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ORIGINAL ARTICLE

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Risk for gestational diabetes and hypertension for women with twin pregnancy compared to singleton pregnancy

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Abstract *Objectives:* This study was undertaken to determine the incidence of pregnancy induced hypertension (PIH) and gestational diabetes (GDM) in twin pregnancies (TP) in comparison with singleton pregnancies (SP), and to test whether TP with GDM have a higher risk than TP without GDM, as is known to be the case in SP. *Materials and methods:* Eighty-nine patients with TP who sought prenatal care between 1 September 1994 and 30 October 1997, were asked to participate. One hundred and seventy-eight of the 1,416 patients were matched in a 1:2 ratio by age, body-mass-index, parity, gestational age at screening, and ethnicity with a singleton pregnancy from our database dating from the same period. The diagnosis "hypertension" or "preeclampsia" was made using clinical criteria including a repeated blood pressure above 140/90 mm Hg. Maternal and fetal outcome were compared between SP and TP, between TP with and without pathological screening, between TP with and without GDM. *Results:* Patients with TP did not have a higher rate of GDM but of PIH (GDM 3.4% vs. 3.4%, p=0.63; PIH 2.8% vs. 9.0%, p=0.036). Expectant mothers of twins whose glucose screening test was pathological have a higher incidence of hypertension than those whose screening test was normal (17.9% vs. 4.9%, p=0.048). Twins of gestational diabetics have a higher rate of admission to the neonatal intensive care unit than twins of healthy pregnant patients (100% vs. 31%, p=0.028). *Conclusions:* TP are associated with a higher risk of hypertension than SP but not for GDM. Patients expecting twins who show a carbohydrate intolerance are at a higher risk for hypertension and fetal diabetes-associated complications.

Keywords Gestational diabetes · Twin pregnancy · Pregnancy induced hypertension · Screening · Hypertension

A part of this study was presented at the 62nd Congress of the American Diabetes Association

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Introduction

The obstetrician is increasingly confronted with multiple gestations as the demands in reproductive medicine rise [2, 12]. The complication rate correlates to the number of fetuses. The perinatal morbidity of twins is two to three times higher than in singleton pregnancies (SP) [5, 18]. The higher risks may be associated with the tension of the uterus (e.g., hypertension) and factors, such as age, which necessitated the particular reproductive procedure.

With an incidence of 5%, gestational diabetes (GDM) is one of the most common diseases during pregnancy [8]. The maternal risk factors that promote the development of GDM, such as age, body-mass-index, and weight gain, have been well documented. Unlike other pregnancy associated illnesses, once diagnosed GDM is easy to treat thus effectively lowering the risks.

GDM and TP have several evident risk factors in common, such as maternal age, weight gain, and body-mass-index. Regarding the cause of GDM, several authors hold the hormones (e.g., gestagens, estrogens, human placental lactogen) responsible which rise beginning in the 20th gestational week. Twin pregnancies (TP) generally have higher concentrations of these hormones [15]. A higher incidence of carbohydrate intolerance in TP is therefore probable.

Several studies have investigated this question, but the results varied greatly due to statistical disparities. Most studies involved fewer than 50 patients and others did not

Table 1 Comparison of anamnestic data between single and twin pregnancies

Parameter	Single pregnancies (n=178)	Twin pregnancies (n=89)	p
Age (years)	29.8±4.66	29.8±4.73	0.97
Body-mass-index (kg/m^2)	24.5±4.79	24.9±4.76	0.40
Weight gain (kg)	13.6±5.31	14.5±4.98	0.20
Parity (mean ± SD)	0.66	1.39	<0.01
Smoking	10.1%	21.3%	0.02
Ethnic origin			0.30
Western European	76.4% (136)	68.5% (61)	
Turkish, Greek, Albanian	22.5% (40)	31.5% (28)	
Asian	1.1% (2)	0.0% (0)	
Delivery (weeks + days)	39+6	36+2	<0.01
Gestational age at GCT (weeks + days)	34+0	30+3	<0.01
1-h GCT	129±24	130±26	0.97
3-h OGTT (75 g)			
Fasting	85±10	86±12	0.77
1-h	159±26	169±36	0.12
2-h	119±28	128±26	0.15
Gestational diabetes (O'Sullivan criteria)	7.9% (14/178)	6.7% (6/89)	0.81
Gestational diabetes (Carpenter/Coustan criteria)	3.4% (6/178)	3.4% (3/89)	0.99
Hypertension	2.8% (5/178)	9.0% (8/89)	0.036

match the SP and TP by the aforementioned criteria [1, 4, 6, 9, 10, 11, 13, 14, 16, 17].

This study was undertaken to determine the incidence of pregnancy induced hypertension (PIH) and GDM in TP in comparison with SP. A further interest was whether TP with GDM have a higher risk of pregnancy-associated illnesses than TP without GDM, as observed in SP.

Materials and methods

Study center

The 50 g glucose challenge test is currently recommended by the German Diabetes Association, but is not covered by German health insurance providers. Since 1993, every patient seeking prenatal care at our clinic has been given the 50 g glucose challenge test. Our clinic performs 3,800 deliveries per year.

Screening and diagnosis

According to the screening test criteria of the ADA, the patient was given 50 g glucose to consume within 5 min. Exactly 1 h later, a blood sample was drawn (capillary whole blood). If the blood glucose concentration was $\geq$140 mg/dl, the patient underwent the oral glucose tolerance test (OGTT) after having consumed a carbohydrate rich diet for several days.

The OGTT was performed with 75 g glucose, and the blood glucose concentration was measured in the fasting state and exactly after 1 and 2 h. Like many centers in Germany we used the cut-off criteria of O'Sullivan (90/165/145 mg/dl). For a better comparison to international data we based our calculations on the criteria of Carpenter/Coustan (90/180/155 mg/dl). Patients who had two or three measurements exceeding the cut-off points were classified as "gestational diabetics" (GDM). Their treatment consisted of diet (25–35 kcal/kg), self-monitoring glucose profile, and insulin if necessary. Patients with one abnormal value were classified as "impaired glucose tolerant" (IGT). They received nutritional counseling and the OGTT was repeated after 10 days.

Patients and control group

All patients seeking prenatal care between 1 September1994 and 30 October 1997 were asked to participate in our test and the study.

Eighty-nine patients pregnant with twins participated. We matched them with a 1:2 ratio to 178/1,416 of our patients with a single pregnancy who participated during the same period. The criteria used to match patients included: age, body-mass-index, parity, gestational age at screening, and ethnicity.

The diagnosis "hypertension" was made using clinical criteria. A repeated blood pressure exceeding 140/90 mm Hg was used as the cutoff value for the diagnosis of hypertension.

Outcome

In addition to the aforementioned criteria, the rate of admission to the neonatal intensive care unit (NICU) was evaluated. Typical diabetes associated fetal complications (hyperbilirubinemia, hypoglycemia, and pulmonary maladaption) were based on clinical criteria and summarized as "diabetes associated morbidity." Pulmonary maladaption was summarized from the diagnosis "respiratory distress syndrome" and "tachypnea."

Statistics

For normally distributed data, the student-t-test was used, otherwise the Mann-Whitney-U-test. For categorical data, the chi-square test was used. A significant difference was defined as a p-value <0.05.

Results

Incidence of gestational diabetes in twin pregnancies

The comparison of the clinical data between the TP and SP is shown in Table 1.

Significant differences were found in parity, gestational age at delivery, and gestational age at screening. No differences were found concerning the age, BMI, weight gain, and ethnic origin. TP showed a tendency of higher

Table 2 Comparison of anamnestic data of twin pregnancies distributed by GCT (± SD)

Parameter	Twin pregnancies, normal screening (n=61)	Twin pregnancies, pathological screening (n=28)	p
Age (years)	29.7±4.92	30.0±4.35	0.71
Body-mass-index (kg/m^2)	24.7±4.62	25.5±5.11	0.64
Weight gain (kg)	14.1±4.63	15.3±5.68	0.47
Parity (mean)	1.5±1.23	1.3±0.97	0.43
Gestational age at GCT (weeks + days)	30+6	29+2	<0.01
50 g-screening (mg/dl)	115±15.5	161±14.8	<0.01
Delivery (weeks + days)	36+2	36+4	0.77
Smoking	9.8% (6)	10.7% (3)	0.58
Hypertension	4.9% (3)	17.9% (5)	0.048

Table 3 Comparison of anamnestic data and outcome of twin pregnancies with and without gestational diabetes (GDM, Carpenter/Coustan criteria). *NICU* neonatal intensive care unit

Parameter	Twin pregnancies without GDM (n=86)	Twin pregnancies with GDM (n=3)	p
Age (years)	29.7±4.70	32.0±6.24	0.63
Body-mass-index (kg/m^2)	25.0±4.80	21.8±1.75	0.27
Weight gain (kg)	14.6±4.99	11.0±3.61	0.20
Gestational age at GCT (weeks)	30+4	28+1	0.08
Gestational age at delivery (weeks)	36+3	34+1	0.11
50 g-screening (mg/dl)	128±25.7	168±5.3	<0.01
Hypertension	9.3% (8)	0% (0)	0.75
Admission to NICU	31% (54/172)	100% (6/6)	0.028
Diabetes associated morbidity	30.7% (51/166)	75.0% (9/12)	0.50

measurements in the OGTT after 1 and 2 h, but the difference was not statistically significant.

The diagnosis GDM was found in 6.7% (6/89) of TP vs. 7.9% (14/178) of SP (p=0.81) based on the O'Sullivan criteria. Using the criteria of Carpenter/Coustan, the rate falls to 3.4% (3/89) of TP and 3.4% (6/178) of SP (p=0.99).

Incidence of hypertension in twin pregnancies

Thirteen of 267 patients developed hypertension. In 9.0% (8/89) of the cases, the rate of hypertension was higher in TP than in SP (2.8% 5/178, p=0.036). There was no association between smoking habits and hypertension.

There was no significant difference between SP with and without GDM in developing hypertension (2.3 vs. 16.7%, p=0.16). In contrast, 17.9% of TP with a pathological screening test had hypertension while only 4.9% of TP with a normal screening test had hypertension (p=0.048). The anamnestic data of TP distributed by the GCT are shown in Table 2. The logistic regression analysis showed no influence of parity and gestational age at GCT on the development of hypertension.

Outcome of patients with TP with and without GDM

Three of 89 patients with TP developed gestational diabetes. In a comparison of outcome of TP with and without GDM, the newborns of TP with GDM had a higher rate of admission to the NICU (100% vs. 31%) and a higher diabetes associated morbidity which was not statistically significant (Table 3).

Discussion

Incidence of gestational diabetes in twin pregnancies

The increased complications in perinatal outcome caused by gestational diabetes are well documented [8]. Twin pregnancies have a higher general perinatal risk, e.g., placental insufficiency, which may be exacerbated by GDM. Knowledge regarding the rate of GDM and other risk factors in TP is, therefore, of interest. Most of the available studies, as well as our matched-pair study, did not show a higher incidence of GDM in twin pregnancy. Like the results of Schwartz, we found no significant differences in OGTT results in fasting, 1-, and 2-h measurements, but rather a tendency to higher results in TP. Schwartz found a significant difference in the 3-h measurement, which we did not perform [14].

Incidence of hypertension in twin pregnancies

The higher incidence of hypertension has been well described [3]. We found a significant difference in the rate of hypertension between SP and TP (2.8% vs. 9.0%, p=0.036) which is in accord with the findings of Coonrod et al., who reported a 3.5 fold risk in TP.

An association between hyperglycemia and hypertension was been described by Innes et al., who found the

strongest association of the 2-h post-load glucose level with an OR of 1.48 per 10 mg/dl increase [7]. In our population, we found a higher incidence of hypertension in TP with a pathological GCT in comparison to TP with a normal GCT (17.9 vs. 4.8%, p=0.048). We could not repeat those findings in comparison of the TP with and without GDM, possibly due to the small number. But this finding supports the theory that insulin resistance precedes the clinical onset of hypertension in pregnancy.

Outcome of patients with TP with and without GDM

No studies are available on the causes of GDM complications in twin pregnancies. In this study, we found a higher perinatal risk for twins whose mother is affected by this common gestational disease even in a small population.

This study's findings suggest that women with twin pregnancies have a higher incidence of hypertension but no significant changes in glucose tolerance than women with singleton pregnancies. Impaired glucose tolerance in women with TP is a risk factor for hypertension. Therefore, strict management of these high-risk patients is necessary.

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