

Gestational Diabetes Mellitus and Prisca Test for Increased Risk for Trisomy 21 And Other Aneuploidy in Pregnant Woman in Bitola in 2020 Year

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1. Abstract

1.1. Background: Gestational diabetes mellitus (GDM) is one of the most common medical complications of pregnancy. The aim of this study was to analyze the presents of GDM in all pregnant women in our town for one year period. We analyze risk for trisomy 21 and other aneuploidy in pregnant women with GDM compared to pregnant women without GDM.

1.2. Methods: We conducted a one year follow up study on all pregnant women with and without GDM in Clinical Hospital Bitola from January 2020 to January 2021 year. The pregnant women range in age from 20 to 43 years. We separated the patients in two groups.

1.3. Results: Over a one year period, screening was carried out in 175 pregnancies. Median maternal age was 32.2 years. The prevalence of GDM was 17%. GDM is present in all ages of the participants. We conclude that predisposition to GDM is higher in advanced maternal age. Significant increased free β -hCG concentration, increased maternal weight, increased Crown – rump length and decreased nuchal translucency has been reported in pregnant women that were diagnosed with GDM.

1.4. Conclusion: GDM is the most common medical and metabolic complication seen in pregnancy. Women who are at high risk of developing GDM should be appropriately screened to reduce maternal and fetal morbidity. Early diagnosis of ‘diabetes in pregnancy’ enables prompt evaluation and treatment. It is clear that GDM does appear to carry increased risk of perinatal complications to both the parturient and her fetus/neonate

2. Introduction

Gestational diabetes mellitus (GDM) is one of the most common medical complications of pregnancy and represents a major risk factor for both adverse maternal-fetal outcomes [1,2] and long-term maternal complications [3, 4].

In recent years, its incidence has dramatically increased worldwide, in parallel with the rising incidence of overweight/obesity and common type 2 diabetes mellitus [2].

In women, the rising obesity has led to an increase in the incidence of gestational diabetes mellitus as well as associated pregnancy and perinatal complications. Known non-modifiable risk factors for predisposition to GDM include advanced maternal age, ethnicity, and family history of type two diabetes mellitus [5].

Maternal obesity independently contributes to the development of GDM [6]. Various organizations attempted to establish population-based protocols to diagnose GDM [7].

In 1999, the WHO recommended a screening test of a 75-g anhydrous glucose load, following an overnight fasting for 8–14 h, between 24 and 28 weeks’ gestation.

In 2010, the International Association of Diabetes and Pregnancy Study Group (IADPSG) panel recommended a universal screening, consisting of a 75 g oral glucose tolerance test (OGTT) to be performed at 24–28 weeks of gestation in all pregnant women, with lower glucose cut-offs for the diagnosis of GDM with respect to the past [8]. They recommended measuring glucose at gestational age at screening 28 week and values of glucose, FBS <5.3 mmol/L, after first hour <10.6 mmol/L and after two hours <9 mmol/L.

Prisca test identifies a population of women whose fetuses are at increased risk for trisomy 21 and other aneuploidy, with a detection rate of approximately 90% and a false-positive rate of 5%. Prisca is performed between 11 and 13 weeks of gestation, and it is obtained by the combination of maternal age, ultrasound fetal nuchal translucency measurement, and the maternal serum markers free β -human chorionic gonadotropin (β -hCG) and pregnancy-associated plasma protein A (PAPP-A) [9].

Nuchal translucency refers to a fluid-filled subcutaneous space present in all fetuses, posterior to the cervical spine, physiologically varying from 0.7 mm at 10 weeks of gestation to 1.5 mm at 13 weeks [10]. Increased nuchal translucency measurements are significantly associated with aneuploidy and structural malformations [10,11].

Free β -human chorionic gonadotropin is a pregnancy-specific hormone produced by trophoblast cells, which regulates placental development [12]. Pregnancy-associated plasma protein A is a proteolytic enzyme produced by the placenta and deciduas and is believed to have a critical function in the normal placental development. Abnormal concentrations of either free β -human chorionic gonadotropin or pregnancy-associated plasma protein A are associated with adverse pregnancy outcomes, such as pre-eclampsia, pre-term delivery, spontaneous fetal loss, low birth weight, and small for gestational age [13-18].

The aim of this study was to analyze the presents of gestational diabetes in all pregnant women in our town for one year period. We analyze risk for trisomy 21 and other aneuploidy in pregnant women with GDM compared to pregnant women without GDM.

3. Methods

3.1. Study population

We conducted a one year follow up study on all pregnant women with and without GDM in Clinical Hospital Bitola from January 2020 to January 2021 year. The pregnant women range in age from 20 to 43 years. We separated the patients in two groups: pregnant women with GDM and without GDM.

Ethics Committee of Health Organization Clinical hospital "D-r Trifun Panovski" approved the study, and all of the procedures were performed in accordance with ethical approval institutional guidelines. The study protocol followed

the ethical guidelines of the most recent Declaration of Helsinki. All participants provided informed consent prior to enrolment in the trial.

A follow-up - participants were analyzed at 11-13 gestational age for Prisca screening and at 28 gestational week for oral glucose tolerant test.

3.2. Laboratory methods

Maternal weight was measured using a digital weight scale eighth a precision of 0.1 kg. The serum was separated and pregnancy

associated plasma protein-A and free beta human chorionic gonadotrophin hormone were measured using solid phase, enzyme labeled chemiluminescent immunometric assay (Siemens Healthcare Diagnostics, Inc., Llanberis, UK).

Transabdominal and transvaginal ultrasound examination was performed by certified maternal fetal medicine specialists. The ultrasound scan included a full structural survey, and nuchal translucency was measured according to established guidelines. Ultrasound examinations were performed with high resolution equipment (Voluson E Expert 2008, General Electric, Austria or Siemens G50 Ultrasound, Siemens Medical Solutions USA, Inc.)

Risks for chromosomal abnormalities were calculated using the software Prisca - mathematical model which gives individual risks for trisomy 21, 18 and 13. This mathematical model takes into consideration the maternal age, the serum levels of various biochemical markers and the fetus ultrasound measurements. In addition, a number of factors play an important role in the calculation of the risk as they will affect the values of the maternal serum biochemical analytes. This includes gestational age, weight, race, smoking, diabetic status of the individual, the number of fetuses present, and whether in vitro fertilization treatment was used for conceiving.

A calculated risk $\geq 1:250$ were defined as high-risk for Down syndrome and $\geq 1:300$ was defined as high-risk for Edward syndrome.

The data are presented as mean \pm standard deviation (SD). The results were done with the SPSS version 13.

4. Results

Over a one year period, screening was carried out in 175 pregnancies. Median maternal age was 32.2 years (range 20 to 43 years). Of all pregnant women, 164 were Christian and 11 Muslim.

The prevalence of gestational diabetes was 17% (33 Christian, 2 Muslim).

Fasting plasma glucose levels 5.1-6.9 mmol/L and two hours plasma glucose levels of 8.5-11.0 mmol/L were set up as cut-off levels (Table 1).

In the present Table 1 we can see that gestational diabetes is present in all ages of the participants. The youngest pregnant woman with gestational diabetes is 23 years old and the oldest pregnant woman with gestational diabetes is 42 years old.

We analyzed patients in all age groups, and we discovered in age group 20 – 25 years 21(12%) examinee pregnant women, only 5 have gestational diabetes, in age group 26-30 years 48 (27%) examinee pregnant women 7 have gestational diabetes.

At age group 31 – 35 years 65(37%) examinee pregnant 11 have gestational diabetes, and at age group 36-40 years, 35 (20%) examinee pregnant women 10 have gestational diabetes. At age group 41-45 years, 6 (4%) examinee pregnant women, 2 have gestational diabetes.

We can concluded that predisposition to gestational diabetes mellitus is higher in advanced maternal age.

After oral glucose tolerant test we analyze risks for chromosomal abnormalities with Prisca –screening. A calculated risk $\geq 1:150$ were defined as high-risk for Down syndrome and $\geq 1:150$ was defined as high-risk for Edward syndrome (Table 2).

In addition, a significant increased free β -hCG concentration has been reported in pregnant women that were diagnosed with gestational diabetes mellitus. Nuchal translucency was decreased in

pregnant women that were subsequently diagnosed with gestational diabetes mellitus.

We notes that maternal weight in pregnant women with gestational diabetes mellitus is higher compared to pregnant women without gestational diabetes mellitus.

Crown – rump length in pregnant women with gestational diabetes mellitus is higher compared to pregnant women without gestational diabetes mellitus.

Table 1: Present glucose levels in all participants in the study and presents of gestational diabetes by age.

Age (years)	Number of participants	GDM	Mean glucose level before	Mean glucose values measured	Mean glucose values measured
			oral glucose tolerant test in all patients	at first hour of	at second hour of
			(mmol/L)	oral glucose tolerant test in all patients	oral glucose tolerant test in all patients
			(mmol/L)	(mmol/L)	(mmol/L)
20	1		5.2	8.2	6.5
21	2		5	8.5	5.8
22	3		5.2	9.2	6.4
23	4	2	5.5	10	7.2
24	4	1	5.8	8.1	8.2
25	7	2	5.7	9.7	7.1
26	7	1	6.1	9.1	7.7
27	8		5.2	7.8	6.1
28	8		5.5	8.6	6.9
29	12	4	5.4	9.4	6.7
30	13	2	5.6	9	6.7
31	12	4	5.5	9	6.7
32	13	2	5.5	8.9	6.5
33	18	1	5.2	8.6	6
34	14	3	5.4	9.3	6.1
35	8	1	5.4	8.4	7
36	15	5	5.6	9.9	7.3
37	6		5.2	7.9	6.7
38	7	2	5.5	9.6	7
39	6	3	5.2	10.7	6.6
40	1		5.3	8.8	7.5
41	3	1	4.9	8.3	5.8
42	2	1	6.6	11.3	8.4
43	1		4.9	8.3	5.8

Table 2: Results from PRISCA screening in all pregnant women

Variable	Pregnant women with gestational diabetes mellitus (n=35)	Pregnant women without gestational diabetes mellitus (n=140)
Maternal age (years)	32.9±12.7	32.2±6.3
Maternal weight (kg)	73.2±11.31	66.9±12
Mode of conception		
spontaneous	33	137
In vitro fertilization	2	3
Smoking status		
Smoker	1	17
Non – smoker	34	123
Diabetes mellitus		
Mother with diabetes mellitus	0	0
Mother without diabetes mellitus	35	140
Number of fetuses		
singleton	35	135
twins	0	5

Crown – rump length (mm)	66.98±8.41	60.7±6
Pregnancy associated plasma protein-A (mIU/ml)	3.96±3.95	3.9±3
Free beta human chorionic gonadotropin hormone (ng/ml)	62.27±10.6	44.6±11
Nuchal translucency (mm)	0.78±0.12	0.89±0.15
Chromosomal abnormality		
Normal	32	114
Trisomy 21 and trisomy 13/18	1	26
Biochemical trisomy 21 risk	2	8
Biochemical trisomy 21 risk > 1:50	1	4
Biochemical trisomy 21 risk 1: 50 –1:100	1	4
Combinated trisomy 21 risk	1	8
Combinated trisomy 21 risk > 1:50	1	5
Biochemical trisomy 21 risk and combinated trisomy 21 risk	1	3
Just biochemical trisomy 21 risk	2	15
Just combinated trisomy 21 risk	1	5
Combinated trisomy 21 risk and trisomy 13/18 risk	0	3
Biochemical trisomy 21 risk, combinated trisomy 21 risk and trisomy 13/18 risk	0	0
Just with trisomy 13/18 risk.	0	0

5. Discussion

The prevalence of GDM in our study was 17% (33 Christian, 2 Muslim). It was estimated that worldwide about 15.1% of pregnancies were affected by GDM [19], 11.5% in Asia [20], 5.4% in Europe [21] and 5.1% in sub-Saharan Africa respectively [22].

Advanced maternal age is an independent risk factor for GDM [23]. At age group 36-40 years we have 35 (20%) examinee pregnant women 10 with GDM diabetes. At age group 41-45 years we have 6 (4%) examinee pregnant women, 2 with GDM diabetes. We concluded that predisposition to GDM diabetes mellitus is higher in advanced maternal age.

Maternal age is an established risk factor for GDM, but there is no consensus on the age above which there is significantly increased risk of GDM. In the literature, the lowest cut-off is ≥ 25 years, as recommended by the American Diabetes Association [24]. Some studies [25,26] have suggested that GDM risk increases linearly with maternal age, another studies [27] showed that the incidence of GDM increased with age, peaked at 35-39 years and then declined in women aged 40-50 years.

Furthermore, other study showed the highest age-specific prevalence of GDM in women aged 30–34 years. These contradictions detract from the provision of effective preconception counseling to women [28].

In our study we measured significant increased free β -hCG concentration has been reported in pregnant women that were diagnosed with GDM. Other study determine significant reduction in PAPP-A and free β -hCG concentrations has been reported in pregnant women that were subsequently diagnosed with GDM [29-31]. While in a more recent study, it was suggested that high free β -hCG levels in the first trimester of pregnancy decrease the risk for GDM [32]. On the contrary, in two other studies no significant association was observed between GDM and both markers [33, 34].

Nuchal translucency was decreased in pregnant women that were subsequently diagnosed with GDM diabetes mellitus. No significant difference in the NT measurement between women with GDM and NGT was observed in other study [35].

We notes that maternal weight in pregnant women with GDM diabetes mellitus is higher compared to pregnant women without GDM diabetes mellitus. Women who develop GDM have higher gestational weight gain through 24 weeks. Gestational weight gain is a significant risk factor for GDM in the overweight or obese patient but not in patients who were underweight or had a normal BMI before pregnancy [36]. The association between the rate of gestational weight gain and GDM was primarily attributed to increased weight gain in the first trimester. The association was stronger in overweight or obese and nonwhite women. High rates of gestational weight gain, especially early in pregnancy, may increase a woman's risk of GDM. Gestational weight gain during early pregnancy may represent a modifiable risk factor for GDM and needs more attention from health care providers [37].

6. Conclusion

GDM is the most common medical and metabolic complication seen in pregnancy. Women who are at high risk of developing GDM should be appropriately screened to reduce maternal and fetal morbidity. Patients with GDM are at risk of developing type two diabetes in the future and should be monitored regularly. Early diagnosis of 'diabetes in pregnancy' enables prompt evaluation and treatment. It is clear that GDM does appear to carry increased risk of perinatal complications to both the parturient and her fetus/neonate. Such risks appear to be reduced by glycemic control, which can be accomplished with diet, exercise or pharmaceutical intervention. The evolution of technologies and clinical knowledge has made it possible for such patients to experience pregnancies similar to those of the normal population, but patient management can be clinically challenging.

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