	0	0.3
Umbilical Cord Compression				
Cases per 1000 births	11.7(289)	9.0(227)[c]	4.3(1)	11.0(38)
Deaths per 100 cases	10.7(31)	12.3(28)	0	2.6(1)
Perinatal mortality rate	1.3	1.1	0	0.3
Rh Erythroblastosis Fetalis				
Cases per 1000 births	10.1(250)	2.3(83)[d]	0	4.3(15)[d]
Deaths per 100 cases	29.2(73)	18.1(15)	0	20.0(3)
Perinatal mortality rate	2.9	0.6[d]	0	0.9[a]
Placental Growth Retardation				
Cases per 1000 births	9.3(178)	14.5(217)[d]	0	13.6(32)[a]
Deaths per 100 cases	8.4(15)	15.2(33)	0	9.4(3)
Perinatal mortality rate	0.8	2.2[d]	0	1.3
Postnatal Infections				
Cases per 1000 births	9.0(224)	8.8(226)	12.8 (3)	6.6(23)
Deaths per 100 cases	25.9(58)	62.0(140)[d]	33.3(1)	47.8(11)
Perinatal mortality rate	2.3	5.5[d]	4.3	3.2
Placenta Previa				
Cases per 1000 births	7.8(193)	6.0(146)[c]	4.4(1)	4.9(17)
Deaths per 100 cases	9.3(18)	15.1(22)	0	5.9(1)
Perinatal mortality rate	0.7	0.9	0	0.3
Incompetent Cervix				
Cases per 1000 births	4.3(110)	5.3(136)	0	0.8(3)[c]
Deaths per 100 cases	7.4(8)	6.6(9)	0	0
Perinatal mortality rate	0.3	0.4	0	0
Syphilis, + Serologic Test				
Cases per 1000 births	5.4(138)	55.2(1416)[d]	25.3(6)[d]	39.7(141)[d]
Deaths per 100 cases	0.7(1)	0.2(3)	0	0
Perinatal mortality rate	0	0.1	0	0
Breech Delivery and Forceps				
Cases per 1000 births	39.2(1002)	34.0(883)[c]	33.8(8)	33.0(118)
Deaths per 100 cases	0.9(9)	1.5(13)	0	0
Perinatal mortality rate	0.4	0.5	0	0
Cesarean Section				
Cases per 1000 births	60.4(1543)	52.4(1363)[d]	25.3(6)[a]	53.6(192)
Deaths per 100 cases	0.8(12)	0.3(4)	16.7(1)	1.0(2)
Perinatal mortality rate	0.5	0.2	4.2	0.6
Twins				
Cases per 1000 births	20.6(508)	26.1(663)[d]	8.6(2)	13.0(46)[c]
Deaths per 100 cases	1.4(7)	1.2(8)	0	0
Perinatal mortality rate	0.3	0.3	0	0
Other Disorders				
Perinatal mortality rate	6.9	11.3[d]	4.3	11.0[c]
TOTAL				
Perinatal mortality rate	34.4	50.5[d]	23.3	40.7

Number of cases in parentheses.
[a]$P < .05$ compared with whites
[b]$P < .02$
[c]$P < .01$
[d]$P < .001$

Cases were placed in the *abruptio placentae* category when gross inspection showed an adherent retroplacental clot with depression or disruption of the underlying placental tissue or when there were otherwise classical findings including external or occult bleeding.[7] The infants whose deaths were attributed to abruptio placentae had evidences of antenatal hypoxia, i.e., aspirated squamous cells in their lungs and petechiae on the serosal surfaces of their visceral organs. *Congenital anomalies* were recorded when one or more major malformations were recognized in the neonatal period. A malformation was considered to be major when it had the potential for shortening lifespan. Death was ascribed to such malformations when they were judged too severe to permit fetal or neonatal survival.

Cases were placed in the category of *large placental infarcts* when one or more infarcts were greater than 3 cm in diameter. To attribute death to such infarcts, 25 per cent or more of the placenta had to be infarcted and there had to be no other explanation for the previously mentioned postmortem evidences of antenatal hypoxia.[8] The diagnosis *amniotic fluid infection* was made when there was acute inflammation in the subchorionic plate of the placenta. For this diagnosis, the fetal membranes had to be intact at the onset of labor when the labor was preterm, i.e., less than 259 days from the start of the last menstrual period. Previous studies have shown that bacteria are responsible for most if not all of these infections.[9, 10] All of the infants whose deaths were attributed to this disorder had acute congenital pneumonia. *Premature rupture of the fetal membranes* was diagnosed when the membranes spontaneously ruptured before the onset of labor prior to 37 weeks of gestation. Deaths in this category were due to congenital pneumonia or to the consequences of immaturity. Cases over 37 weeks of gestation were given this diagnosis when labor did not begin for 20 or more hours following membrane rupture. Death was attributed to this diagnosis when the infants died with bacterial pneumonia. Premature rupture of the fetal membranes can be either the cause or the consequence of amniotic fluid infections. When both were present with fetal or neonatal death resulting, premature rupture of the membranes was considered the primary diagnosis.

The diagnosis of *hydramnios* was made when excess amniotic fluid was judged to have initiated premature labor. Death was ascribed to the disorder when the infant died of the consequences of immaturity. *Umbilical cord compression* included cases of cord prolapse and a few instances in which there were tight knots in the cord or the cord was very tightly wound around the infant's neck. Death was ascribed to such compression when the previously mentioned evidences of antenatal hypoxia were present and there was no other explanation for death. The diagnosis *Rhesus erythroblastosis fetalis* was based on rising titers of maternal Rhesus antibodies, positive direct Coomb's test on the cord blood, hepatosplenomegaly and anemia in the newborn. Infants who died had erythroblastic hyperplasia in their bone marrows, spleens and liver. *Placental growth retardation* was the diagnosis when the placenta was 40 per cent or more below normal weight at term.[11] Death was attributed to such growth retardation when the neonate had the previously mentioned evidences of antenatal hypoxia and there was no other explanation for death.

The category *postnatal infections* included pneumonias, meningitis, uncontrolled diarrhea, septicemia, and upper respiratory tract infections. *Placenta previa* was diagnosed when the placenta encroached on the cervical os. Fetal or neonatal deaths in this category were due to premature separation of the placenta, blood loss or to the consequences of premature delivery.[12] *Incompetent cervix* was a clinical diagnosis. Deaths in this category were due to congenital pneumonia or the consequences of immaturity. Incompetent cervix is a cause of amniotic fluid infections so when both were present incompetent cervix was considered the primary diagnosis. Death was attributed to *congenital syphilis* when the infant's organs had chronic inflammation and fibrosis in association with spirochetes. The category *breech delivery and forceps* included both breech deliveries and cases in which forceps were used above the pelvic outlet. All the deaths in this category were due to trauma. Tentorial tears were the most frequent type of fatal damage in this category. Death was attributed to *cesarean section* when the gestational age of the fetus had been overestimated and a prematurely born infant died of the consequences of immaturity. Details of the *monovular twin transfusion syndrome* have been previously described.[13]

Enough clinical and placental data were available to determine outcomes on 58,296 cases for premature rupture of the fetal membranes. The number of cases with data adequate to analyze for other diagnoses were: breech delivery and forceps 55,371, cesarean section 55,371, incompetent cervix 54,908, hydramnios 54,842, syphilis 54,804, abruptio placentae 54,295, Rh erythroblastosis fetalis 54,161, neonatal infections 54,161, placenta previa 53,947, umbilical cord compression 53,746, major congenital malformations 48,938, large placental infarcts 47,846, placental growth retardation 36,731, and amniotic fluid infections 31,088. The last two figures were smaller than the rest because the placenta had to be weighed and a full set of microscopic sections prepared from well-preserved tissues to determine whether these disorders were present. Most of the placentas "lost" were discarded nights and weekends. This failure to weigh and prepare microscopic sections from the placenta affected all four racial groups to about the same degree. In the study as a whole, 45 per cent of the infants were White and 48 per cent Black. The respective figures for those with complete placental examinations were 44 per cent and 47 per cent.

The diagnosis of urinary tract infection was made when 15 or more leukocytes were found/high powered microscopic field in two or more catheterized or clean catch urine specimens and there were 100,000 or more bacteria/ml of urine. The diagnosis of maternal hypertension was made when two or more diastolic blood pressures exceeded 85 mm Hg during pregnancy.

The number of cases of each disorder was determined for Blacks, Whites, Orientals, and Puerto Ricans. Next, the case fatality rates for the established disorders were determined, and finally the perinatal mortality rate for each disorder in each racial group. All of these data were stratified by

a number of maternal and fetal factors known to influence the pathogenesis of one or more of the disorders under analysis. As an example of how the stratified analyses were undertaken, each disease analysis was separately undertaken for the following number of maternal visits for antenatal medical care: under 4, 5-7, 8-11, over 11. Other maternal pregnancy factors for which stratified analyses were undertaken were: trimester when registered for antenatal medical care, peak recorded diastolic blood pressure, lowest hemoglobin value, acetonuria, urinary tract infections, total weight gain, type of work outside home, number of cigarettes smoked per day, number of years smoked before pregnancy, parity, marital status, family income, years of formal education, height, prepregnancy body weight, total weight gain during pregnancy, length of gestation, and the combined duration of the first and second stages of labor in hours. Newborns were placed in birth weight percentile growth categories based on recently published, improved fetal growth standards.[14] Stratified analyses were then undertaken for infants' ABO blood types. Chi square was the statistical method used in the study. The application of multivariate analytic techniques to these data has been explored and found to be inappropriate.

Results

The perinatal mortality rate was 34.4/1000 total births for Whites, 50.5 for Blacks, 40.7 for Puerto Ricans, and 23.3 for Orientals (Table 1). Blacks had more amniotic fluid infections, premature rupture of the fetal membranes, major congenital malformations, and placental growth retardation than Whites (Table 1). Most other disorders were less common in Blacks than in Whites. Once established, amniotic fluid infections, large placental infarcts, abruptio placentae, and postnatal infections were more often fatal in Blacks than in Whites (Table 1). The net result of these differences was that amniotic fluid infections, premature rupture of the membranes, large placental infarcts, placental growth retardation, and postnatal infections had significantly higher perinatal mortality rates in Blacks than in Whites. Only Rh erythroblastosis fetalis had a significantly higher perinatal mortality rate in Whites than in Blacks.

Puerto Ricans had more placental growth retardation and premature rupture of the fetal membranes than Whites (Table 1) and less frequent major congenital malformations, abruptio placentae, hydramnios, incompetent cervix, and twins. Once established, large placental infarcts, major congenital malformations, and abruptio placentae were more often fatal in Puerto Ricans than in Whites. The net result of these differences was that large placental infarcts had a higher perinatal mortality rate in Puerto Ricans than in Whites (Table 1). The perinatal mortality rate for Rh erythroblastosis fetalis was greater for Whites than for Puerto Ricans. There were too few Orientals in the study to make intergroup comparisons for individual disorders. However, Orientals had a lower total perinatal mortality rate than any other group (Table 1).

Stratifying the data by various non-racial factors greatly reduced most of the interracial differences. Placental growth retardation occurred at the same rate in Whites and Puerto Ricans when mothers under 101 lbs in prepregnancy body weight were excluded from the analyses (9/1000 births). Differences between Whites and Blacks markedly decreased or disappeared for placental growth retardation, placenta previa, and breech delivery-forceps when mothers registered and started their antenatal medical care in the first trimester of pregnancy (9 vs. 11, 8 vs. 8, and 34 vs. 34/1000 births, all $P > .1$).

Cesarean section rates became almost the same in Whites and Blacks when cases with labors longer than 20 hours were excluded from the analyses (14 vs. 16/1000, $P > .1$). The occurrence of umbilical cord compression was equally common in Whites and Blacks when first pregnancies and pregnancies beyond the third were excluded from the analyses (9/1000). The perinatal mortality rates for postnatal infections were markedly reduced and the perinatal mortality rate difference between Whites and Blacks decreased when mothers made eight or more visits for antenatal medical care (12 per cent vs. 17 per cent, $P > .1$).

The largest remaining unexplained disease difference between Blacks and Whites, an excess of amniotic fluid infections, was reduced by 40 per cent but was still statistically significant ($P < .01$) when mothers who had urinary tract infections during pregnancy were excluded from the analyses. Neither the exclusion of multiple births from the analyses* nor stratification of the data by birth weight percentiles or any other non-racial factor listed in the methods section significantly affected this excess of amniotic fluid infections in Blacks. Such stratification also failed to affect significantly interracial differences in the frequencies of premature rupture of the membranes, congenital anomalies, and abruptio placentae.

Acetonuria was detected on one or more occasions in 18.3 per cent of White, 13.3 per cent of Oriental, 4.0 per cent of Puerto Rican, and 13.0 per cent of Black mothers during pregnancy. These differences were not significantly changed when the data were stratified by the time of starting antenatal medical care, the number of antenatal medical visits, and the number of urine specimens in which acetone was measured.

Discussion

The study found significant interracial differences in the occurrence, case fatality, and perinatal mortality rates of the most common fetal and placental disorders. Most of these differences appear to be non-racial in origin. Interracial differences in the occurrence of placenta previa, placental growth retardation, and breech delivery disappeared when the analyses were restricted to mothers who entered the antenatal medical care system in the first trimester of pregnancy. The high frequency of placental growth retardation in Puerto Ricans proved due to the greater proportion of Puerto Rican mothers with prepregnancy body weights under 101 lbs.**

*A detailed study of the causes of perinatal death in twins has been published elsewhere.[15]

**A recently completed study in our laboratory found that mothers with such low prepregnancy body weights had much lighter placentas than heavier mothers, independent of racial or ethnic origin.

There were no significant interracial differences in the occurrence of postnatal infections but the case fatality and perinatal mortality rate for such infections was greater in Blacks than in Whites. Most of this mortality excess in Blacks occurred after the infants had gone home from the hospital neonatal nursery. Review of the medical records showed that a higher proportion of Black than of White families did not receive medical aid for the fatal infections or received it too late to save the infant. As a group, mothers of these infants made few visits for antenatal medical care.

Rh erythroblastosis fetalis was much more frequent in Whites than in Blacks or Puerto Ricans. As is well known, a higher proportion of Whites than of Blacks or Puerto Ricans are Rh negative so that Whites more often become Rh sensitized during pregnancy.

Part of the greater frequency of amniotic fluid infections in Blacks than in Whites and Puerto Ricans may be explained by the greater frequency of gestational urinary tract infections in Blacks. Some amniotic fluid infections appear to be the consequence of bacterial spread from mothers' urinary tracts.[16] The number of amniotic fluid infections was reduced more in Blacks than in Whites and Puerto Ricans when mothers with urinary tract infections were excluded from the analyses. No explanation is currently available for the remaining excess of amniotic fluid infections in Blacks by comparison with the other groups. The explanation of this phenomenon will also help to explain part of the excess premature fetal membrane ruptures in Blacks because many such premature ruptures are the consequence of amniotic fluid infections.***

Maternal acetonuria has a special significance in perinatal mortality. It increases in frequency and is a marker for high perinatal mortality rates for a wide variety of fetal and placental disorders when mothers have low weight gains or urinary tract infections during pregnancy.[15, 16] It presumably reflects an underlying maternal acidosis. Since low maternal weight gains and urinary tract infections were more common in Black than in White pregnancies, finding more acetonuria in the Blacks might have provided a partial explanation for their excessive perinatal mortality rates. However, acetonuria was more common in White than in Black mothers during pregnancy.

***The extraplacental membranes in such cases show a much older and more advanced inflammatory process at the point of rupture than at other sites.

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