Perinatal Outcomes in Infants of Mothers with Diabetes in Pregnancy

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ABSTRACT **Background:** The incidence of gestational diabetes mellitus (GDM) is increasing in parallel to the worldwide obesity and type 2 diabetes pandemic. Both GDM and pre-gestational diabetes mellitus (PGDM) are associated with short- and long-term consequences in the offspring. There are few recent studies addressing outcomes of newborns born to women diagnosed with GDM and PGDM in Israel.

Objectives: To assess perinatal complications in offspring of women with GDM and PGDM.

Methods: The authors conducted a single-center retrospective case-control study of outcomes of all newborns whose mothers had been diagnosed with diabetes in pregnancy compared to randomly assigned controls born on the same date, whose mothers had no diabetes.

Results: In the study period 2015–2017, 526 mothers diagnosed with GDM or PGDM and their newborn infants were identified. The authors randomly assigned 526 control infants. The rate of women with diabetes in pregnancy was 5.0%. Mothers with GDM and PGDM had higher rates of pre-eclampsia, multiple pregnancies, and preterm deliveries. Mothers with PGDM had significantly higher rates of intrauterine fetal demise (4.3%), congenital anomalies (12.8%), and small-for-gestational-age neonates (10.6%) compared to controls (0%, 3.2%, and 4.2%, respectively, $P < 0.001$). The risks for preterm or cesarean delivery, large-for-gestational-age neonate, respiratory morbidity, hypoglycemia, and polycythemia were increased in offspring of mothers with diabetes, especially PGDM.

Conclusions: Despite all the advancements in prenatal care, diabetes in pregnancy, both PGDM and GDM, is still associated with significant morbidities and complications in offspring. Better preconception and inter-pregnancy care might reduce these risks.

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KEY WORDS: gestational diabetes mellitus (GDM), neonatal outcomes, offspring morbidity, perinatal outcomes, pre-gestational diabetes mellitus (PGDM)

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The incidence of gestational diabetes mellitus (GDM) is increasing in parallel to the obesity and type 2 diabetes pandemic worldwide [1]. The reported rates of GDM from recent years range from 7.2% in France [2] to 13–15% in Australia and the United States, which is similar to the rate reported in the Hyperglycemia and Adverse Pregnancy Outcome study (HAPO study) [3,4]. Approximately 90% of women with diabetes in pregnancy have GDM, while the rest have pre-gestational diabetes mellitus (PGDM), either type 2 or Type 1 diabetes. Both gestational and pre-gestational maternal diabetes are associated with short and long-term consequences in the offspring [2,5,6]. Good treatment and control of diabetes before and during pregnancy result in improved outcomes and decreased neonatal complications [7,8]. Offspring of diabetic mother are also at risk of developing long-term metabolic complications and diabetes at older age [6,9].

Relatively few studies exist that address the outcomes of pregnancy in women diagnosed with diabetes in Israel in recent years. In this study, our aim was to study current prevalence of diabetes in pregnancy and its complications for the newborn. We also evaluated the relation between the type of diabetes (gestational or pre-gestational), the treatment protocol during pregnancy, and perinatal complications.

PATIENTS AND METHODS

Our case-control study was based on medical records of women diagnosed with diabetes during pregnancy who delivered at Bnai Zion Medical Center between 1 January 2015 and 31 December 2017. The study was approved by Bnai Zion Medical Center ethics committee (0075-18-BNZ). GDM or PGDM was identified using all ICD-9 diagnoses and key words related to these conditions. The data regarding the offspring were identified. Every infant born to a mother with diabetes during pregnancy was matched to an infant born at the closest time to a mother without diabetes in pregnancy. For every mother–infant pair in the study and control groups data were collected from the electronic medical records including maternal age and ethnicity, type of diabetes in pregnancy (GDM or PGDM),

treatment given to the mother (diet, oral hypoglycemic, or insulin), preeclampsia as reported by the obstetrician, gestational age at delivery, and mode of delivery (vaginal, assisted vaginal delivery, or cesarean delivery). Neonatal data included gender, single or multiple gestation, birth weight, small for gestational age (SGA, below the 10th percentile) or large for gestational age (LGA, above the 90th percentile), congenital anomalies, birth trauma (Erb's palsy, clavicular or long bone fracture), respiratory distress (based on clinical signs of dyspnea or tachypnea with or without the need for oxygen or respiratory support persisting for longer than 2 hours after delivery). Additional data included specific diagnosis of transient tachypnea of the newborn (TTN) or respiratory distress syndrome (RDS) based on chest X-ray and clinical course, hypoglycemia (blood glucose routinely drawn within one hour of birth and then at 2, 4, 8 hours that is below 40 mg/dl) [6], or polycythemia (defined as hematocrit above 65% in a peripheral venous sample; peripheral capillary samples are routinely drawn for hematocrit measurement within the first 2 hours after birth and only if the value is > 65% is a venous sample drawn to verify) [6]. Last, data on neonatal jaundice (based on age adjusted bilirubin levels criteria [Bhutani's nomograms] or bilirubin level above 7.0 mg/dl [Bhutani's 40th percentile defining benign neonatal hyperbilirubinemia or physiologic jaundice] at discharge to home at 40 hours of age) [6] and cardiomyopathy (based on finding of thickening of the interventricular septum on echocardiography were collected). This evaluation was performed whenever there were cardio-respiratory symptoms or evidence of other neonatal complications related to maternal diabetes**)** [6]. In addition, we reviewed all intrauterine death cases and their relation to diabetes in pregnancy. Data were collected in an Excel spreadsheet (Microsoft Excel (Version 15.0, Microsoft Corp, Richmond, CA, USA).

All data were tested for normal distribution by applying Kolmogorov-Smirnov test. Kruskal-Wallis one-way analysis of variance, Chi-square, and binary univariate or multivariate logistic regression were used as appropriate to study the associations between pregnancy outcomes and study groups. Statistical analysis was performed using SigmaPlot, version 11.0 (Systat Software Inc. San Jose, CA, USA) and Minitab®, version 16.2.2 (Minitab Inc. State College, PA, USA; Coventry, UK). Statistical significance was set at $P < 0.05$.

RESULTS

The rate of women with diabetes in pregnancy in our population was 5.0%. No ethnic differences were found between the diabetic and control groups. Mothers with diabetes were older and had higher rates of multiple pregnancies and preeclampsia. Notably, the rates of intrauterine fetal death and neonatal congenital anomalies were significantly higher only in mothers with pre-gestational diabetes [Table 1].

Interestingly, gestational age at delivery was lower in women with diabetes in pregnancy although median birth-weights were not significantly different from controls [Table 1]. Using multiple logistic regression model we found that prematurity (gestational age at birth below 37 weeks) was significantly associated not only with maternal diabetes, especially PGDM, but also with multiple gestation and preeclampsia in these mothers [Table 2]. The rate of large for gestational (LGA) infants was higher in all women with diabetes in pregnancy whereas SGA rate was higher only in mothers with PGDM [Table 1].

Cesarean delivery rate was significantly higher in mothers with diabetes both PGDM (68.1%) and GDM (47.6%) compared to only 25.9% in control women [Table 1]. Multiple logistic regression model showed that delivery by cesarean section was also significantly associated with multiple gestation, preeclampsia, and LGA babies [Table 2].

There were no significant differences in birth trauma rates between women with diabetes and controls [Table 1]. There were no cases of neonatal asphyxia in either study or control groups.

Although respiratory morbidity was higher among all infants born to mothers with diabetes in pregnancy [Table 1], using a multiple logistic model to assess whether the risk for respiratory morbidity was also associated with cesarean delivery and prematurity, we found that respiratory morbidity after delivery was significantly associated only with PGDM [Table 2]. Notably 80.0% of the infants with respiratory morbidity in the PGDM group had RDS compared to only 34.9% in the GDM group and 14.3% in the controls (the rest were diagnosed with TTN) ($P = 0.013$). The median gestational age of infants with respiratory morbidity in the PGDM group was also significantly younger (31.4 weeks) compared to either the GDM group (34.7 weeks) or the controls (39.3 weeks) ($P < 0.001$).

Hypoglycemia was more frequent in newborns of mothers with diabetes in pregnancy, especially those with PGDM [Table 1]. Of the infants born to mothers with PGDM, 30% presented with symptomatic hypoglycemia compared to only 2.9% in infants of mothers with GDM and none in the control group ($P = 0.037$). However, the rates of infants who needed intravenous treatment for hypoglycemia were not significantly different (58.3%, 50.0%, and 33.3% in the PGDM, GDM, and control groups, respectively, $P = 0.607$). Using a multiple logistic model, we found that hypoglycemia was also significantly associated with prematurity and LGA infants [Table 2].

Polycythemia was more frequent in all infants born to mothers with diabetes in pregnancy, especially in infants born to mothers with GDM [Table 1]. The rates of significant polycythemia (hematocrit > 70%) were 13.3% and 14.0% in infants born to mothers with PGDM and GDM significantly higher compared to 2.7% in the controls ($P < 0.001$). However, partial exchange transfusions were performed only in 11.1% of infants with symptomatic polycythemia, all were born to mothers with GDM. Based on multiple logistic analysis polycythemia was al-

Table 1. Maternal and neonatal characteristics in control versus mothers with diabetes (gestational or pre-gestational)

	Control (n=526)	Gestational diabetes (n=479)	Pre-gestational diabetes (n=47)	*P* value
Age of mother in years*	31.0 (27.0–34.0)	**33.0 (29.0–37.0)**	**33.0 (29.0–38.0)**	**< 0.001**
Ethnicity, Jewish**	387 (73.7%)	359 (75.1%)	33 (70.2%)	0.719
Preeclampsia** OR, 95%CI	8 (1.5%) 1	**22 (4.6%) 3.1, 1.4–7.1**	**5 (10.6%) 7.7, 2.4–24.6**	**< 0.001**
Multiple gestation** OR, 95%CI	13 (2.5%) 1	**42 (8.8%) 3.8, 2.0–7.2**	**6 (12.8%) 5.8, 2.1–16.0**	**< 0.001**
Intrauterine fetal death** OR, 95%CI	0 1	2 (0.4%) 1.2, 0.2–8.5	**2 (4.3%) 15.6, 3.4–70.9**	**< 0.001**
Congenital anomalies** OR, 95%CI	6 (3.2%) 1	21 (4.4%) 1.4, 0.7–2.6	**6 (12.8%) 4.4, 1.6–11.7**	**0.007**
Gender, male**	275 (52.4%)	283 (59.1%)	24 (51.1%)	0.085
Gestational age in weeks*	39.7 (38.8–40.4)	**39.1 (38.1–39.9)**	**38.4 (36.1–39.1)**	**< 0.001**
Preterm delivery< 37 wks** OR, 95%CI	26 (4.9%) 1	**54 (11.3%) 2.44, 1.5–4.0**	**15 (31.9%) 9.01, 4.4–18.7**	**0.001**
Cesarean delivery** OR, 95%CI	136 (25.9%) 1	**228 (47.6%) 2.6, 2.0–3.4**	**32 (68.1%) 6.1, 3.2–11.6**	**< 0.001**
Birth weight in grams*	3300 (3000–3610)	3300 (2900–3623)	3370 (2585–3696)	0.835
Small for gestational age** OR, 95%CI	22 (4.2%) 1	22 (4.6%) 1.1, 0.6–2.0	**5 (10.6%) 2.7, 1.0–7.6**	**< 0.001**
Large for gestational age** OR, 95%CI	34 (6.5%) 1	**50 (10.4%) 1.7, 1.1–2.7**	**12 (25.5%) 5.0, 2.4–10.4**	**< 0.001**
Birth trauma** OR, 95%CI	3 (0.6%) 1	4 (0.8%) 1.5, 0.3–6.6	1 (2.2%) 4.0, 0.4–38.9	0.459
Respiratory morbidity** OR, 95%CI	14 (2.7%) 1	23 (4.8%) 1.8, 0.9–3.6	**10 (22.2%) 10.4, 4.3–25.2**	**< 0.001**
Hypoglycemia (glucose < 40 mg/dl)** OR, 95%CI	9 (1.7%) 1	**34 (7.1%) 4.4, 2.1–9.3**	**13 (28.9%) 23.3, 9.3–58.7**	**< 0.001**
Polycythemia (hematocrit > 65%)** OR, 95%CI	33 (6.3%) 1	**180 (37.7%) 9.1, (6.1–13.5)**	**12 (26.7%) 5.4, (2.6–11.5)**	**< 0.001**
Neonatal jaundice (bilirubin > 7 mg/dl)**	286 (54.6%)	280 (59.1%)	29 (64.4%)	0.212
Hypertrophic cardiomyopathy** OR, 95%CI	0 1	**7 (1.5%) 8.5, 1.0–69.2**	1 (2.2%) 2.6, 0.6–12.4	**0.015**

Bold indicates significant differences compared to control group
Odds ratio and 95% confidence interval were calculated using univariate binary logistic regression analysis
*Kruskal–Wallis one-way ANOVA on ranks, data are presented as median (with interquartile range)
**Chi-square test, data are presented as n (%)
OR = odds ratio
95%CI = 95% confidence interval

Table 2. Binary multivariable logistic regression analysis for main outcomes

Outcome	Significant variables	Odds ratio	95% confidence interval	*P*
Cesarean delivery	GDM	2.2	1.7–2.9	< 0.001
	PGDM	4.7	2.4–9.2	< 0.001
	Multiple gestation	23.9	8.5–67.3	< 0.001
	Pre-eclampsia	3.4	1.5–7.9	0.004
	LGA	2.3	1.4–3.5	< 0.001
Preterm delivery < 37 weeks	GDM	1.8	1.1–3.0	0.032
	PGDM	7.0	3.1–15.5	< 0.001
	Multiple gestation	13.6	7.5–24.6	< 0.001
	Preeclampsia	3.1	1.3–7.5	0.014
Respiratory morbidity	GDM	0.9	0.4–2.0	0.83
	PGDM	3.4	1.3–9.2	0.017
	Preterm delivery < 37weeks	10.9	5.6–21.2	< 0.001
	Cesarean delivery	3.8	1.9–7.8	< 0.001
Hypoglycemia	GDM	3.6	1.7–7.6	0.001
	PGDM	11.7	4.3–32.0	< 0.001
	Preterm delivery < 37weeks	6.0	3.2–11.3	< 0.001
	LGA	2.6	1.2–5.6	0.012
Polycythemia	GDM	11.1	7.3–17.2	< 0.001
	PGDM	4.0	2.3–11.6	< 0.001
	SGA	6.3	4.9–20.8	< 0.001
	LGA	2.2	1.3–3.6	0.001
	Multiple gestation	0.14	0.05–0.36	< 0.001

GDM = gestational diabetes mellitus, PGDM = pre-gestational diabetes mellitus, LGA = large for gestational age, SGA = small for gestational age

so associated with SGA and LGA (compared to AGA infants), and multiple gestation [Table 2].

Hypertrophic cardiomyopathy is a relatively rare complication, it was diagnosed more frequently among newborns to mothers with diabetes in pregnancy, but this was statistically significant only in GDM [Table 1], more likely to be also LGA (odds ratio [OR] 4.6, 95% confidence interval [95%CI] 1.0–20.2, $P = 0.044$).

Three-quarters (74.8%) of the women with GDM were treated with diet changes and the rest received medical treatment, either oral hypoglycemic (8.5%) or insulin (16.7%) during pregnancy. There were no significant differences in any of the perinatal and neonatal outcomes studied.

DISCUSSION

Despite all of the advancements in prenatal care and treatment, diabetes in pregnancy, both gestational and pre-gestational, is still associated with significant morbidities and complications in the neonates, and these issues require careful observation of the newborn. Moreover, as demonstrated in Table 1, there was a trend for more frequent complications (notably cesarean delivery rate, LGA rate, hypoglycemia, and respiratory morbidity) with more severe disease (PGDM vs. GDM) probably due to worse diabetic control throughout pregnancy.

THE RATE OF DIABETES IN PREGNANCY AND MATERNAL CHARACTERISTICS

We collected data on 526 women with diabetes in pregnancy who delivered between 2015 and 2017 in a single medical center, representing 5% of all deliveries during these years. Although this rate is within the 2–8% reported in the literature [10], it is relatively low compared to the rate of approximately 7.5% reported in other developed countries [2,4,11]. Possible explanations include different criteria used to define gestational diabetes [3,11] and partial implementation of GDM screening and treatment in the community where most women were treated.

In accordance with the literature we found that women with diabetes in pregnancy were older [12,13] and had higher rates of preeclampsia [14,15].

The rate of multiple pregnancies (twins and triplets) was higher among diabetic mothers, in accordance with the increased risk for diabetes described in such pregnancies [16].

NEONATAL COMPLICATIONS

INTRAUTERINE FETAL DEMISE AND CONGENITAL ANOMALIES

The association between intrauterine fetal death or congenital anomalies and diabetes in pregnancy was significant only in mothers with PGDM, as described in previous studies [14]. The main cause is probably related to the diabetic embryopathy of early pregnancy (6–7 weeks of gestation), which results in spontaneous

abortions and congenital anomalies [6]. Late intrauterine fetal death is probably associated with the factors that increase the risk for perinatal asphyxia [17], including poor glycemic control, vasculopathy, and hypoxia in macrosomic fetuses. The higher rates of intrauterine death in mothers with PGDM is probably also associated with the high frequency of congenital anomalies in this group

PRETERM DELIVERY

Gestational age at delivery was lower among women with GDM and even younger in women with PGDM. Previous studies found that women with PGDM were at especially high risk for indicated premature delivery and spontaneous premature delivery compared to women without diabetes [18]. The reason for the increased rate of non-indicated premature deliveries is unknown but could be related to multiple gestation or increased risk of urinary tract infections in poorly controlled diabetics [19]. There are many causes for indicated premature deliveries including preeclampsia, fetal distress, macrosomia or suspected intrauterine growth restriction (IUGR), uncontrolled diabetes, or aggravation of diabetic morbidity (e.g., nephropathy). In our study 14% of preterm deliveries in mothers with diabetes in pregnancy were associated with preeclampsia, 9% with SGA infants (IUGR), and 12% with LGA infants (possibly due to poorly controlled diabetes).

MODE OF DELIVERY

The rate of cesarean deliveries was significantly higher in mothers with diabetes in pregnancy and higher compared to previous reports in the literature (48 vs. 28% for GDM and 68 vs. 51-57% for PGDM) [2]. We do not have the indication for cesarean deliveries; however, this increased rate is probably related to the higher complication rates of macrosomia, preeclampsia, and SGA in this population. In our study 8.5% of mothers with diabetes in pregnancy who delivered by cesarean section had preeclampsia, and 16% and 6.5% of infants born by cesarean delivery to mothers with diabetes in pregnancy were either LGA or SGA, respectively. Macrosomia could lead to difficulties in delivery because of wide shoulder girdle, as well as birth trauma, such as brachial plexus injuries, fractures of the clavicle or humerus, and even asphyxia. Macrosomia is the most common cause for medical indication for cesarean delivery in mothers with diabetes in pregnancy, when the risk of shoulder dystocia is high. In the current study 68% of LGA infants to mothers with diabetes in pregnancy were born by cesarean delivery. This high rate might also explain the non-significant increase in birth trauma in this population compared to controls.

LARGE FOR GESTATIONAL AGE AND SMALL FOR GESTATIONAL AGE

SGA rates were significantly higher in women with PGDM. This association is well known in the literature with quite similar reported odds (OR 3.3, 95%CI 1.6–7) [20]. This finding could be related to diabetic nephropathy and vasculopathy, which also affect the placenta. According to the Pedersen hypothesis on diabetic fetopathy, macrosomia is related to poor glycemic control, high glucose levels in the mothers and hence in their fetuses that leads to increased insulin secretion, and high insulin levels in the fetus that result in accelerated growth that lead to high frequency of macrosomic infants, as seen in our results. The increased odds for macrosomia (LGA) in both GDM and PGDM in our study are similar to those cited in the literature (1.6 and 4.0-6.6, respectively) [2].

RESPIRATORY DISTRESS

Although the rates of respiratory distress were higher in all infants born to mothers with diabetes in pregnancy, when this finding was analyzed in a multivariate model along with mode of delivery, it was found that respiratory morbidity was significantly associated to cesarean deliveries, most probably in the mechanism of delayed absorption of fetal lung fluids that leads to the clinical presentation of transient tachypnea of the newborn (TTN) or retained fetal lung fluids. Although this mechanism was also described in association with gestational diabetes, in our multivariate analysis, the association of respiratory morbidity in the newborn to diabetes in the mother was significant only in infants born to mothers with PGDM who were born more premature and were diagnosed with respiratory distress syndrome (RDS) due to lung immaturity secondary to surfactant deficiency. It is known that hyperinsulinemia in the fetus during pregnancy disturbs the process of lung maturation by inhibiting surfactant secretion under the influence of corticosteroids [21].

HYPOGLYCEMIA

We used the definition of threshold glucose of less than 40 mg/dl to define hypoglycemia. The association between hypoglycemia and maternal diabetes in pregnancy was significant, especially among mothers with PGDM. Early hypoglycemia in the first hours of life in infants born to mothers with diabetes in pregnancy is common, and was described in 5% to 27% of these newborns [6,22], similar to our findings, especially in mothers with PGDM. There are several possible explanations for the increased hypoglycemia rates in women with diabetes in pregnancy including relative hyperinsulinemia secondary to intrauterine hyperglycemia, especially among LGA neonates. Hypoglycemia is also more common in SGA infants due to PGDM vasculopathy and possible placental insufficiency or preeclampsia. Also preterm infants are at an increased risk of hypoglycemia because of relatively scarce glycogen storages.

POLYCYTHEMIA

The frequency of polycythemia was higher among infants born to mothers with diabetes in pregnancy, especially in those born to mothers with GDM, and macrosomic (LGA) infants. These results are in agreement with other studies that demonstrated increased metabolism secondary to hyperglycemia and hyperin-

sulinemia in fetuses of diabetic mothers, which leads to relative hypoxia resulting in increased secretion of erythropoietin and polycythemia [23]. Polycythemia as a result of placental transfusion to the fetus in cases of hypoxia secondary to maternal or fetal distress could explain the association we found between polycythemia and SGA infants, which was probably secondary to IUGR. The rate of polycythemia in our study is higher than the 5% described in the literature [6,22] perhaps due to delayed cord clamping, which is a much more common practice or to the policy of encouraging exclusive breastfeeding, which might be associated with mild dehydration and a rise in hematocrit levels.

HYPERTROPHIC CARDIOMYOPATHY

Hypertrophic cardiomyopathy was more frequent among infants born to mothers with GDM who were macrosomic (LGA). The cardiomyopathy develops under the influence of hyperinsulinemia, which causes increased deposition of glycogen and fat in the cells of the myocardium. Although the rate of cardiomyopathy in infants born to mothers with PGDM was higher, it did not reach statistical significance (probably due to the small number of PGDM mothers in our study) as opposed to findings in other studies [24].

TREATMENT OF GESTATIONAL DIABETES

The most common treatment of gestational diabetes is diet and adopting healthy life practices. The recommended first line of medical therapy for diabetes in pregnancy when diet is insufficient is insulin. In recent years there is an increasing trend to use oral hypoglycemic drugs also in pregnancy. In this study, which was based on hospital medical records, we lacked data on the reasons for the treatment choice as well as on the level of diabetic control during pregnancy because most of pregnancy follow-ups were conducted in community clinics. We found no significant differences in pregnancy outcomes between newborns of mothers treated with diet compared to neonates of women with GDM who received medical treatment (either insulin or oral hypoglycemic) during pregnancy. This study outcome is different from Billionnet and colleagues [2] who found significantly worse outcomes in the insulin treated GDM group.

LIMITATIONS

This study has some limitations that might preclude generalization of findings to the population in general. The main limitations of our study are the retrospective nature of the study and the relatively small number of mothers (especially with PGDM) and their infants who were treated at a single medical center in Haifa, Israel. Another limitation was lack of data on the way the diagnosis of diabetes in pregnancy was made and the criteria used for diagnosis. We also lacked data on the level of glycemic control before and during pregnancy and the type or indications for the treatment chosen (diet, insulin, or oral hypoglycemic). We did not find cases of perinatal asphyxia in either the study or control groups, and we lacked data related to cesarean delivery indication or cause for preterm delivery.

Despite all these limitations, we believe that this study provides an updated perspective on the prevalence of diabetes in pregnancy and highlights the complications and associated neonatal morbidities. Better preconception and inter-pregnancy care and tighter diabetic control before and during the pregnancy might reduce the risk of congenital anomalies as well as the rates of LGA neonates, caesarean deliveries, and preeclampsia as published in a recent study [25].

CONCLUSIONS

Both gestational and pre-gestational maternal diabetes are associated with consequences in the offspring. We addressed outcomes of newborns of mothers with diabetes in pregnancy in Israel in recent years. Mothers with pre-gestational diabetes had higher rates of intrauterine fetal demise, congenital anomalies and small-for-gestational-age neonates. The risks for preterm or cesarean delivery, large-for-gestational-age neonates, respiratory morbidity, hypoglycemia, and polycythemia were increased in offspring of mothers with diabetes in pregnancy. Despite all advancements in prenatal care, diabetes in pregnancy is still associated with significant morbidities and complications in offspring.

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Capsule

The commensal skin microbiota triggers type I IFN-dependent innate repair responses in injured skin

Skin wounds heal by coordinated induction of inflammation and tissue repair, but the initiating events are poorly defined. **Di Domizio** and colleagues uncovered a fundamental role of commensal skin microbiota in this process and showed that it is mediated by the recruitment and the activation of type I interferon (IFN)-producing plasmacytoid DC (pDC). Commensal bacteria colonizing skin wounds trigger activation of neutrophils to express the chemokine CXCL10, which recruits pDC and acts as an antimicrobial protein to kill exposed microbiota, leading to the formation of CXCL10–bacterial DNA complexes. These complexes and not complexes with host-derived DNA activate pDC to produce type I IFNs, which accelerate wound closure by triggering skin inflammation and early T cell-independent wound repair responses, mediated by macrophages and fibroblasts that produce major growth factors required for healing. These findings identify a key function of commensal microbiota in driving a central innate wound healing response of the skin.

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Capsule

Seeking broad protection from SARS-CoV-2

As scientists develop therapeutic antibodies and vaccines against severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the risk of emergent coronaviruses makes it important to also identify broadly protective antibodies. **Wec** et al. isolated and characterized hundreds of antibodies against the viral spike protein of SARS-CoV-2 from the memory B cells of a survivor of the 2003 outbreak caused by the related coronavirus, SARS-CoV. In both of these viruses, the spike protein facilitated viral entry by binding to the angiotensin-converting enzyme 2 (ACE2) receptor on human cells. The antibodies targeted multiple sites on the spike protein, but of nine antibodies that showed strong cross-neutralization, eight targeted the domain that binds to ACE2. These eight antibodies also neutralized a bat SARS-related virus. Illuminating the epitopes on the viral spike protein that bind cross-neutralizing antibodies could guide the design of broadly protective vaccines.

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