

Well-managed gestational diabetes mellitus is no longer a risk factor for neonatal RDS – a case-control study

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Abstract

BACKGROUND Diabetes in pregnancy used to be considered associated with a higher risk of respiratory distress syndrome (RDS) in neonates. However, whether well-managed gestational diabetes remains an independent risk factor is unclear. This study was to determine the associations of them.

METHOD This was a case-control study conducted at the Obstetrics & Gynecology Hospital of Fudan University, Shanghai, China. We collected data from 101 RDS infants and 101 RDS infants from among 1749 infants, through a standardized protocol with predefined inclusion and exclusion criteria. Two investigators enrolled in recording same data twice to minimize bias. Assessment of diabetes management was based on HbA1c and random blood glucose measurements. Univariable and multivariable logistic regression was performed to calculate the odds ratio (OR). An intergroup analysis was conducted between RDS infants and those without RDS, and a subgroup analysis was conducted between RDS neonates born to women with gestational diabetes and those born to women without gestational diabetes.

RESULTS The mean (\pm SD) gestational age of the RDS infants was 35.9 (\pm 1.9) weeks, which was similar to that of the non-RDS infants (35.7 \pm 1.3) weeks). The HbA1c levels at diabetes diagnosed, the HbA1c levels right before delivery and the RBG levels before delivery had no significant differences, and all of them were below a well-controlled level. In the intergroup analysis, the morbidity of gestational diabetes between the two groups showed no significant differences in the adjusted analyses (adjusted OR 1.40, 95% CI 0.59-3.36). However, the case group had significantly more placental abnormalities (adjusted OR 3.61, 95% CI 1.63-8.00), fetal distress (adjusted OR 4.20, 95% CI 1.87-9.46), and asphyxia (adjusted OR 3.74, 95% CI 1.59-8.81) than the control group. In the subgroup analysis, the total dose of the PS applications, incidence of complications, and need for respiratory support (total and separate) were not significantly different between the two groups.

CONCLUSIONS Well managed gestational diabetes is no longer a significant risk factor for RDS, while acute or chronic ischemia factors are. Diet and exercise are sufficient for the GDM management target of HbA1c below 6.5%.

Background

Respiratory distress syndrome (RDS) is one of the most common and severe respiratory diseases in neonates. Although RDS most occurs in early preterm babies (GA lower than 34 weeks), RDS still was founded in a significant number of late preterm infants (GA between 34 weeks and 36 weeks and 6 days) and term infants[1]. Due to the increased complications and higher mortality that they experience, these patients are noteworthy as well. Gestational diabetes mellitus (GDM) was considered associated with an increased risk of neonatal complications, including the higher incidence of RDS[2, 3]. Some previous studies have demonstrated that RDS occurs more frequently in infants whose mothers have GDM[4, 5] due to hyperinsulinemia induced by hyperglycemia. Hyperinsulinemia appears to delay surfactant

synthesis by interfering with lung maturation[6–8]. However, a recent secondary analysis study based on the results of a randomized controlled trial suggested that GDM was not a risk factor for RDS[9]. Additionally, another study focusing on preterm infants (22–33 weeks gestation) reached a similar conclusion[10]. These contradictions didn't reveal whether a well managed GDM is still increase the risk of neonatal RDS, and whether nowadays therapy for GDM is suitable. Hence, we conducted a case-control study containing 101 RDS infants and 101 non-RDS infants to test the hypothesis that well-managed gestational diabetes does not increase and exacerbate RDS in late preterm or term infants.

Methods

Study subjects

This is a unmatched case-control study which comprised 202 neonates with a GA was higher than 34 weeks who were admitted to the neonatal intensive care unit (NICU) at the Obstetrics & Gynecology Hospital of Fudan University, Shanghai, China, from 1st June 2017 to 1st June 2019. All datas were collected anonymously medical record system of Obstetrics and Gynecology Hospital of Fudan University and collection was authorized. We excluded infants with severe cardiac malformation and incomplete antenatal record data, as well as infants who died during hospitalization, from the analysis. The case group comprised 101 infants with radiographically confirmed RDS (further criteria below). The control group consisted of 101 non-RDS infants who were admitted with a diagnosis of transient tachypnea, asphyxia, congenital pneumonia, hyperbilirubinemia, or low birth weight. We randomly selected controls from the neonates admitted to the same ward over the same time period as with the case group; identical inclusion and exclusion criteria were applied. Randomization was based on a random number table linked to the patient identification number of each infant.

Diagnostic criteria for RDS, GDM, and PGDM

The oral glucose tolerance test (OGTT) was used to diagnose GDM and PGDM at the Obstetrics & Gynecology Hospital of Fudan University. Positive results for fasting, one-hour postprandial, and two-hour postprandial blood glucose concentrations were levels higher than 5.1, 10.0, and 8.5 mmol/L, respectively[11]. The diagnostic criteria for RDS included (1) a clinical picture of infants with the onset of progressive respiratory failure shortly after birth with respiratory failure that manifested by an increase in the work of breathing and an increase in the oxygen requirement; (2) a characteristic chest radiograph featuring low volume, the classic diffuse ground-glass appearance and air bronchograms.

Definition of well-managed GDM[12–14]: Glycated hemoglobin (HbA1c) was lower than 6.5%, or the concentrations of fasting, one-hour postprandial, and two-hour postprandial blood glucose were all lower than 5.3 mmol/L, 7.8 mmol/L, and 6.7 mmol/L, respectively. Additionally, random blood glucose (RBG) < 11.1 mmol/L was considered a reference standard for well-managed diabetes.

Definition of confounders:

Maternal: (1)pregnancy induced hypertension(PIH) was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg) at ≥ 20 weeks of gestation in the absence of proteinuria or new signs of end-organ dysfunction[15]. (2)Premature rupture of fetal membranes(PROM) means fetal membranes break 8 hours or earlier before delivery. (3)Maternal prenatal fever was defined as body temperature is above 38.0°C whenever before, during or after delivery.

Neonatal: (1)Hyperglycemia and hypoglycemia was defined according to Pediatric Endocrine Society guideline[16]. (2)Jaundice referred to a series of criteria based on different age[17]. (3)pulmonary arterial hypertension(PAH) was diagnosed by echocardiography according to criteria reported by others[18]. (4)Infection and potential infection:including septicemia, intrapartum fever of mother ($T > 38.0^{\circ}\text{C}$), congenital pneumonia. (5)Placental abnormality includes placental abruption, velamentous insertion, battledore placenta, placental implantation, placenta previa, and placental adhesion. (6)Umbilical cord abnormality refers to prolapse, presentation, tying of umbilical cord and cord around the neck; (7)The criteria of asphyxia, which is our routine suggested by Newborn Professional Committee of Chinese Medical Association, is (a)Apgar score is less than 7 at 1 min or 5 min after birth and (b)umbilical artery serum pH is blow 7.15[19]. (8)Anemia was defined as hemoglobin of umbilical cord blood is below 17.0 g/dL for term infants and 16.0 g/dL for preterm infants.

Statistical analysis

We summed the data as frequencies or percentages for categorical variables and as the means and standard deviations or medians and interquartile ranges for continuous variables, according to the distribution. Differences between the groups were compared by the chi-square or Fisher's exact test for categorical variables, Student's t-test, or Mann-Whitney U test for continuous variables, depending on the distribution. Binary logistic regression was used to assess associations of GDM or PGDM with RDS; the model was first unadjusted and then adjusted for GA, asphyxia, and other potential risk factors. A nominal 2-sided probability value < 0.05 was considered to indicate statistical significance. All of the calculations were performed using SPSS 23.0 (SPSS Inc. Chicago, IL).

Results

We reviewed the medical records of patients admitted to the neonatal intensive care unit (NICU) at the Obstetrics & Gynecology Hospital of Fudan University. After excluding 33 neonates according to the exclusion criteria, 1446 late preterm and term infants were eligible for analysis. All 101 infants who developed RDS were allocated to the case group. For the control group, 101 neonates were selected randomly from the 1345 other neonates with non-RDS diseases. An intergroup comparison and a subgroup comparison were performed (Fig. 1).

Clinical data: The clinical characteristics of the case group and control group are presented in Table 1. The preterm birth rate and low birth weight rate were both significantly different between the two groups ($P < 0.05$) after adjusting for maternal age, the occurrence of elderly pregnancy, PIH, cesarean rate, sex, gestational age, and birth weight.

Table 1
Comparison of maternal and neonate basic characteristics

Characteristic	Case group	Control group
Diagnosis for admission	RDS (101/101)	Infection and potential infection [‡] (5/101); Low birth weight (19/101); Hyperbilirubinemia (16/101) TTN (61/101)
Maternal characteristics		
Maternal age (mean ± SD)	31.7 ± 4.6	31.5 ± 4.6
Elderly pregnancy (%) [†]	29.0	24.8
PIH (%)	11.0	7.9
Cesarean rate (%)	23.0	32.7
Infant characteristics		
Sex (male%)	57.0	47.5
Gestational age (weeks, mean ± SD)	35.9 ± 1.9	35.7 ± 1.3
Preterm birth (n, %)*	72, 72.0%	60, 59.4%
Birth weight (g, mean ± SD)	2590 ± 642	2494 ± 492
Low birth weight(%)*	42.0	60.4
BW to GA	11	28
SGA (%)	84	71
AGA (%)	5	2
LGA (%)		
Complications during hospitalization		
Hypoglycemia (%)	12.0	6.9
Hyperglycemia (%)	10.0	3.0
Neonatal jaundice (%)	51.0	57.4
PAH (%)	13.0	0
Neonatal infection (%)	27.0	2.0
Anemia (%)	11.0	3.0
PIH: pregnancy induced hypertension; NICU: neonatal intensive care unit;		

Characteristic	Case group	Control group
TTN:Transient Tachypnea of Newborn;PAH:pulmonary arterial hypertension		
Preterm birth was defined as gestation age is smaller than 34 weeks.		
SGA, AGA, LGA was categorised individually according to the birth weight below the 10th centile,between 10th and 90th centile, and above 90th .		
† Elderly pregnancy:maternal age is grater than 35 years.		
‡ Infection and potential infection:including septicemia, intrapartum fever of mother (T > 38.0°C), congenital pneumonia.		
* there is a significant difference (P < 0.05, in chi-square test)		

We analyzed the HbA1c and RBG levels of mothers with diabetes in the two groups to determine whether their GDM was well-managed. Table 2 and Fig. 1 illustrate the diabetes features of those with GDM and PGDM in the two groups diabetes features, including morbidity, treatment, rate of tests (HbA1c, RBG), and mean gestational age before diagnosis, were similar for both groups (Table 2). Levels of HbA1c at diabetes was diagnosed, HbA1c right beofre delivery and RBG before delivery had no significant difference, and all of them were below a well-controlled level. These results indicated that both groups of diabetic mothers were well managed (Fig. 2).

Table 2
Comparison of diabetes features between RDS infants and non-RDS infants

	RDS	Non-RDS	P-value
GDM (N/all subjects)	15/101	13/101	0.41
PGDM (N/all subjects)	2/101	3/101	0.56
GDM & PGDM (N/all subjects)	17/101	16/101	0.49
Treatment (N/all subjects)	14/101	13/101	0.94
Diet and exercise	2/101	3/101	
Insulin			
Number of HbA1c records at diagnosis (N / number of diabetes patients)	14/17	9/16	0.17
Number of HbA1c records right before delivery (N / number of diabetes patients)	13/17	13/16	0.42
Number of RBG records right before delivery (N / number of diabetes patients)	15/17	15/16	0.35
Mean result of OGTT(mmol/L) (fasting, 1 h, 2 h)	4.8, 10.6, 8.5	4.8, 9.9, 9.3	—
GA at diagnosis (weeks)	17.6	19.1	0.44
GDM: gestational diabetes mellitus; PGDM: pregestational diabetes mellitus;			
OGTT: Oral glucose tolerance test; RBG: random blood glucose; GA: gestational age			
* there is a significant difference (P < 0.05, in t-student test).			

Univariable and multivariable logistic regression was performed to confirm whether well-controlled diabetes (GDM and PGDM) was still a risk factor for RDS in late preterm and term infants (Table 3). After adjusting for confounders, the incidence of diabetes showed no significant differences between the cases and the controls. This means that well-controlled diabetes was no longer a risk factor for these babies.

Table 3

Risk factors associated with RDS in the univariable analysis and after adjustment for diabetes

Risk factors	RDS n = 101	Non-RDS n = 101	Crude OR OR (95% CI)	Adjusted OR OR (95% CI)
GDM and PGDM	18, 18.0%	16, 15.8%	1.17 (0.56–2.44)	1.40 (0.59–3.36)
Corticosteroid	34, 34.0%	26, 25.7%	1.49 (0.81–2.73)	1.14 (0.52–2.59)
PROM	13, 13.0%	19, 18.8%	0.65 (0.30–1.39)	0.65 (0.24–1.75)
Placental abnormality [†]	39, 39.0%	12, 11.9%	4.74 (2.30–9.79)*	3.61 (1.63–8.00)*
Umbilical cord abnormality [‡]	13, 13.0%	16, 15.8%	0.79 (0.36–1.75)	0.70 (0.26–1.91)
Eclampsia	27, 27.0%	30, 29.7%	0.88 (0.47–1.62)	0.78 (0.36–1.68)
Maternal prenatal fever	6, 6.0%	13, 12.9%	0.43 (0.16–1.19)	0.35 (0.10–1.24)
FIUD	40, 40.0%	14, 13.9%	4.14 (2.07–8.28)*	4.20 (1.87–9.46)*
Asphyxia	32, 32.0%	10, 9.9%	4.28 (1.97–9.31)*	3.74 (1.59–8.81)*
Preterm birth	72, 72.0%	60, 59.4%	1.76 (0.97–3.17)	1.66 (0.77–3.60)
GDM and PGDM: gestational diabetes mellitus or pregestational diabetes mellitus;				
PROM: premature rupture of fetal membranes; GBS: group B streptococcus;				
FIUD: fetal distress in the uterus;				
† placental abnormality includes placental abruption, velamentous insertion, battledore placenta, placental implantation, placenta previa, and placental adhesion.				
‡ umbilical cord abnormality refers to prolapse, presentation, tying of umbilical cord and cord around the neck;				
* there is a significant difference (P < 0.05, in chi-square test).				

To investigate whether babies born to mothers with gestational diabetes had poorer outcomes than those born to mothers without gestational diabetes, we grouped RDS neonates into two subgroups: the non-diabetic group and the diabetic group, and a subgroup analysis was conducted between these two groups. Table 4 displays the RDS characteristics of these neonates. The transfer rate of the diabetic group was significantly lower than that in the non-diabetic group, indicating that the number of severe cases in the diabetic group was less than that in the non-diabetic group. And for mild and moderate patients, who didn't need transfer for further and more advanced treatment, the total dose of PS applications, incidence of complications, and respiratory support rates (total and separate) (Table 4) as well as different respiratory support duration (Fig. 3) showed no significant differences between the two groups. All of these results showed that situation of RDS neonates did not deteriorate because of GDM

and PGDM. Table 5 shows that there was a higher usage rate of hood oxygen, while the usage rates of other respiratory supports were similar. As hood oxygen was often utilized before RDS was diagnosed, gestational diabetes might have led to a more prolonged latent period of RDS.

Table 4

Comparison of RDS features and outcomes between infants born to mothers with and without gestational diabetes

	Maternal diabetes	No maternal diabetes	P-value
RDS (n)	18	83	—
Initial symptoms (n,%)	17, 94%	81, 97%	> 0.05
tachypnea	13, 72%	40, 48%	
subcostal retractions	4, 22%	19, 22%	
audible grunting	1, 2%	1, 5%	
cyanosis			
Frequency of PS applications [†]	17/18	76/83	0.57
1 time	1/18	7/83	
2 times			
Total dose of PS applications [†]	155 ± 43 mg	146 ± 49 mg	0.56
Transfer [‡]	2/18	28/83	0.046*
Complications			
PPHN	2/18	11/83	0.58
Metabolic acidosis	5/18	15/83	0.26
Pneumonia	4/18	15/83	0.45
Pneumothorax	0/18	8/83	0.20
Septicemia	1/18	3/83	0.55
Other infection	2/18	25/83	0.08
PS: pulmonary surfactant;			
† Usage frequency and the dose of PS application are counted from admission to discharge for every single infant. The dose was summarized as a mean dosage per kilogram of birth weight.			
‡ Because of intractable complications such as PPHN, severe infection, and surgical diseases, some neonates need to be transferred to specialized pediatric hospitals for further and more advanced treatment. This always means a worse situation for patients.			
* there is a significant difference (P < 0.05, in Fisher's exact test).			

Table 5

Comparison of the usage rates of different types of respiratory support between babies born to mothers with gestational diabetes and babies born to mothers without gestational diabetes

	gestational diabetes (N/all subjects)	No gestational diabetes (N/all subjects)	P-value
Hood oxygen	11/18 (61.1%)	26/83 (31.3%)	0.019*
CPAP	13/18 (54.2%)	45/83 (72.2%)	0.127
MV	5/18 (27.7%)	23/83 (27.8%)	0.601
CPAP: Continuous Positive Airway Pressure; MV: Mechanical ventilation			
* there is a significant difference (P < 0.05, in chi-square test).			

Discussion

This study has three clinically relevant findings: (1) The similarity in morbidity, severity, and outcomes between infants born to mothers with GDM and infants born to mothers without GDM revealed that well-managed gestational diabetes did not increase the incidence of RDS in late preterm or term infants. (2) For RDS infants, GDM did not exacerbate their situation including complications, need for pulmonary surfactant (frequency and dose), and need for respiratory support (frequency and duration). (3) Furthermore, some intra-uterine or extra-uterine hypoxic-ischemic factors seem to be related to increased risk of neonate RDS.

Comparison with other studies

There has been a long-standing debate regarding the effect of gestational diabetes on neonatal RDS. Consistent with our present observations, numerous other studies have also revealed that the risk of RDS in infants born to mothers with gestational diabetes approached that of infants born to mothers without diabetes. For example, Martina conducted research on 76320 infants who were very preterm and very low birth weight and showed no association between GDM and RDS[20]. A 1999 case-control study, which included 45 diabetic pregnancies, indicated that fetal lung maturity was not delayed by diabetes[21], but it may have driven more TTN. Some additional studies came to a similar conclusion[22, 23]. However, few of these studies have evaluated glycemic indicators, such as HbA1 or RBG during gestation, so they could not illustrate whether proper management of GDM having no detrimental effect to RDS.

Nevertheless, some other studies have suggested that diabetes during pregnancy is an independent risk factor. The most compelling evidence supporting this point was derived from a scholarly paper[24], a cohort study on 805 infants of diabetic mothers and 10,152 infants of non-diabetic mothers, which reported a 23.7 risk ratio (RR) of GDM. Apart from this, later research also adds more evidence to support

this, such as a meta-analysis on 24 studies[25], a prospective study on 444 infants (GA > 34 weeks), and a cohort study involving 57,629 mothers with diabetes[4].

There are potential reasons for this observation. First, diabetes of the mother may cause fetal hyperglycemia and later hyperinsulinemia, which works as an inhibitor of the key enzyme of lipid synthesis[6, 26] and production of the vital protein SP-B [27]. Second, preterm births were significantly more common in women with diabetes, which directly led to immature fetal lungs and a lack of pulmonary surfactant[28, 29]. This preterm risk seems to be higher for pregestational diabetes type I than for type II[30]. In addition, macrosomia, which is more likely to result in cesarean section (CS), was more prevalent in babies with diabetic mothers[29, 31], and CS is related to an increased risk of RDS[32]. A study based on a pregnancy cohort with 110879 women confirmed this point. It was found that GDM was associated with a 1.63 RR of RDS, and a 1.40 RR of neonate hypoglycemia[33], which means that infants were influenced by hyperinsulinemia before delivery. There are a small number of papers that studied the effect of different types and severity of gestational diabetes on RDS. Francisco et al. reported that women with diet-controlled GDM and normoglycemic women had infants with appropriate lung maturation, while the insulin-treated group had more immature lungs[34]. This implied that worse islet cell function of the mother drove more noticeable adverse effects on the fetal lung. However, none of these studies have detailed glycemic and HbA1c levels during pregnancy to illustrate whether the conflicting results may be due to poor diabetes management.

Strengths and Limitations of our study: To our knowledge, this is the first study concerned with the details and validity of diabetes control during pregnancy. To shed light on this problem, we focused on diabetes indicators at different times: HbA1c and OGTT at diagnosis and HbA1c and random blood glucose right before delivery. These results not only confirmed that diabetes was well-managed in our study but also indicated that an HbA1c of 6.5% is a safe threshold for gestational diabetes to avoid additional RDS risk (Fig. 2). As far as the reliability of the data was concerned, although not every pregnant woman had their diabetes monitoring recorded due to limitations of the retrospective study, most of them (13/17 to 15/16) (Table 2) provide credible results. With a standardized protocol to collect all of the data, information bias was minimized.

Another advantage is that we elaborated on the effect of diabetes on RDS infant outcomes in more detail for several different aspects, including counts and doses of PS usage, complications, and the duration of respiratory support. The relationship between different types respiratory support and gestational diabetes confirmed that well-managed diabetes did not aggravate RDS, even if the duration was somewhat discrete. This point was also supported indirectly by comparisons of other complications, such as PPHN, pneumonia, or pneumothorax. However, what hampered us in obtaining a firmer conclusion was the low morbidity of nonpreterm RDS, resulting in the small number of neonates in the case group. This also means that additional research, which includes a larger sample size and premature infants, is needed to illustrate whether GDM has a different effect on various gestation ages. There are some minor limitations in our study. For example, limited by time and labor cost, it was difficult to collect information on all 1345 contemporary infants without RDS for the control group. We used a simple randomization to select and

review approximately 1/10 of the records, which may have resulted in a sampling error. In addition, as an obstetrics and gynecology hospital, our NICU lacks advanced equipment and surgical collaborators to rescue critical patients; we must transfer these patients to specialized pediatric hospitals. The absence of their detailed information forced us to conclude that they had a worse prognosis, which may have introduced bias in the comparison of complications. However, this bias does not change the conclusion that diabetes did not increase the risk of RDS.

On account of the detailed examination in this study, there is an interesting finding in our work: RDS resulted in an increased usage rate of hood oxygen, which is the primary respiratory support used in TTN or for the initial stage of RDS in our routine procedures. This means that GDM can prolong the latent period of RDS, or some RDS was possibly derived from TTN. Another study showing a higher incidence of TTN in gestational diabetes babies supported this point[21] indirectly. The potential latent period seemed to provide a time window to take precaution and prevent RDS development from TTN by early detection with sensitive methods, such as lung [35]ultrasonography. Lung ultrasonography can differentiate RDS from TTN through echogenicity discrepancies. This discrepancy is caused by a substantial difference in the pathological mechanism. Furthermore, as suggested by the logistic regression analysis adjusted for confounders, the independent risk factors for RDS of late-preterm babies included placental abnormalities, umbilical cord abnormalities, and fetal distress in the uterus; but not gestational diabetes. These factors are all related to acute or chronic ischemia in fetuses or neonates, indicating that hypoxic-ischemic injury plays an essential role in RDS etiology, which is in accordance with some previous reports[36–38].

It should be noted that the most appropriate comparison was between infants born to mothers with well-managed GDM and infants born to mothers with poorly managed GDM. Nevertheless, there were very few pregnant women with poorly managed GDM in Shanghai, China, due to improved antenatal examinations. Therefore, our study was a case-control study designed to compare RDS infants and non-RDS infants and examine the well-managed GDM incidence of their mother to determine the odds ratio (OR).

Conclusion

Well-managed gestational diabetes did not increase the incidence of RDS in late preterm or term infants. And for those infants with RDS, GDM or PGDM of their mothers did not exacerbate their complications, need for pulmonary surfactant, or frequency and duration of respiratory support use. These results indicated that current GDM management targets including (1)FBG below 11.1 mmol/L, (2)HbA1c was lower than 6.5%, and(3)OGTT results below 5.3 mmol/L, 7.8 mmol/L, and 6.7 mmol/L are enough for reducing risk of neonatal RDS. Besides, this study also implied that management methods of diet and exercise are sufficient to reach this GDM management target. Additionally, our research showed some intra-uterine or extra-uterine hypoxic-ischemic factors, such as asphyxia, placental abnormality, and fetal distress, are likely to relate to neonatal RDS. This needs some more basic researches to illustrate the mechanism.

Abbreviations

GDM

gestational diabetes mellitus;

PGDM

pregestational diabetes mellitus;

GA

gestational age;

RDS

respiratory distress syndrome;

HbA1c

Glycated hemoglobin;

RBG

random blood glucose;

OGTT

oral glucose tolerance test;

PROM

premature rupture of fetal membranes;

GBS

group B streptococcus;

FIUD

fetal distress in the uterus;

PIH

pregnancy induced hypertension;

TTN

Transient Tachypnea of Newborn;

OR

odds ratio;

LBW

low birth weight;

ELBW

extremely low birth weight;

NICU

neonatal intensive care unit;

CPAP

Continuous Positive Airway Pressure;

MV

Mechanical ventilation;

Declarations

Ethics approval and consent to participate This study was approved by the ethics committee of Obstetrics and Gynecology Hospital of Fudan University(No. 2019-35). Even if there are neonates enrolled in this study, written informed consent was not required by the ethics committee because all data were analysed anonymously.

Consent to publish Not applicable.

Availability of data and materials The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.All datas were collected from database of medical record system of Obstetrics and Gynecology Hospital of Fudan University and collection was authorized.

Competing interests There is no conflict of interest associated with this manuscript.

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Author Contributions M.D JMW and Doctor GNX proposed the idea of this research and designed the protocol. M.D QY, performed the data acquisition and analyses. Doctor GNX and M.D QY wrote the report. FL, YY, CQL, XFW have been involved in revising the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

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Figures

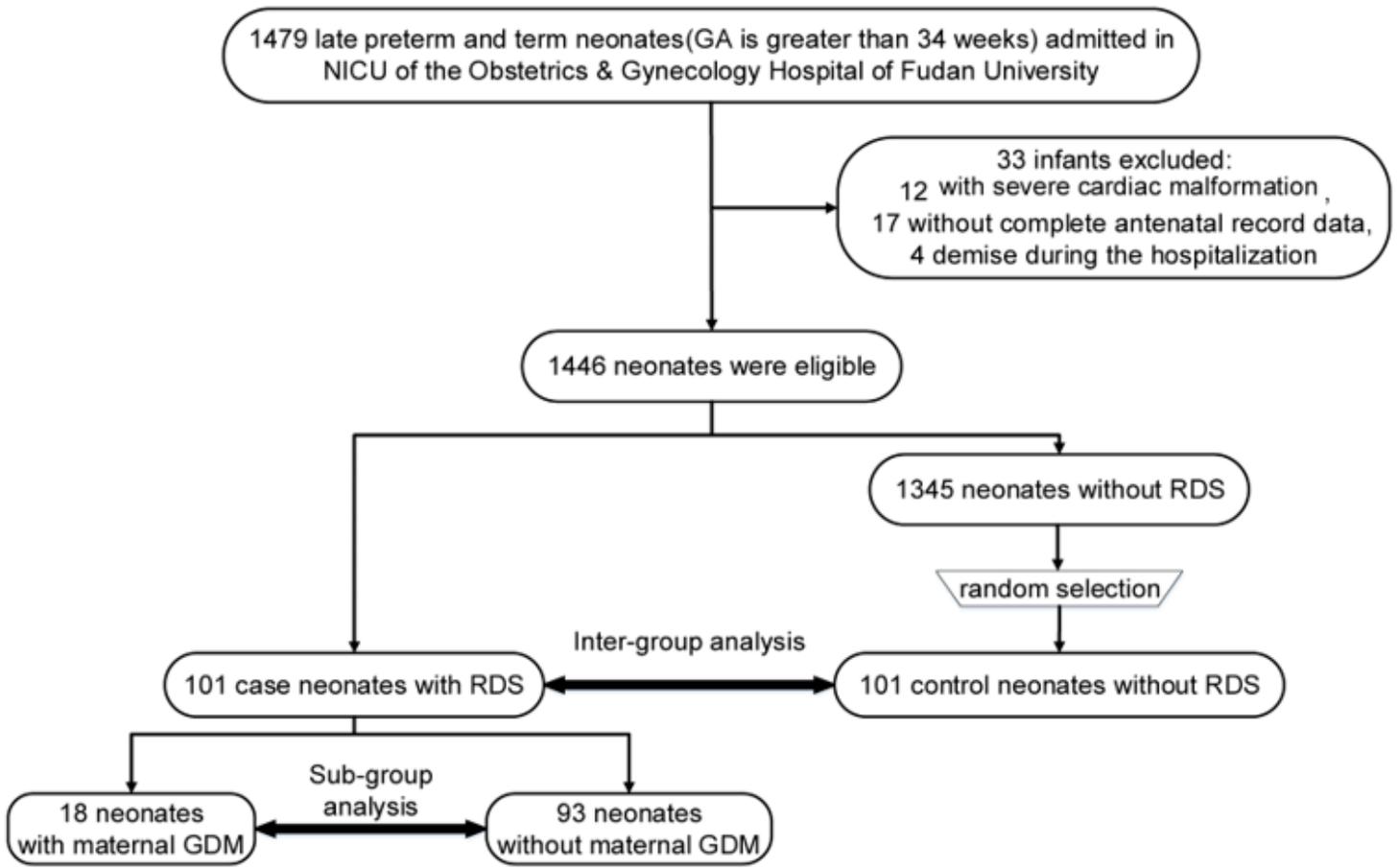


Figure 1

Flow diagram of participants.

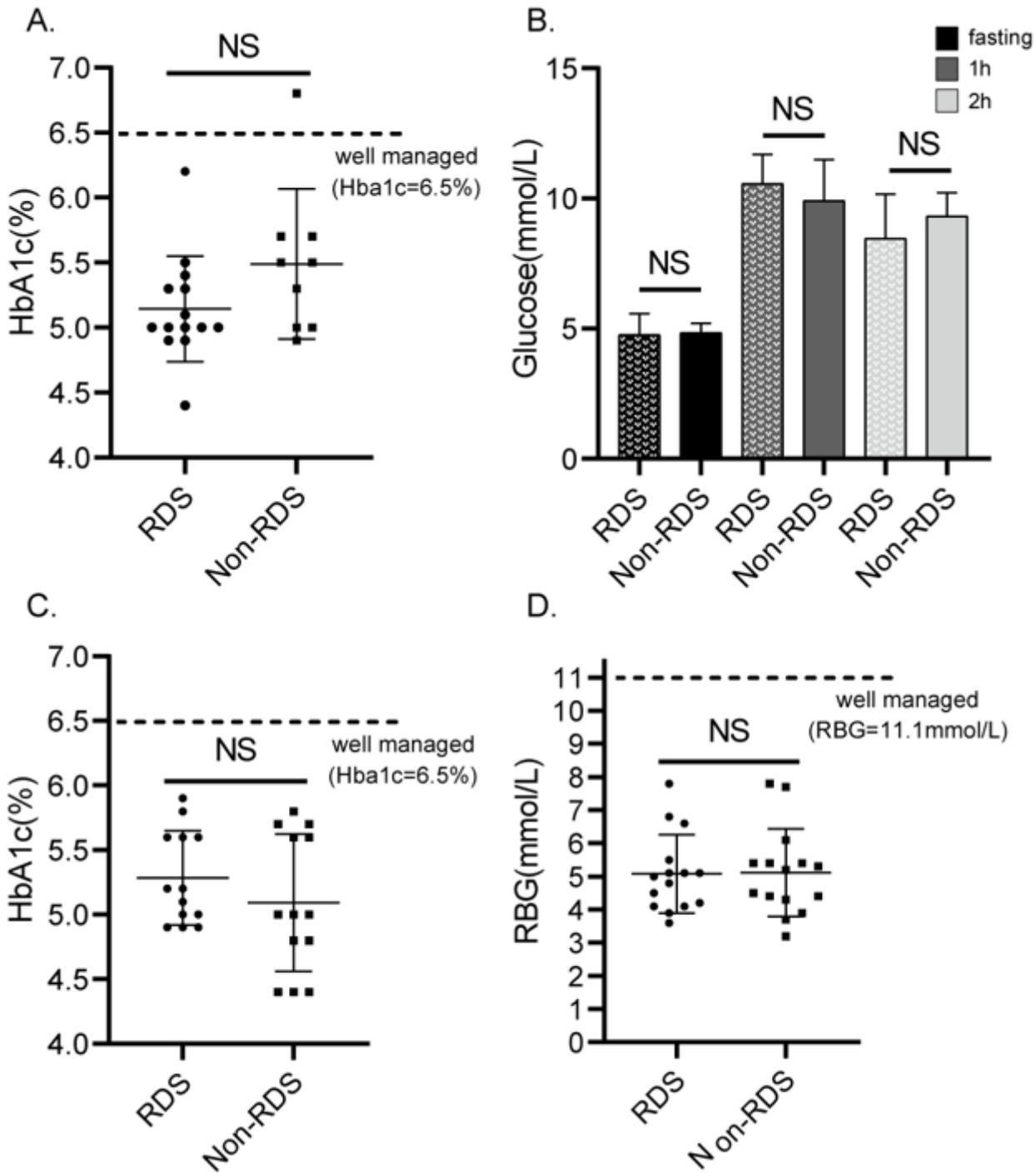


Figure 2

The comparison of laboratory test results for diabetes indicators between neonates with and without RDS. A. OGTT results for diabetes diagnosis, B. HbA1C results at diabetes diagnosis, C. HbA1C right before delivery, D. RBG right before delivery. NS: there is no significant difference; $P > 0.05$, which was calculated with Student's t-test for variables with a normal distribution.

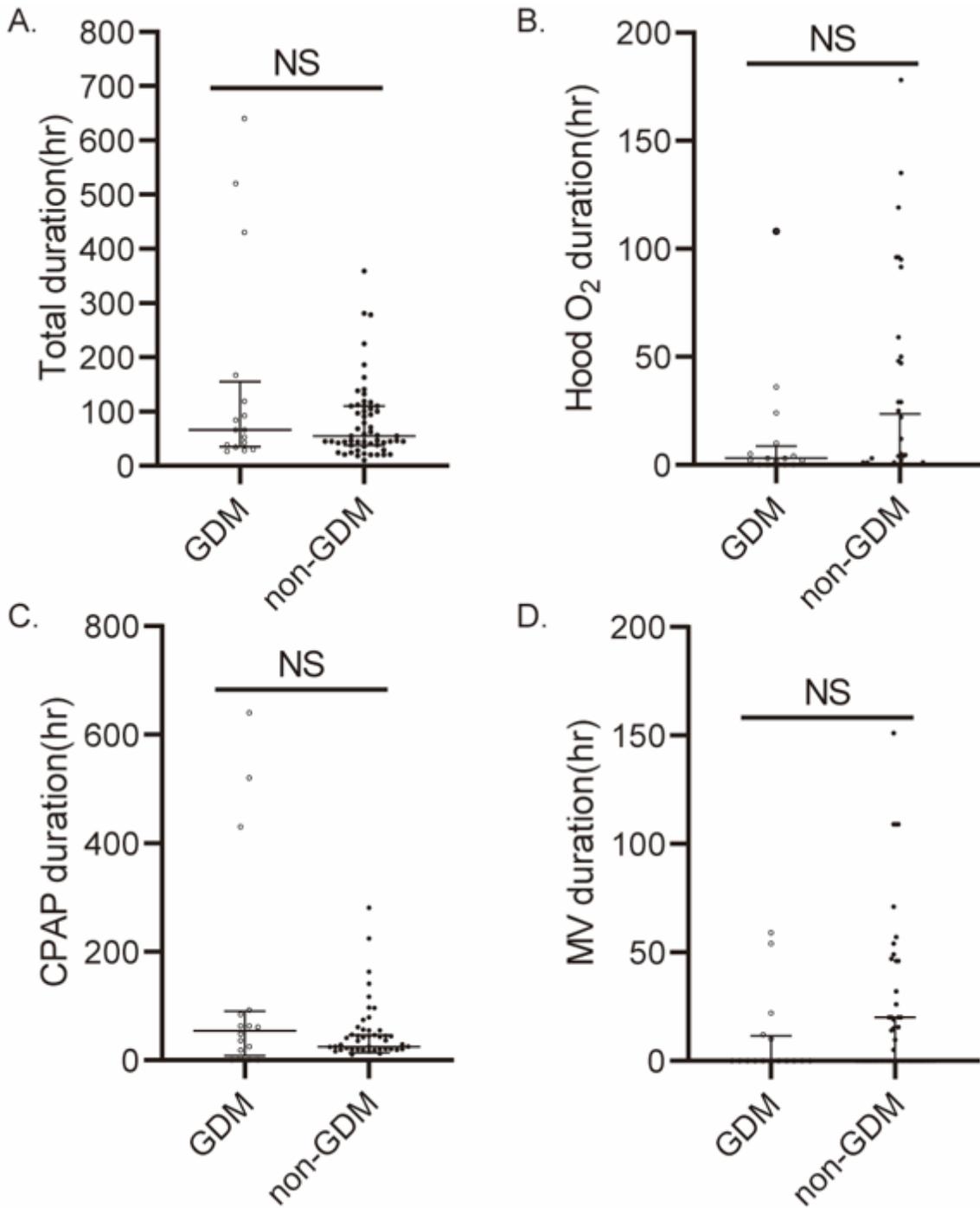


Figure 3

Comparison of different durations of respiratory support between babies born to mothers with gestational diabetes and babies born to mothers without gestational diabetes. A, B, C, D present separate comparisons for treatment durations of hood oxygen, CPAP, MV, and total respiratory support, respectively, between infants born to mothers with gestational diabetes and infants born to mothers without gestational diabetes. NS: there was no significant difference; $P > 0.05$, which was calculated with the Mann-Whitney U test for a nonnormal distribution.

Supplementary Files

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