

Current Patterns of Neonatal Morbidity and Mortality in Infants of Diabetic Mothers

STEVEN G. GABBE, RICHARD I. LOWENSOHN, PAUL Y. K. WU, AND GONZALO GUERRA

Recent advances in antepartum fetal evaluation have contributed to a marked reduction in fetal deaths in pregnancies complicated by overt diabetes mellitus. To determine the effect of these changes on neonatal morbidity and mortality, a retrospective analysis of complications in 322 infants of diabetic mothers (IDM) in White classes B–R was undertaken. The majority (89 per cent) of the IDM were delivered at term with a mean gestational age of 38 weeks. Neonatal morbidity correlated significantly with gestational age, occurring in 80 per cent of the preterm and 40 per cent of the term infants. The overall incidence of complications was: hyperbilirubinemia 37 per cent, hypoglycemia 31 per cent, hypocalcemia 13 per cent, polycythemia 8 per cent, and necrotizing enterocolitis 2 per cent. Respiratory distress syndrome (RDS) occurred in 9 per cent and congenital malformations in 6 per cent of the infants. Nine infants died, and four of these deaths were due to anomalies. These data indicate that (1) a reduction in fetal mortality has been accompanied by a reduction in neonatal mortality; (2) neonatal morbidity has been decreased but remains significant in the IDM; and (3) congenital anomalies have replaced RDS as a major cause of neonatal death for the IDM. *DIABETES CARE* 1: 335–339, NOVEMBER–DECEMBER 1978.

The risk of a sudden intrauterine death increases as term is approached in the pregnancy complicated by overt diabetes mellitus.¹ Attempting to decrease these losses, obstetricians have electively terminated such pregnancies between 35 and 38 weeks' gestation. This approach was associated with significant neonatal morbidity, and often mortality, due to hyaline membrane disease (HMD).²

Antepartum evaluation of fetal well-being using both biochemical and biophysical indices, and assessment of pulmonary maturation by the lecithin/sphingomyelin (L/S) ratio have permitted an expectant course of management. The present study was undertaken to determine if patterns of neonatal morbidity and mortality had been altered by this approach.

PATIENTS AND METHODS

In 1971, the following plan of management was adopted at Los Angeles County Women's Hospital for the care of the

pregnant patient with diabetes mellitus, White classes B–R. All patients were followed weekly in the clinic, and insulin and dietary management were combined to maintain fasting serum glucose at 100 to 110 mg. per deciliter and postprandial concentrations at 140 mg. per deciliter. At 34 weeks' gestation, all patients were hospitalized for bed rest, diabetic control, and intensive antepartum surveillance using daily 24-hour urinary estriol excretion and weekly contraction stress tests (CST).^{3,4} An L/S ratio was determined between 37 and 38 weeks' gestation and was evaluated before the elective delivery of any patient.⁵ Termination of pregnancy was considered (1) if a patient reached 38 weeks' gestation and had an L/S ratio of 2.0 or greater, (2) if estriol excretion fell significantly or the CST was positive and an L/S ratio was mature, or (3) if estriol values dropped and the CST was positive even with an immature L/S ratio. During labor, continuous electronic monitoring of fetal heart rate and uterine contractions was utilized. To avoid traumatic morbidity, delivery by elective cesarean section was planned for any fetus thought to weigh over 4,000 gm.

All IDM were treated in the neonatal special care nursery and followed with frequent determinations of serum glucose, calcium, bilirubin, and hematocrit.

The data were obtained by reviewing the charts of all diabetic women and their infants delivered during the years 1971 to 1976. Statistical significance was determined using chi-square analysis unless otherwise indicated.

RESULTS

During this six-year period, 322 women with overt diabetes mellitus were treated by this protocol. Their classification by White's criteria¹ was: class B, 237; class C, 47; class D, 29; class F, 6; and class R, 3. The perinatal mortality rate for all classes was 38/1000, not significantly different from the rate of 23/1000 in the hospital as a whole. However, the perinatal mortality rate of 49/1000 for classes C-R was significantly greater ($P < 0.05$). Three stillbirths occurred in the diabetic population for a fetal death rate of 9/1000, a figure not significantly different from the 12/1000 recorded in the general hospital population. The neonatal death rate in classes B-R was 29/1000, almost three times greater and significantly higher than that of the hospital as a whole. Of the nine neonatal deaths, four were due to anomalies, including two ventricular septal defects and one coarctation of the aorta. Necrotizing enterocolitis accounted for two deaths, while HMD, Group B streptococcal sepsis, and erythroblastosis fetalis were responsible for one each. The only infant to die of HMD was delivered by emergency cesarean section at 38 weeks' gestation after a 50 per cent fall in urinary estriol levels. The baby had an Apgar score of 3 at one and five minutes and succumbed despite an L/S ratio of 2.6. There were no deaths due to trauma or iatrogenic prematurity and no intrapartum losses.

Delivery was accomplished by cesarean section in 54 per cent of the diabetic patients. Of these 173 procedures, 85 per cent or 147 were primary operations. Morbidity was not significantly different in infants delivered without labor or after spontaneous or induced labor. Neonatal complications

could not be correlated with route of delivery. The incidence of Apgar scores below 7 at five minutes was 6 per cent (20/322).

Mean gestational age at delivery was 38.0 weeks. There was no significant difference in gestational age by class. Eighty-two per cent of the patients (288/322) were delivered at or beyond 36 weeks' gestation and 34 per cent (111/322) after 38 weeks.

Sixty-one per cent (198/322) of the infants did experience some morbidity. The overall incidence of morbidity was 59 per cent in class B (140/237), 74 per cent in class C (34/47), and 76 per cent in classes D-R (29/38). Hypoglycemia (a serum glucose below 30 mg. per deciliter in infants over 2,500 gm. or less than 20 mg. per deciliter in infants below 2,500 gm.) was recorded in 31 per cent (100/322) of IDM. Thirty-seven per cent (118/322) were noted to have a serum bilirubin above 10 mg. per deciliter. Hypocalcemia, a serum calcium below 7 mg. per deciliter, was found in 13 per cent (41/322) of IDM, while polycythemia, a central venous hematocrit of 65 per cent or greater, occurred in 8 per cent (27/322). Twenty neonates or 6 per cent were noted to have a congenital malformation on physical examination or X-ray. RDS occurred in 9 per cent (28/322) of IDM and traumatic morbidity in 2 per cent (7/322). Seven infants developed necrotizing enterocolitis, and two of these died. These data are shown in table 1 and figure 1.

Mean birth weights were $3,563 \pm 97$ gm. for class B, $3,520 \pm 455$ gm. for class C, and $2,985 \pm 790$ for classes through R. Seventy infants or 22 per cent weighed over 4,000 gm. All seven episodes of traumatic morbidity occurred in macrosomic IDM who were delivered vaginally ($P < 0.001$). Twenty-three infants or 7 per cent weighed less than 2,500 gm. These infants had a significantly higher incidence of hypocalcemia (38 per cent, $P < 0.01$), RDS (25 per cent, $P < 0.001$), and anomalies (28 per cent, $P < 0.001$).

As shown in figure 2, the number of IDM with morbidity was directly correlated with gestational age ($r = 0.95$). A progressive downward trend from 80 per cent at 34 to 36 weeks to 40 per cent at 40 weeks' gestation was observed. The incidence of RDS fell markedly after 35 weeks' gestation.

TABLE 1
Number of infants at number of weeks' gestation with selected morbidity

	Weeks of gestation												
	31	32	33	34	35	36	37	38	39	40	41	42	43
Deliveries	2	1	3	8	20	40	42	96	49	39	16	5	1
Congenital anomalies	1	0	1	1	1	5	3	6	1	0	1	0	0
Polycythemia	0	0	0	1	1	8	2	6	8	0	1	0	0
Necrotizing enterocolitis	0	0	0	0	1	2	2	1	0	0	1	0	0
Respiratory distress syndrome	2	0	1	1	6	7	4	4	0	2	1	0	0
Neonatal deaths	2	0	0	0	1	2	0	4	0	0	0	0	0

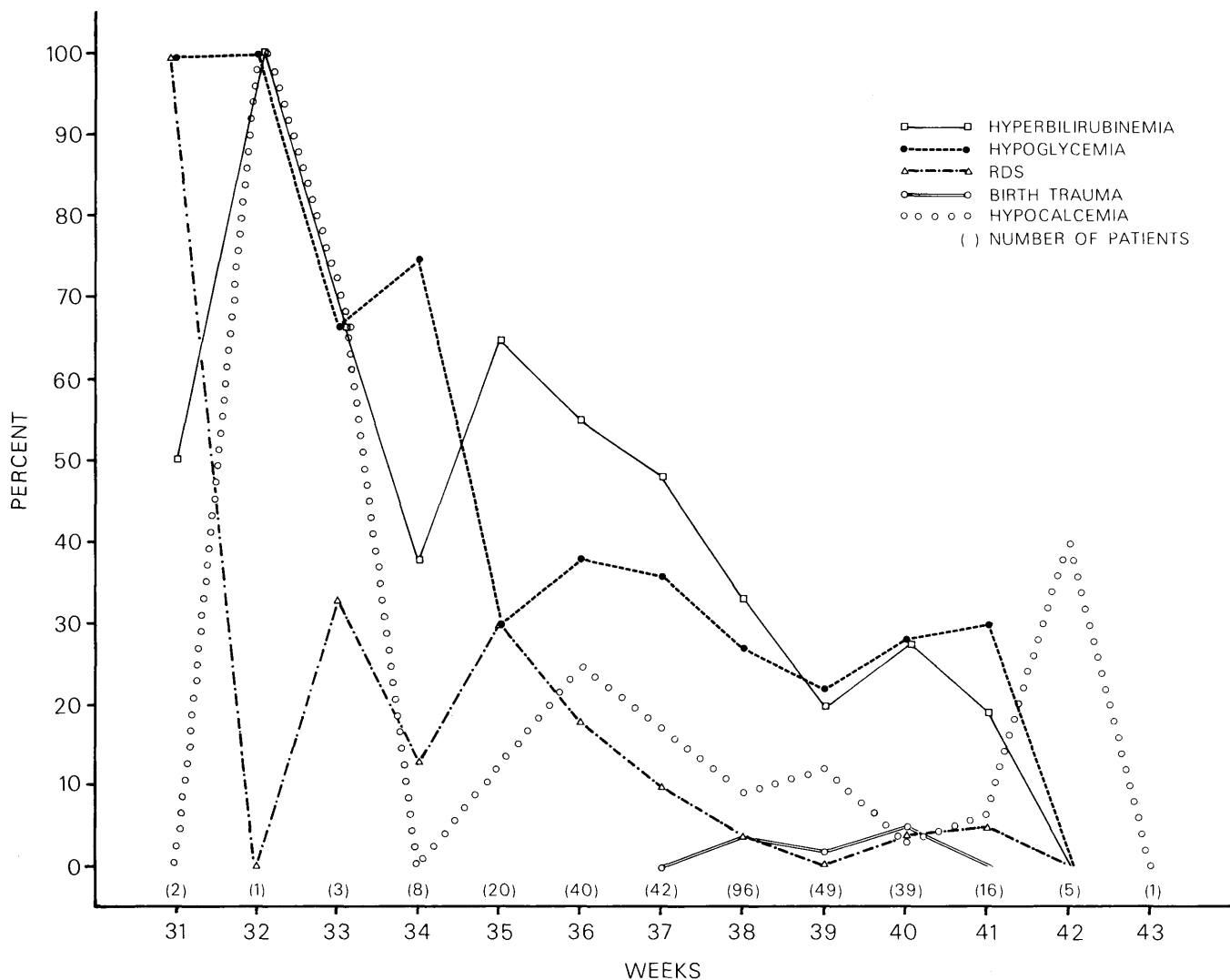


FIG. 1. Neonatal morbidity 1971 to 1976 (322 births). Number of infants with morbidity is plotted against gestational age. Number of births at each gestational age is given in parentheses.

DISCUSSION

During the past six years, we have observed a significant reduction in fetal deaths and neonatal mortality due to HMD in the IDM. Intensive care of maternal diabetes has been combined with biophysical and biochemical assessment of fetal status to produce fetal and perinatal mortality rates not significantly higher than those of the general hospital population. Daily 24-hour urinary estriol assays and weekly CST have proved reliable indicators of fetal well-being and permitted prolongation of pregnancy with little risk of unexpected intrauterine death.

HMD is no longer a major contributor to neonatal morbidity or mortality in the IDM. Only one neonatal death has been attributed to HMD during the past six years. The incidence of RDS was 9 per cent. This observation contrasts with the findings of Robert and her coworkers who retrospectively evaluated 805 IDM delivered between 1958 and 1968 and noted the risk of RDS to be 23.7 times greater than in control neonates.⁶ The elimination of confounding factors such as gestational age and route of delivery demonstrated that RDS still was 5.6 times more likely to develop in the IDM. It would appear that the key difference is in the use of the L/S ratio in our series, which was not available for clinical use before 1970. It is important to note that 39

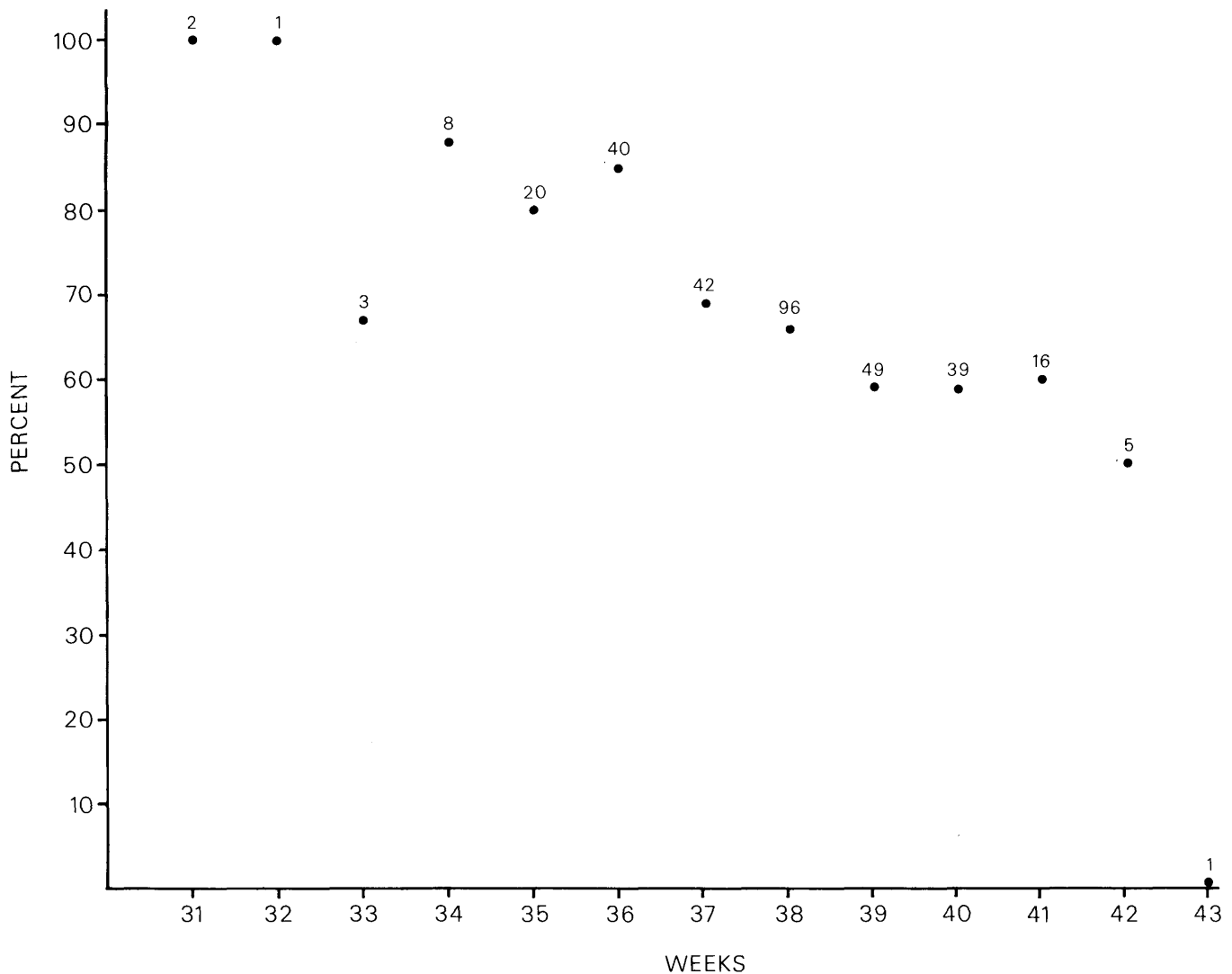


FIG. 2. Neonatal morbidity, 1971 to 1976, in infants of the diabetic White classes B-F. Percentage of infants with morbidity is plotted against gestational age at delivery. Number of births for each gestational age is plotted next to each point.

per cent (11/28) of our cases of RDS occurred at 37 weeks' gestation or longer. Our incidence of RDS with an L/S ratio over 2.0 was only 3 per cent, however, which is no different from that of our normal population.⁷ Route of delivery was not correlated with the development of RDS. By prolonging pregnancy, we may permit the fetus to synthesize not only adequate surface-active lecithin but also phosphatidylglycerol, an important factor in alveolar stabilization that is not produced by the fetal lung until 37 to 38 weeks' gestation.⁸

With the elimination of deaths due to trauma, a reduction in fetal deaths, and a decrease in mortality associated with HMD, congenital malformations have emerged as the most important cause of mortality in IDM. One-third of the deaths

in our series were due to anomalies. Several large centers have had a similar experience.^{9,10}

Although expectant management has decreased the incidence of RDS, considerable complications still occur. Almost two-thirds of the IDM did experience some morbidity such as hypoglycemia, hyperbilirubinemia, hypocalcemia, or polycythemia. With the exception of necrotizing enterocolitis, such problems are rarely fatal; however, neonatal morbidity has been associated with long-term impairment of neurologic function.^{11,12} The latter studies must be interpreted cautiously, as they do include large numbers of IDM who were delivered prematurely.

Prevention and early detection of congenital malforma-

tions, reduction of neonatal morbidity, and evaluation of long-term development are now the important challenges in caring for the pregnant diabetic woman and her infant.

From the Departments of Obstetrics and Gynecology and Pediatrics, University of Southern California School of Medicine, Los Angeles County Women's Hospital, Los Angeles, California 90033.

Address reprint requests to Steven G. Gabbe, Dept. of Obstetrics and Gynecology, Hospital of the U. of Pennsylvania, 3400 Spruce St., Phila., Pa. 19104.

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