

Is There a Tendency for Thrombosis in Gestational Diabetes Mellitus?

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OBJECTIVES

Impact of gestational diabetes mellitus (GDM) on the coagulation system, dynamics involved at a pathophysiological level and the exact mechanism remain unclear.

Aims: To evaluate the association between diabetes-related parameters and hemostatic factors to search for a tendency of thrombosis in GDM.

METHODS

Nineteen pregnant women who had GDM, 16 healthy pregnant and 13 healthy nonpregnant controls admitted to the Endocrinology outpatient clinics were enrolled in the study. Fasting and postprandial glucose, hemoglobin A1c and insulin levels, and insulin resistance; fructosamine, thrombin activatable fibrinolysis inhibitor (TAFI), tissue factor pathway inhibitor (TFPI), plasminogen activator inhibitor Type-1 (PAI-1), tissue-type plasminogen activator (t-PA), fibrinogen, plasminogen and hemoglobin levels, platelet counts, prothrombin time (PT), and activated partial thromboplastin time (aPTT) were studied. Statistical Analysis Used: One-way analysis of variance, Kruskal–Wallis, and *post hoc Tukey honestly significant* difference or Conover's nonparametric multiple comparison tests for comparison of the study groups.

RESULTS

The mean age SD of the GDM patients, and healthy pregnant and nonpregnant control groups were 31.2 ± 6.0 years, 26.8 ± 5.0 years, and 32.0 ± 8.7 years, respectively. The main characteristics of the study population are summarized in Table 1. There were no differences between the groups in regards to the mean age, FBG and insulin levels, and HOMA-IR. Compared with controls, BMI was significantly higher in GDM patients ($P < 0.01$). There was no statistically significant difference between pregnant women with and without GDM in terms of mean BMI. PPBG levels in GDM patients were significantly higher than both pregnant and nonpregnant healthy control groups ($P < 0.01$, for each). In the pregnant group without GDM, HbA1c and fructosamine levels were lower compared to the control and GDM groups ($P < 0.05$, $P < 0.01$; respectively).

Hemoglobin levels and platelet counts were not significantly different between the study groups [Table 2]. PT and aPTT were significantly lower in GDM patients compared to the controls ($P < 0.05$). Fibrinogen and plasminogen levels were significantly higher in the GDM group compared to the healthy pregnant and nonpregnant control groups ($P < 0.05$, for each). TAFI, TFPI, PAI-1, and t-PA levels were not found to be significantly different between groups. Although no statistically significant difference was demonstrated between the groups, average PAI-1 level was remarkably higher while t-PA level tended to be lower in GDM patients compared the other study groups.

CONCLUSIONS

There is general opinion based on encouraging data that GDM, which complicates pregnancy by exposing prothrombosis and hypofibrinolysis that may be dangerous both for the mother and the baby. We believe that levels of coagulation factors may vary in different stages of pregnancy and postpartum period with diverse etiopathogenesis. Similar to previously reported studies, our study suggests that GDM may play a role in the pathogenesis leading to a thrombotic tendency similar to DM. Further clinical studies at larger scales are needed to further delineate the relationship between GDM and homeostasis.

References

- Mitanchez D, Yzydorczyk C, Simeoni U. What neonatal complications should the pediatrician be aware of in case of maternal gestational diabetes? *World J Diabetes*. 2015 Jun 10;6(5):734-43
- Lemkes BA, Hermanides J, Devries JH, Holleman F, Meijers JC, Hoekstra JB. Hyperglycemia: a prothrombotic factor? *Thromb Haemost*. 2010 Aug;8(8):1663-9
- Collis RE, Collins PW. *Haemostatic management of obstetric haemorrhage*. Anaesthesia. 2015 Jan;70 Suppl 1:78-86, e27-8.
- Alzahrani SH, Ajjan RH. Coagulation and fibrinolysis in diabetes. *Diabetes and vascular disease research* 2010; 7: 260-273.
- Abdel Gader AG, Khashoggi TY, Habib F, Awadallah SB. Haemostatic and cytokine changes in gestational diabetes mellitus. *Gynecol Endocrinol*. 2011; 27(5):356-60.
- Kvasnicka J, Bendl J, Zivný J, Umlaufová A, Maslowská H. *Changes in hemostasis and fibrinolysis in gestational diabetes*. *Cas Lek Cesk*. 1996 Feb 14;135(4):106-10
- Iwaki T, Urano T, Umemura K. PAI-1, progress in understanding the clinical problem and its aetiology. *Br J Haematol*. 2012; 157(3):291.
- Bellart J, Gilabert R, Fontcuberta J, Carreras E, Miralles RM, Cabero L. *Coagulation and fibrinolysis parameters in normal pregnancy and in gestational diabetes*. *Am J Perinatol*. 1998 Aug;15(8):479-86.

Graphs and tables

	Controls (n=13)	Pregnant without GDM (n=16)	Pregnant with GDM (n=19)	p-value
Age (years)	32,0±8,7	26,8±5,0	31,2±6,0	0,071
BMI (kg/m ²)	25,6±3,46 ^a	28,0±5,14	30,1±3,13 ^a	0,013
FBG (mg/dl)	90,0 (12,50)	84,0 (15,75)	90,0 (33,00)	0,185
PPBG (mg/dl)	91,0 (15,00) ^{ab}	110,0 (25,50) ^{bc}	151,0 (39,00) ^{ac}	<0,001
Insulin (IU/ml)	13,5 (3,90)	15,7 (27,65)	12,9 (9,17)	0,127
HOMA-IR	2,8 (1,18)	2,7 (2,48)	3,9 (5,23)	0,222
HbA1c (%)	5,5 (0,35) ^b	5,1 (0,35) ^{bc}	5,9 (0,90) ^c	<0,001
Fructosamin	206,0 (61,25) ^b	177,4 (35,1) ^{bc}	208,0 (148,40) ^c	0,045

	Controls (n=13)	Normal pregnant (n=16)	Pregnant with GDM (n=19)	p-value
Hemoglobin (mg/dL)	13,0±1,83	12,3±1,59	12,3±1,11	0,317
Platelet (x10 ³ /L)	236,0 (51,00)	232,5 (69,25)	226,0 (151,00)	0,712
PT (sec)	11,17±0,89 ^a	11,01±0,78	10,54±0,52 ^a	0,041
aPTT (sec)	29,91±3,50 ^a	27,31±2,37	26,92±3,10 ^a	0,020
Fibrinogen (mg/dL)	342,38±61,52 ^{ab}	475,81±65,41 ^{bc}	553,79±77,66 ^{ac}	<0,001
Plasminogen (%)	108,31±9,71 ^{ab}	135,75±22,45 ^{bc}	150,84±13,21 ^{ac}	<0,001
TAFI (%)	37,0±11,68	41,8±21,29	39,9±21,04	0,802
TFPI (ng/mL)	1,01 (0,31)	0,91 (0,33)	0,91 (0,14)	0,088
PAI-1 (ng/mL)	4,7±2,34	5,6±2,77	7,2±3,24	0,053
t-PA (ng/mL)	6,4 (4,09)	5,8 (4,65)	4,6 (3,97)	0,298