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Der Pharmacia Lettre, 2016, 8 (20):63-67
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Clinical outcomes of pregnancy in women with type 1 diabetes

Hamri Ahlem^{1*}, Bouzidi Zoubir², Boukhris Nadia^{1,3} and Tahraoui Abdelkrim¹

¹Laboratory of Neuro- endocrinology Applied Biology Department; Badji Mokhtar University
Annaba, 23000, Algeria

²Specialized Hospital El Bouni Annaba, 23000, Algeria

³Service de médecine interne CHU IBNSINA Annaba

ABSTRACT

The prevalence of all types of diabetes mellitus is increasing worldwide. Diabetes is a common metabolic complication of pregnancy. For many years, pregnancy complicated by type 1 diabetes was associated with a particularly poor prognosis, and while this has changed dramatically over the last 2 decades, a lot has yet to be done. The number of pregnant women with pre-existing diabetes is increasing, mainly from an increase in type 2 diabetes, but also an increase in type 1 diabetes. Overall, type 1 diabetes accounts for approximately 5% to 10% of all diabetes outside of pregnancy, and in pregnancy put together with type 2 account for 10% of diabetic pregnancies. Management of the pregnant diabetic woman is a complex task that ideally begins before conception. Specific attention is required for diabetic pregnancies in different trimesters of pregnancy. Diabetes, especially type 1 diabetes, can be a challenge in pregnancy, but with education, close monitoring, and latest therapeutic modalities, these women can have healthy newborns. Close attention to diet, glycemic control, metabolic stresses, and early diagnosis and monitoring of complications can make pregnancy a successful experience for women with diabetes.

Key words: women, pregnancy, Type 1 diabetes mellitus.

INTRODUCTION

Pregnancy complicated by diabetes constitutes a challenge for diabetologists, obstetricians, And pediatricians worldwide[1] .It is an important medical, social, and financial problem.

The number of pregnant women diagnosed with diabetes either before or during pregnancy is increasing for several reasons. First, the global epidemics of obesity affects also females in reproductive age. Moreover, women tend to postpone their decision to become a mother, mainly due to social and economic factors. This increases the prevalence of gestational diabetes mellitus and pregestational type 2 diabetes. Additionally, the number of women with pregnancy complicated by type 1 diabetes, an autoimmune disease characterized by total β -cell destruction and requiring intensive insulin therapy, is also on the rise.

Not a long time ago, type 1 diabetic women were discouraged from making maternity plans

Because of the high prevalence of chronic diabetic complications and fear of their progress, difficulties in reaching satisfactory glycemic control, and high number of pregnancy outcomes [2, 3]. Diabetes during pregnancy is still generally classified using the original system proposed by Priscilla White almost 60 years ago. [4] White's classification relates the onset of diabetes, its duration, and the degree of vasculopathy to the outcome of pregnancy. Because there were differences and some confusion in the interpretation of class A diabetes, particularly when the patient required insulin for therapy, a revision made by Hare and White proposed that class A diabetes should

include women known to have diabetes before pregnancy and who are treated with diet alone.[5] Thus, White's class 'A' classification includes only patients with pre-gestational diabetes and defines gestational diabetes as a completely separate group.

Practically speaking, women with pregnancies complicated by diabetes mellitus may be separated into one of two groups:

1. Gestational diabetes: women with carbohydrate intolerance of variable severity, with onset or first recognition during the present pregnancy.
2. Pre-gestational diabetes: women known to have diabetes before pregnancy.

The objective of this study was to examine the relationship between prepregnancy care, glycemic control, maternal hypoglycemia, and pregnancy outcomes in women with type 1 diabetes.

MATERIALS AND METHODS

Subjects

A total of 160 women was recruited in this study and unscrews in 4 groups:

Group 1:40 women control

Group 2:40 women reached of diabetes of the type 1 and not pregnant

Group 3:40 nondiabetic pregnant women

Group 4:40 pregnant diabetic women

These women were recruited in the service of diabetologie of the polyclinic LARBI KHROUF (ALGERIA);

All diabetic women received insulin (for type I diabetes).

Control and other women were matched with respect to age and body mass index. All individuals were none smokers. None had taken vitamin supplements.

Blood samples

Fasting venous blood samples were collected by venipuncture into heparinized tubes. Plasma was obtained by centrifugation at $2000 \times g$ for 15 min at room temperature, and was used immediately for the determination of glycosylated hemoglobin (HbA1C) and glycemia; plasma was left stored at -20°C up to one week.

Laboratory methods

Plasma determination

HbA1C levels were determined by isolab column chromatography (Kaplan and al.1982). The hour of the taking away will have imperatively to be indicated.

Statistical Analysis:

All data are presented as mean \pm SEM. The comparison between groups was carried out by Minitab using Student test.

RESULTS

Variations of glycemia concentration in: control, diabetic, pregnant and diabetic pregnant women:

Figure 1 show the variation of glycemia levels in 4 groups of women .Data are expressed as mean \pm standard deviation.

The data analyses showed a very high significant difference ($P \leq 0.0001$) among the following groups (control, diabetic), (control, diabetic pregnant), (pregnant, diabetic pregnant) respectively (control: $0,788 \pm 0,105$ vs. diabetic: $0,998 \pm 0,141$), (control: $0,788 \pm 0,105$ vs. diabetic pregnant: $1,017 \pm 0,139$), (pregnant: $0,815 \pm 0,155$ vs. diabetic pregnant: $1,017 \pm 0,139$) but there is no significance between the rest of the groups ($P > 0.05$) (Fig.1).

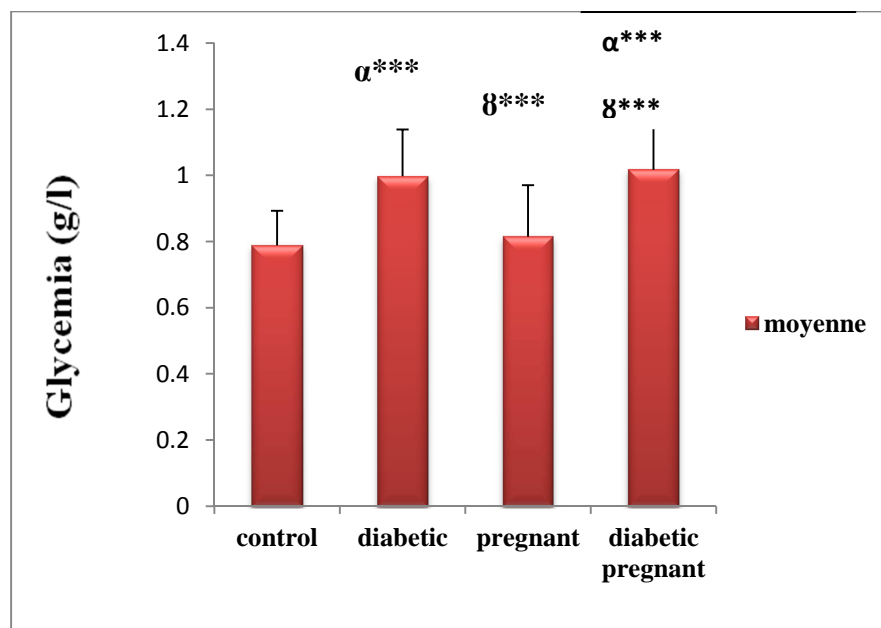


Figure 1: variation of glycemia levels (g/l) in: control, diabetic, pregnant and diabetic pregnant women
 (m \pm SD; n control =40, n diabetic =40, pregnant=40, diabetic pregnant=40)
 (α) Comparison between: control/diabetic, control/pregnant, control/diabetic pregnant
 (β) Comparison between: diabetic and diabetic pregnant
 (γ) Comparison between: pregnant and diabetic pregnant
 (Ns: Non significant difference ; $P > 0.05$; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$)

Variations of HbA1c concentration in: control, diabetic, pregnant and diabetic pregnant women:

Figure 2 show the variation of HbA1c levels in 4 groups of women .Data are expressed as mean \pm standard deviation. The data analyses showed a very high significant difference ($P \leq 0.0001$) among (control, diabetic), (control, diabetic pregnant) respectively (control: 5.428 ± 0.525 vs. diabetic: 6.315 ± 0.477), (control: 5.428 ± 0.525 vs. diabetic pregnant: 6.07 ± 0.371). Between (control, pregnant), (pregnant, diabetic pregnant) there is very significant difference ($P < 0.01$) respectively (control: 5.428 ± 0.525 vs. pregnant: 5.795 ± 0.399), (pregnant: 5.795 ± 0.399 vs. diabetic pregnant: 6.07 ± 0.371) , on the other hand there is a low signification (< 0.05) between diabetic and diabetic pregnant women (diabetic: 6.315 ± 0.477 vs. diabetic pregnant: 6.07 ± 0.371) (Fig.2).

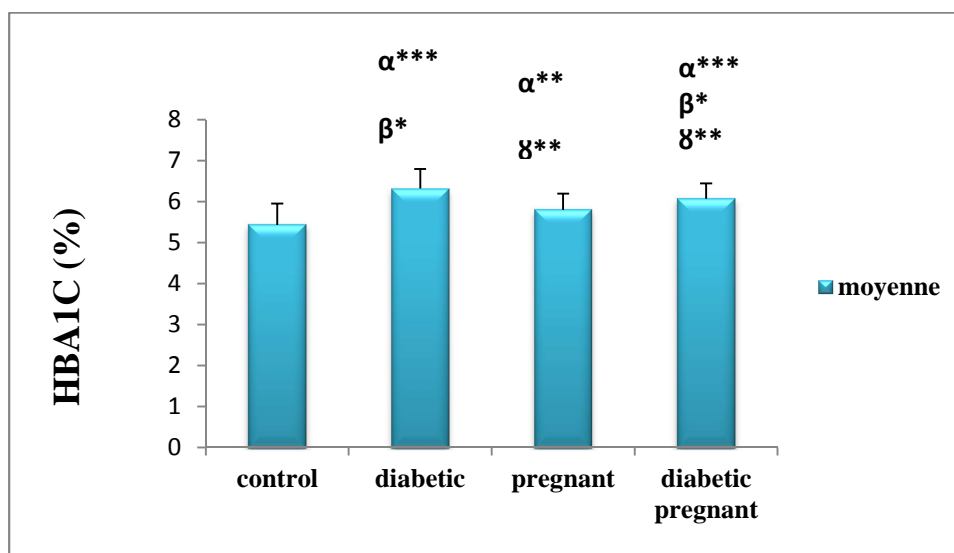


Figure 2: variation of HbA1c levels (%) in: control, diabetic, pregnant and diabetic pregnant women
 (m \pm SD; n control =40, n diabetic =40, pregnant=40, diabetic pregnant=40)
 (α) Comparison between: control/diabetic, control/pregnant, control/diabetic pregnant
 (β) Comparison between: diabetic and diabetic pregnant
 (γ) Comparison between: pregnant and diabetic pregnant
 (Ns: Non significant difference ; $P > 0.05$; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$)

DISCUSSION

In the past few years, it has become increasingly clear that autoimmunity plays a key role in type 1 diabetes. [6, 7] It is currently believed that type 1 diabetes mellitus is actually a slow process in which insulin-secreting cells are gradually destroyed, leading to islet cell failure and hyperglycemia. The exact mechanism of the inheritance of type 1 diabetes is not known. Formerly, it was suggested that the risk of inheriting diabetes in offspring with one affected parent was in the range of 1–6%.[8] Based on recent information,[9] it has become clear that type 1 diabetes is transmitted less frequently to the offspring of diabetic mothers (1%) than to children of diabetic fathers (6%). This preferential paternal transmission rate may be related to greater transfer of DR4 alleles to the offspring of DR4 fathers than to the offspring of DR4 mothers.[10] Family studies have shown that the estimated risk of type 1 diabetes in offspring in a family with one affected sibling but unaffected parents is 5–6%.[11].

Pregnancy itself is usually regarded as a diabetogenic state in which postprandial glucose levels are elevated and insulin sensitivity is decreased. [12] Classically, the decreased response to insulin activity observed in pregnancy has been attributed to increases in hormones such as cortisol, progesterone, estrogen, prolactin, and human placental lactogen.[13]Most recently, new molecules such as leptin, tumor necrosis factor- α (TNF- α), and resistin have been implicated in this matter. Kirwan and colleagues [14] showed that TNF- α is the strongest independent predictor of insulin sensitivity during the late gestational period. In vitro studies showed that TNF- α disrupted insulin signaling and inhibited glucose uptake [14].

Several reports have shown that in physiological pregnancy, glucose levels are lower compared with the prepregnancy state. For example, in nondiabetic women, the upper level of glycated hemoglobin (HbA_{1c}), a long-established parameter for assessing glycemic control, fell from 6.3% to 5.7% in early pregnancy and further to 5.6% in late pregnancy [15, 16]. This is attributed mainly to a decrease in the fasting glucose level during normal pregnancy [16]. As the maternal and fetal glucose levels are in equilibrium, in physiological conditions, the fetus develops in a low glycemic environment. The rise of maternal and, subsequently, fetal glucose and insulin levels is a major pathophysiological mechanism in pregnancy complicated by diabetes. Observational studies have demonstrated that type 1 diabetic women have an increased risk of maternal and fetal outcomes. For early pregnancy, the list of such outcomes includes a progression of chronic diabetic complications in the mother, spontaneous abortion, and fetal malformations. For late pregnancy, an increased risk of pre-eclampsia, hydramnios, and operative delivery in mothers as well as macrosomia and stillbirth in neonates are observed [17, 18, 19, 20]. The risk of congenital abnormalities is as high as 25% in type 1 diabetic women with HbA_{1c} above 10%; however, it is much lower in type 1 diabetic subjects with better glycemic control [21]. Nevertheless, even in women with excellent glucose levels, this risk is higher than in the general female population [20]. It is important that optimal medical care is provided to type 1 diabetic women, from pregnancy planning, through the entire pregnancy and during the labor, as there is clear evidence that such care can reduce the risk of maternal and fetal complications [17, 18, 22, 23].

HbA_{1c} concentrations > 7.0% are assumed to be associated with rates of congenital malformations and macrosomia no greater than those in pregnancies in non-diabetic women.[24] However, our study shows that such levels of control are not good enough to prevent these complications. This indicates that current criteria for strict glycaemic control are not “safe” enough or that HbA_{1c} does not sufficiently reflect short term glucose variability (hypoglycemia and hyperglycemia).[25] Recently, the second possibility has indeed been shown with the continuous glucose monitoring system. [26, 27]. Congenital malformations were related (but not significantly) to HbA_{1c}, but the incidence was higher than that of the general population, even with normal and almost normal HbA_{1c} values. This also points to an effect of glucose variability rather than of HbA_{1c}. The same can be concluded from the high incidence of macrosomia.[28] This incidence was much higher than that published by other authors, despite overall adequate HbA_{1c} levels. [29, 30, 31, 32] HbA_{1c} was the most powerful predictor for macrosomia, but its predictive capacity was only weak (explained variance < 5%).[28]

It is strongly advised that all pregnancies in women with type 1 diabetes are planned. Thus, effective contraception is recommended to all type 1 diabetic women in childbearing age until the optimal glycemic control is reached. This should enable them to enter the pregnancy period with the desired glucose

Levels. [33].The general goal during pregnancy complicated by type 1 diabetes is to achieve glucose levels as close as possible to those observed in nondiabetic pregnant women. Thus, the recommended values of fasting and postprandial glycemia levels are much lower than in type 1 diabetes outside of pregnancy.

CONCLUSION

In women with T1DM, pregnancy increased the risks of hypoglycaemia, diabetic ketoacidosis, pregnancy-induced hypertension, infections and worsening of diabetic microvascular disease. Moreover, T1DM during pregnancy had an impact on the embryo and the fetus, and may have increased the risk of spontaneous miscarriages, malformations, premature births, and fetal and neonatal complications. However, intensive glycaemic control and preconceptional care have been shown to decrease the rate of fetal demise and malformations. Also, the use of insulin analogues during pregnancy is now regarded as safe. Tight glucose control and frequent follow-up are recommended throughout pregnancy in women with T1DM. Their obstetric management should take place in a maternity hospital with an appropriate perinatal environment and in close collaboration with diabetologists.

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