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Diabetic pregnancy in over 35 years old women

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Summary. - 87 pregnancies in diabetic women older than 35 years at time of conception were studied. 3% were insulin-dependent diabetes mellitus (IDDM), 52% non insulin-dependent diabetes mellitus (NIDDM) and 45% gestational diabetes mellitus (GDM). Mean age was 38 ± 3 years; BMI was 33.2 ± 7.0 kg/m^2; gestation rate was 5 ± 3 and number of alive children was 2 ± 2. Only 3% of pregnancies were planned. Mean time of reference to diabetic care unit was 17 ± 10 weeks. 95% of the women required human insulin. Mean total daily insulin dose was 0.49 ± 0.28 UI/kg/d, increasing with gestational age. Mean fasting glycemia was 6.85 ± 1.93 mmol/l and mean post-prandial glycemia was 8.29 ± 2.52 mmol/l. Mean time of delivery was 38 ± 2.1 weeks (less than 37 weeks in 9%). Cesarian section was performed in 44% of 34 cases. Death *in utero* occurred in 11% of 54 cases, postnatal death in 4%, congenital malformations in 4%, macrosomia in 40%. 9% of infants received intensive neonatal care. No difference was found between NIDDM and GDM about outcome of pregnancy. These results underlined importance of early screening for GDM as most cases seem to be undiagnosed pregravid diabetes mellitus (DM).

Key words: diabetic pregnancy, gestational diabetes, gestation in old women.

Riassunto *(Diabete in gravidanza in donne con età superiore a 35 anni)*. - Sono state studiate 87 gravide diabetiche con età superiore ai 35 anni al momento del concepimento. Il 3% era IDDM, il 52% NIDDM ed il 45% GDM. L'età media era di 38 ± 3 anni; il BMI era pari a 33,2 ± 7 kg/m^2 ; il numero di gravidanze era pari a 5 ± 3 con un numero di figli viventi pari a 2 ± 2. Solo il 3% delle gravidanze era pianificato. L'epoca media di assistenza presso il servizio di diabetologia era pari a 17 ± 10 settimane. Il 95% delle donne richiedeva una terapia insulinica, la cui dose giornaliera era pari a 0,49 ± 0,28 UI/kg, con aumento durante la gravidanza. I valori medi della glicemia a digiuno erano pari a 6,85 ± 1,93 mmol/l, mentre quella postprandiale era di 8,29 ± 2,5 mmol/l. L'epoca media del parto era di 38 ± 2,1 settimane (inferiore a 37 nel 9%). Il taglio cesareo veniva praticato nel 44%. La mortalità intrauterina si aveva nell'11% (di 54 casi), mentre il 9% dei neonati riceveva una terapia intensiva. Tra NIDDM e GDM non si osservavano differenze. Questi risultati sottolineano l'importanza di uno screening precoce per il GDM poiché la maggior parte dei casi sembra avere un diabete non diagnosticato prima del concepimento.

Parole chiave: diabete e gravidanza, diabete gestazionale, gravidanza in donne anziane.

Introduction

Gestational diabetes mellitus (GDM) and non insulin-dependent diabetes mellitus (NIDDM) share same risk factors (familial history of diabetes, obesity, age, etc.) and same metabolic abnormalities (insulino-resistance and hyperinsulinism).

The occurrence of pregnancy in diabetic women older than 35 years is still frequent in Tunisia. It worses maternal and fetal prognosis.

The aim of this study is to describe the outcome of pregnancies in diabetic women older than 35 years and to identify parameters which may influence maternal and neonatal prognosis.

Materials and methods

This retrospective study included 87 cases of pregnancies in diabetic women older than 35 years between 1989 and 1995.

Only 3% (no. 2) of these women were IDDM, 52% (no. 45) were NIDDM and in 45% of them (no. 40) diabetes was first diagnosed during this pregnancy (GDM).

Mean age of NIDDM women was 37.8 ± 3.8 years and for GDM women 37.2 ± 2.4. 72% of all women were between 35 and 40 years old.

(*) in memoriam

Body weight before pregnancy was mostly unknown as women were met late after conception time. Accordingly, body mass index was estimated with reference to the first known weight value during pregnancy. The subjects were over-weighted as mean BMI was 33.5 ± 7.7 kg/m^2 in NIDDM women and 33.5 ± 3.5 in GDM women.

Most of women did not show any microvascular diabetic complications: none suffered from clinical nephropathy and 5% presented background retinopathy (no case of proliferative retinopathy).

10% of these women were known to be hypertensive before pregnancy (16% NIDDM and 3% GDM; $p < 0.05$).

Mean gestation rate was 4.8 ± 2.3 in NIDDM women and 4.5 ± 2.5 in GDM women. Mean number of alive children was 2.2 ± 2.0 in NIDDM women and 2.0 ± 1.6 in GDM women.

A familial history of diabetes was found in 84% of NIDDM women and 54% of GDM women ($p < 0.01$).

Features of obstetrical history are summarized in Table 1. 21% of NIDDM women and 23% of GDM women showed history of previous GDM. 33% of all women were diagnosed as GDM for the first time during this pregnancy. High prevalence of history of macrosomia in the group of GDM women let suppose that most of them had undiagnosed GDM during previous pregnancies. Moreover, high prevalence of previous abortions evocates an undiagnosed permanent diabetes.

Results

Time of reference to diabetic care unit was late: 15 ± 10 weeks for NIDDM women, 21 ± 9 weeks for GDM women. 2 cases (3%) had preconceptional care.

Diabetes regimen: women were treated by diet alone for 2% of NIDDM and 8% of GDM; and by intensified insulinotherapy for 90% of NIDDM and 59% of GDM. Mean time for insulination was 17 ± 10 weeks for NIDDM and 23 ± 13 weeks for GDM.

Table 1. - Obstetrical history of pregnant women

	NIDDM (%)	GDM (%)
Previous GDM (*)	24	15
Cesarian section	33	21
Macrosomia	23	41
Malformation	2	3
Stillbirth	18	13
Abortion	47	51
Postnatal death	23	15

(*) Previous GDM is correlated with history of abortion ($p < 0.05$) and with history of perinatal mortality ($p < 0.05$).
NIDDM: non insulin-dependent diabetes mellitus.
GDM: gestational diabetes mellitus.

Mean insulin dose was 0.53 ± 0.26 UI/kg/d for NIDDM and 0.42 ± 0.28 UI/kg/d for GDM. Insulin dose increased with gestational age from 0.46 ± 0.30 UI/kg/d (at 20 - 25 weeks) to 0.58 ± 0.41 UI/kg/d (after 35 weeks).

Mean fasting glycemia was 7.50 ± 1.70 mmol/l in NIDDM and 5.90 ± 1.60 mmol/l in GDM ($p < 0.01$). Mean post-prandial glycemia was 9.12 ± 2.70 mmol/l in NIDDM and 7.40 ± 2.24 mmol/l in GDM ($p < 0.01$).

Events in obstetrical follow up and outcome are presented in Table 2. No significant differences were found between NIDDM and GDM. Mean time for delivery was 38 ± 2.3 weeks for NIDDM women and 38.6 ± 1.5 weeks for GDM women. Prematurity (delivery before 37 weeks of gestation) concerned 9% of newborn from NIDDM mothers and 14% from GDM mothers.

No case of prematurity was observed in women whose mean fasting glycemia was under 5.5 mmol/l, whereas it concerned 33% of women whose mean fasting glycemia exceeded 6.6 mmol/l ($p < 0.05$).

Newborn weight was 3.812 ± 0.915 kg in NIDDM women offsprings and 3.621 ± 0.505 kg in GDM women offsprings. Mean natal weight was 3.450 ± 0.468 kg when maternal mean post-prandial glycemia was under 6.6 mmol/l, but it reached 3.935 ± 0.371 kg when post-prandial glycemia exceeded 7.7 mmol/l ($p < 0.05$).

Rate of macrosomia was 48% in NIDDM and 30% in GDM; mean time of insulination was 23.7 weeks when macrosomia subsequently occurred and 14.1 weeks in absence of macrosomia ($p < 0.05$).

The frequency of congenital malformations was 3% in NIDDM women offsprings and 5% in GDM women offsprings; a higher fasting glycemia (mean 10.9 mmol/l) was associated to occurrence of congenital malformations (*vs* 6.7 mmol/l in absence of malformation; $p < 0.05$).

Death *in utero* occurred in 18% of NIDDM pregnancies and 13% of GDM pregnancies. Risk factors for death *in utero* were previous history of death *in utero* (40% *vs* 10%, $p < 0.05$) and previous history of abortion (83% *vs* 41%, $p < 0.05$).

9% of infants received intensive neonatal care.

Discussion

Prevalence

A prior study showed that pregnancy in Tunisian women older than 40 years was 0.8% of 27 626 pregnancies [1] within 1.4% of diabetic pregnancies. An other tunisian study on pregnancy in diabetic women found 26% of diabetic pregnant women older than 35 years [2]. GDM was evidenced in most of our patients after the 20th week of gestation. But in 20% of them, diabetes was diagnosed earlier and might be a pre-gravid misdiagnosed diabetes.

Table 2. - Obstetrical outcome

	NIDDM (%)	GDM (%)
Gravid hypertension	15	26
Prematurity	9	33
Malformation	3	5
Stillbirth	10	9
Early postnatal death	0	9
Cesarian section	40	58
Macrosomia	48	30
Hypoglycemia	0	0
Respiratory distress	6	13

NIDDM: non insulin-dependent diabetes mellitus.
GDM: gestational diabetes mellitus.

Engelgau *et al.* [3] reported a 4% US prevalence of diabetes in pregnancy (GDM 88%, NIDDM 4%). Bobrowski and Bottoms [4] estimated risk of elderly multipara 4.5 time greater for GDM and 3.2 for NIDDM.

Diabetic management in pregnancy

Large doses of insulin are required in diabetic pregnancies. Langer *et al.* [5] used initial dose of intensified insulin regimen of about 0.67 UI/kg/d and increased it to 1.19 UI/kg/d at the end of pregnancy. Jovanovic [6] reported a mean dose for lean women from 0.7UI/kg/d to 1.0 UI/kg/d and for obese women about 1.0 UI/kg/d to 3.0 UI/kg/d.

In our study, mean doses of insulin were lower.

30% to 80% of diabetic pregnant women need insulinotherapy according to various criteria; some of the women received insulin since the beginning of care while others needed insulin later. In our study, 98% of NIDDM women and 92% of GDM women receive insulin treatment. In the DIAGEST study [7], insulinotherapy was decided when fasting glycemia exceeded 0.95g/l or post-prandial glycemia exceeded 1.2 g/l and 43% of GDM women received insulin according to these criteria.

Macrosomia

Langer *et al.* [5] found that intensified insulin regimen reduced rate of macrosomia in GDM from 29% to 10%; but monitoring of fasting and pre-meal glycemia did not prevent macrosomia. Cundy and McBride [8] did not found any difference in the incidence of macrosomia between GDM and NIDDM. In our study, macrosomia was correlated to time of insulination: absence of macrosomia was associated to early insulination (mean 14.1 weeks) and its presence to a late insulination (mean 23.7 weeks) ($p < 0.05$). For GDM women, insulination was later (mean: 23 ± 13 weeks) as diagnosis was made after 20 weeks of gestation.

Risk factors for macrosomia are numerous: age, obesity, weight gain during pregnancy, multiple pregnancies, low economic income, glycemic levels. Most of our patients were concerned by a number of these factors. Ferchiou *et al.* [9] found 41% of macrosomia upon diabetic Tunisian pregnancies with correlation to maternal obesity.

Cesarian section

Tunisian study [10] in pregnancies over 40 years found rates of prematurity 24%, cesarian section 22% and early postnatal mortality 4%. Our results are quite similar except a greater rate of cesarian section (48%). Horger and Smythe [11] estimated risk for cesarian section 3.5 time greater in pregnancy over 40 years.

Stillbirth

Raymond *et al.* [12] estimated that risk of stillbirth is increased after 35 years even after exclusion of hypertension and diabetes. O'Sullivan *et al.* [13] found an increase in perinatal mortality in a group of GDM pregnancies (6.5%) compared to a control group (1.5%). A more recent study by Jovanovic [6] did not find any more difference between these groups when glycemic control was achieved.

Congenital malformations

Congenital malformations affected 2.7% of Tunisian pregnancies over 40 [1]. In our study, this rate was 4% and no difference was observed between NIDDM and GDM. This finding is in contradiction with Pettitt *et al.* [14] who reported no prevalence of congenital malformations in GDM pregnancies in Pima Indians.

Conclusions

We found no differences between GDM and NIDDM women in this study: most of these GDM are probably previous unknown diabetes revealed because of screening during gestation.

Diabetic pregnancy needs a careful specialized monitoring to prevent serious maternal and fetal complications. This requirement is much more needed for diabetic women after 35 years as age may add its specific adverse effects on pregnancy outcome.

In 1993 only 58% of Tunisian diabetic women were using contraceptive methods (*vs* 87% for control women) [15].

Our results stress the need of counselling for contraception and preconceptional optimal glycemic control.

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