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Original Research Paper

Biochemistry

STUDY OF CARDIOVASCULAR RISK FACTORS DURING GESTATIONAL DIABETES IN SENEGAL

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ABSTRACT The evolution of gestational diabetes is most often marked by preventable maternal-foetal complications. The objective of this study was to identify factors influencing the development of pregnancy in women with gestational diabetes and treated in gynaecological services in Dakar and its suburbs between 2018 and 2019. A total of 24 women with gestational diabetes were recruited. The mean age of the patients was 29.9 ± 6.45 years (18-45) with a predominance of women over 30 years old. Dyslipidaemias were frequent (91.2%) with a predominance of hypercholesterolemia (n = 13, 54.2%) followed by hyperLDLemia (n = 10, 41.7%). The atherogenic risk was high with the TG / HDL (12.5%) and Apo B / A (20.83%) ratios. A positive correlation was noted between homocysteine and total cholesterol (r = 0.457, p = 0.025), LDL (r = 0.449, p = 0.028), triglycerides (r = 0.540, p = 0.006), apolipoproteins A (r = 0.463, p = 0.023) and B (r = 0.480, p = 0.018), urea (r = 0.0671, p <0.0001) and creatinine (r = 0.0673, p <0, 0001). The development of the pregnancy was marked by caesarean deliveries (54.2%) and macrosomia (8.3%). The factors which were identified in relation to the caesarean section were delayed diagnosis of GD, history of personal abortion (RR (CI) = 2.04 (0.4 - 10.6)), multiparity (RR (CI)) = 2.3 (0.4 - 12.7)) and the advanced age of the woman (RR (CI) = 2.1 (0.5 - 14.4)). The biological monitoring of women with gestational diabetes must consider the dosage of lipid parameters extended to apolipoproteins and homocysteine for a favourable outcome of the pregnancy.

KEYWORDS : Biochemical assessment, Risk factors, Maternal-foetal complications, Gestational diabetes, Senegal.

INTRODUCTION

Gestational diabetes (GD) is defined as a carbohydrate intolerance of varying severity that first appears during pregnancy. It is a common illness affecting 2 to 3% of pregnant women [1]. Its prevalence varies from country to country with a more significant expansion in developing countries. In Senegal, hospital prevalence is 34.5% [2] while at the national level, it remains unclear.

The pathophysiological mechanism is thought to be a disturbance of carbohydrate homeostasis underpinned by insulin resistance causing various metabolic disorders. The latter are responsible for serious consequences in the short, medium, and long term both at the maternal and foetal level [3]. In addition, the diagnosis of gestational diabetes also reveals vulnerable women exposed to several cardiovascular risk factors and maternal-foetal complications [3]. Identifying the risk factors that are most often modifiable would make it possible to better monitor pregnancy and prevent maternal-foetal complications. This work which aims to identify the risk factors related to the course of pregnancy in women with gestational diabetes is done within that framework.

MATERIALS AND METHODS

This is a retrospective and analytical study conducted at seven sites in Dakar and its suburbs in women with gestational diabetes selected according to the WHO 2013 criteria [4]. The study was conducted between July 2018 and July 2019 as part of a collaboration between the medical biochemistry laboratory and the obstetric gynaecology clinic

of Aristide Le Dantec University Hospital (HALD). Data collected were related to age, pregnancy, parity, personal and family history, pregnancy consequences, blood pressure, BMI, laboratory workup with GAJ, homocysteine, insulinemia and the level of peptide C as well as the CRP, the lipid balance combining Apo A1 and B, urea and serum creatinine.

Assays were performed on Abbot® Architect ci4100. Blood glucose, urea, total cholesterol, HDL cholesterol and triglycerides were determined enzymatically. LDL cholesterol by Friedwall's formula [5]. Apo A1 and B as well as CRP were assayed by immuno-turbidimetric method; insulin, C-peptide, and homocysteine by chemiluminescence. Statistical analysis was done with SPSS v.26 software. Bivariate analysis was performed with Spearman's correlation and Fisher's test allowed analysis of distribution parameters. A p value <0.05 was considered significant.

RESULTS

A total of 24 women with gestational diabetes were enrolled. The mean age of the patients was 29.9 ± 6.45 years (18-45) with a predominance of women over 30 years (62.5%). The study population was characterized by a predominance of multiparous women (n = 17; 71%) with a history of personal abortion (n = 14; 58%). Hypertension was found in 7 patients (29%) and the diagnosis of GDM was made in most cases in the 3rd quarter (n = 16, 69.6%). The course of the pregnancy was marked by a predominance of deliveries by caesarean section (n = 13; 54.2%), the birth of 4 premature babies (16.7%), 2 macrosomes (8.3%) and loss of 4 new-borns (16.7%) (Table I).

Table I : Characteristics of the population

		Number (%)
Anthropometric data		
Age (years)	≤ 30	10 (41,7)
	≥30	14 (58,3)
Parity	Primiparous	9 (37,5)
	Multiparous	15 (62,5)
Age of the pregnancy	2nd quarter	8 (33,3)
	3rd quarter	16 (66,7)
Abortion history	None	11 (45,8)
	Personal	11 (45,8)
	Household	2 (8,3)
FRCV		
HTA	No	17 (70 ,8)
	Yes	7 (29,9)
Dyslipidaemia	Yes	22 (91,7)
	No	2 (8,3)
BMI	< 18	0
	18 – 25	6 (25)
	25 - 30	9 (37,5)
	≥ 30	9 (37,5)
Development of the pregnancy		
Delivery	Normal	11 (45,8)
	Caesarean	13 (54,2)
New - born	Alive normal	14 (58,3)
	Macrosomia	2 (8,3)
	Premature	4 (16,7)
	Stillbirth	4 (16,7)

The mean values of the laboratory parameters were within normal limits except for insulin (21.11 ± 44.71 IU / L), C peptide (2.36 ± 2.56 nmol / L) and CRP (15.62 ± 31.11 mg / L) (Table II). Bivariate analysis showed a positive correlation between homocysteine and lipid parameters (total cholesterol ($r = 0.457$, $p = 0.025$), LDL ($r = 0.449$, $p = 0.028$), triglycerides ($r = 0.540$, $p = 0.006$), apolipoproteins A ($r = 0.463$, $p = 0.023$) and B ($r = 0.480$, $p = 0.018$), urea and creatinine were significantly ($p < 0.001$) correlated with homocysteine and peptide C (Table III).

Table II : Distribution of the mean values of biological parameters

Parameters	Average ± ET	Min-Max
Glycaemia (g/L)	0,98±0,18	0,71 – 1,55
Insulin (UI/l)	21,11±44,71	1,20 -216,50
Peptide C (nmol/L)	2,36±2,56	0,56 -11,79
Urea*(mg/l)*	0,145±0,08	0,04 -0,39
Creatinine *(mg /l)*	5,33±1,69	2,3 -9,3
CRP *(mg/l)*	15,62±31,11	0,5 -14,4
Homocysteine (µmol/l)	5,73±2,67	1,78 -12,67
BMI (Kg/m²)	28,84±5,24	20 – 38,70
Cholesterol total *(g/l)*	1,99±0,79	0,78 -3,05
Cholesterol HDL *(g/l))*	0,66±0,29	0,23 -1,46
Cholesterol LDL *(g/l))*	1,19±0,56	0,32 -2,01
Triglycerides *(g/l))*	1,45±0,65	0,33 -3,25
Apolipoproteins A *(g/l)*	1,65±0,59	0,67 -3,10
Apolipoproteins B *(g/l)*	1,16±0,45	0,42 -1,96
CT/ HDL	3,01±0,62	2,08 -3,05
LDL/ HDL	1,80±0,61	1,38 -1,39
TG/HDL	2,52±1,46	1,06 -3,98
Apo B/Apo A	0,72±0,21	0,39 -1,13

Table II : Correlation research in the study population

	Glycemia H0		Peptide C		homocysteine		insulin		CRP		BMI	
	r	p	r	p	r	p	r	p	r	p	r	p
Age	-0,101	0,639	-0,135	0,539	-0,099	0,644	-0,038	0,860	0,116	0,588	0,343	0,101
Total cholesterol	-0,185	0,387	0,146	0,505	0,457	*0,025**	-0,055	0,798	-0,342	0,102	-0,038	0,859
HDL	-0,016	0,941	0,228	0,295	0,397	0,055	0,170	0,426	-0,222	0,298	-0,142	0,508
LDL	-0,223	0,294	0,086	0,698	0,449	*0,028**	-0,073	0,734	-0,323	0,124	-0,046	0,832
Triglycerides	0,077	0,720	0,315	0,143	0,540	*0,006***	-0,125	0,562	-0,003	0,990	0,147	0,494
CT/HDL	-0,117	0,587	0,033	0,881	0,269	0,204	-0,239	0,261	-0,090	0,674	0,072	0,737
LDL/HDL	-0,218	0,306	-0,057	0,795	0,221	0,300	-0,184	0,388	-0,149	0,488	0,027	0,900
TG/HDL	0,098	0,647	0,216	0,322	0,146	0,496	-0,133	0,537	0,147	0,493	0,152	0,479
Apo A	0,087	0,686	0,311	0,149	0,463	*0,023**	0,175	0,413	-0,119	0,579	-0,066	0,760
Apo B	-0,205	0,336	0,139	0,526	0,480	*0,018**	-0,111	0,606	-0,340	0,104	-0,090	0,674
B/A	-0,366	0,079	-0,151	0,492	0,057	0,793	-0,177	0,408	-0,248	0,243	-0,164	0,445
Urea	-0,016	0,940	*0,526*	*0,010***	*0,852*	*0,000***	-0,033	0,879	0,322	0,125	0,155	0,469
Creatinine	0,181	0,397	*0,650*	*0,001***	*0,657*	*0,000***	0,101	0,638	0,211	0,321	0,276	0,192

A high prevalence of dyslipidaemia was found in the population (n = 22, 91.2%) with a predominance of hypercholesterolemia (n = 13, 54.2%) followed by hyperLDLemia (n = 10, 41, 7%). A mixed dyslipidaemia was found in four patients (16.7%) (Figure 1). The atherogenic risk assessed by the CT / HDL and LDL / HDL ratios did not show any increase in risk, while the TG / HDL and Apo B/A ratios respectively showed an increased risk in 3 (12.5%) and 5 women (20.83%) (Figure 2).The study of factors associated with a caesarean section showed a higher risk in women diagnosed in the third quarter of pregnancy (RR (CI) = 6.6 (0.97-44.9), with a history of personal abortion (RR (CI) = 2.04 (0.4-10.6). The risk related to giving birth by caesarean was also increased in women over 30 years (RR (CI) = 2.1 (0.5 - 14.4)), multiparous (RR (CI) = 2.3 (0.4-12.7) and hypertensive (RR (CI) = 1.2 (0.2 - 6.99)).

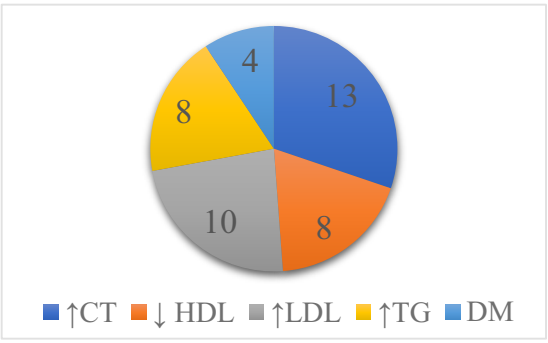

Figure 1 : Distribution of dyslipidaemia in the study population

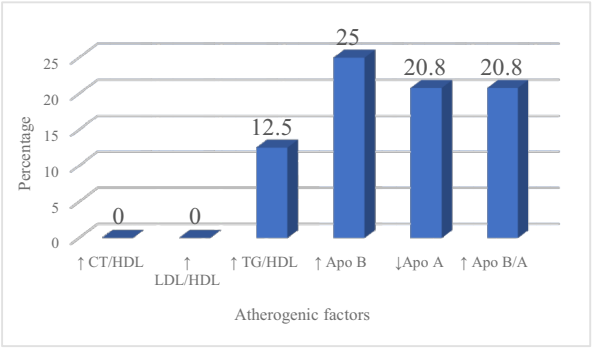

Figure 2 : Distribution of atherogenic risk in the population

Table III: Study of the factors associated with the practice of caesarean in women with gestational diabetes.

Study factors		Caesarean delivery			
		Yes	No	RR (IC=95)	p
Age	≥30 years	9 (37,5)	5 (20,8)	2,1 (0,5 – 14,4)	0,233
	<30 years	4 (16,7)	6 (25)		
Multiparity	Yes	7 (29,2)	8 (33,3)	2,3 (0,4 – 12,7)	0,3
	No	6 (25)	3 (12,5)		
Age of the pregnancy	3rd quarter	11(45,8)	5 (20,8)	6,6 (0,97 – 44,9)	0,055
	2nd quarter	2 (8,3)	6 (25)		
Personal abortion history	Yes	7 (29,2)	4 (16,7)	2,04 (0,4 – 10,6)	0,329
	No	6 (25)	7 (29,2)		
Overweigh	Yes	7 (29,2)	8 (33,3)	1,1 (0,2- 5,6)	0,625
	No	4 (16,7)	5 (20,8)		
Obesity	Yes	4 (16,7)	5 (20,8)	0,53 (0,1 – 2,8)	0,375
	No	9 (37,5)	6 (25)		
HTA	Yes	4 (16,7)	3 (12,5)	1,2 (0,2 – 6,99)	0,605
	No	9 (37,5)	8 (33,3)		
Dyslipidaemia	Yes	12 (50)	10(41,7)	0,07(0,07 –121,7)	0,717
	No	1 (4,2)	1 (4,2)		
Glycemia	Yes	9 (37,5)	8 (33,3)	0,84 (0,14 - 5)	0,605
	No	4 (16,7)	3 (12,5)		
Peptide C	Yes	5 (21,7)	5 (21,7)	0,63 (0,1 - 3,3)	0,448
	No	8 (34,8)	5 (21,7)		
Insulin	Yes	2 (8,3)	5 (20,8)	0,49(0,07-3,61)	0,415
	No	11(45,8)	8 (33,3)		
Inflammation	Yes	6 (25)	5 (20,8)	1,03 (0,2 – 5,2)	0,647
	No	7 (29,2)	6 (25)		

Neonatal complications were frequent t in our population (n = 10, 41.7%). But because of a relatively low number of types of neonatal complications, we did a descriptive analysis which showed that macrosomia (n = 2, 8.3) were mostly found in women over 30 years of age, with dyslipidaemia, blood glucose ≥ 0.92 and in the context of inflammation. As for prematurity, it was predominant in women over 30, overweight and with dyslipidaemia. Stillbirths were frequent in multiparas (16.7%) and in dyslipidaemia (Table IV).

Table IV: Distribution of the population according to neonatal complications

Studied factors		Normal (%)	Macrosomia (%)	Premature (%)	Stillbirth (%)
Age (years)	< 30	7 (29,2)	0	1 (4,2)	2 (8,3)
	≥ 30	7 (29,2)	2(8,3)	3 (12,5)	2 (8,3)
Multiparity	Yes	9 (37,5)	1 (4,2)	2(8,3)	3(12,5)
	No	5 (20,8)	1 (4,2)	2(8,3)	1 (4,2)
Age of pregnancy	2nd quarter	4 (16,7)	1 (4,2)	3 (12,5)	0
	3rd quarter	10 (41,7)	1 (4,2)	1 (4,2)	4(16,7)
Personal abortion history	Yes	8 (34,8)	0	2(8,3)	1 (4,2)
	No	6 (26,1)	2(8,3)	2(8,3)	3 (12,5)
Overweight	Yes	4 (16,7)	0	3(12,5)	2(8,3)
	No	10(41,7)	2(8,3)	1 (4,2)	2(8,3)
Obesity	Yes	6 (26,1)	1 (4,2)	1 (4,2)	1 (4,2)
	No	8 (34,8)	1 (4,2)	3 (12,5)	3 (12,5)
HTA	Yes	4 (16,7)	0	1 (4,2)	2(8,3)
	No	10 (41,7)	2(8,3)	3 (12,5)	2(8,3)
Dyslipidemia	Yes	12 (50)	2(8,3)	4 (16,7)	4 (16,7)
	No	2(8,3)	0	0	0
Glycemia H0 ≥ 0,92	Yes	11(45,8)	2(8,3)	3 (12,5)	1 (4,2)
	No	3 (12,5)	0	1 (4,2)	3 (12,5)
Increase of peptide C	Yes	6 (26,1)	1 (4,3)	1 (4,3)	2(8,7)
	No	8 (34,8)	1 (4,3)	2(8,7)	2(8,7)

Hyperinsulinemia	Yes	2(8,3)	1 (4,2)	1 (4,2)	1 (4,2)
	No	12 (50)	1 (4,2)	3 (12,5)	3 (12,5)
Hyperhomocysteinemia	Yes	1 (4,2)	0	0	0
	No	13 (54,2)	2(8,3)	4 (16,7)	4 (16,7)
Inflammation	Yes	5 (20,8)	2(8,3)	2(8,3)	2(8,3)
	No	9 (37,5)	0	2(8,3)	2(8,3)

DISCUSSION

Our study population consisted of 24 women with a mean age of 29.9 ± 6.45 years (18-45) with more than 62.5% over 30 years old. Most women were in the third quarter of pregnancy at the time of GDM diagnosis (69.6%, n = 16) with a predominance of multiparous at 62.5% (n = 15). According to Vanderijst et al [6], GD appears at the threshold of the 3rd trimester and diabetogenic factors of placental origin are strongly implicated. This causes the β cells to malfunction in coping with the excessive production of insulin leading to insulin resistance.

According to several studies, advanced age is a risk factor for GDM, especially after 35 years. These results are supported by our study, which found a predominance of women over 30. Likewise, the study by Sellami et al found a mean age of 32.6 ± 4.7 years [7]. The study of cardiovascular risk factors in women with gestational diabetes showed a high prevalence of dyslipidaemia at 91.2% (n = 22). In most studies, the lipid balance is rarely normal with the percentages of pregnant women without lipid disorders below 15% [6,7]. Dyslipidaemias were predominantly hypercholesterolemia 54.17% (n = 13) followed by hyperLDLemia 41.67% (n = 10). Mixed dyslipidaemia was observed in 4 women (16.7%). In the literature, the variation of lipid parameters is diversely appreciated. While for many authors elevation in triglyceride levels is constant [8], results are discordant for others. Some have shown either a decrease in HDL-Cholesterol or an increase [9] as evidenced by the work of Sellami et al who found hypoHDLemia (37.1%) as the most frequent lipid abnormality followed by hypertriglyceridemia (31%) [7]. As per Sebai's work, hypercholesterolemia was the most common lipid abnormality with a prevalence of 50% [8]. In our study, hypertriglyceridemia was found in 8 women (33.33%), close to the results of the studies of Sebai and Sellami [7,8]. The atherogenic risk assessed by the CT / HDL, LDL / HDL, TG / LDL and Apo B / A ratios showed that the Apo B / A and TG / HDL ratios were increased in 5 (20.83%) and 3 women, respectively. (12.5%). These results suggest the prescription of the apolipoprotein assay in the analysis of lipid disorders in pregnant women. The CRP and homocysteinemia study showed an increase in CRP in 11 patients (45.83%) with a mean value of 15.62 ± 31.11 mg / L. As for homocysteine, it increased in only 1 woman (4.17%) with a very significant correlation with urea and creatinine. The disturbance of lipid parameters was correlated with homocysteinemia indicating an atherogenic risk in women with gestational diabetes. This atherogenic risk maintained by chronic inflammation can lead to maternal-foetal complications with variable prognosis [10,11]. Although most of our patients had a normal homocysteinemia, it is obvious to include the homocysteine assay in prenatal follow-up, especially in the occurrence of lipid disorders or renal function disturbance knowing that the hyperhomocysteinemia would favour the occurrence of repeated lay-offs, pre-eclampsia, retroplacental hematoma, in utero growth retardation, in utero death as well as vascular pathologies [11]. In our study, no relationship could be established between homocysteinemia and the outcome of pregnancy due to a very small number of patients with hyperhomocysteinemia. The results of our study also showed that advanced age, multiparity, personal abortion history, and the age of pregnancy at the time of GDM diagnosis appear to have an impact on the type of delivery with relative risk. > 2. Late diagnosis of gestational diabetes increases the risk of caesarean section 6 times apart from all other factors. These results show the importance of early detection in the management of gestational diabetes. The study of other factors such as hypertension, obesity, overweight, insulin resistance, variations in blood sugar levels did not show any significant disturbances on the type of childbirth or on the future of the new-born. . However, hypertension increased the risk of giving birth by caesarean section by 1.2 times (CI = 0.2 - 6.99). Insulin resistance and increased BMI do not appear to have an impact on Caesarean section practice according to our study. In a systematic review, Beucher et al had showed that the practice of caesarean section was very variable from one study to another with a prevalence varying from 8.6 to 23.5% [12]. The HAPO study showed a linear and continuous relationship between caesarean section rates and changes in blood sugar, which was not the case in our study [13]. Langer found that the rate of caesarean section was significantly more increased in women with high BMI without GDM management [14]. In addition, we found neonatal complications such as prematurity (n = 4, 16.7%), macrosomia (n = 2, 8.3%) and stillbirth (n = 4, 16.7%).) in our study. Due to their very small staff, we were unable to do statistical analysis to determine their involvement. However, these frequent complications in women in GD with metabolic disorders predominated by neonatal hypoglycaemia were not examined in this present study [15,16]. Bourgade's study reports a predominance of metabolic disorders with jaundice (44.87%) followed by hypoglycemia (16.67%). Macrosomia and prematurity were 10.26% and 8.97%, respectively [16]. We also note limitations in our study, due to a small number (n = 24), an absence of information on the history of dyslipidaemia, indications for caesarean section and neonatal metabolic complications.

CONCLUSION

The development of pregnancy in women with diabetes is very variable. In this study, we report the importance of extending the prenatal assessment to assays of apolipoproteins with the Apo B/A ratio and homocysteine in the follow up of women with gestational diabetes.

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