

Glycosylated haemoglobin and adverse pregnancy outcomes in women with diabetes mellitus type 1 compared to pregnancies in the general population

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Abstract: Aim: to compare pregnancy outcomes in type 1 diabetic pregnancies with the general population and the impact of glycaemic control (HbA1c) on pregnancy outcomes.

Material and methods: The study group included 55 consecutive pregnant women with type 1 diabetes who attended the Outpatient department of Endocrinology, Diabetes and Metabolic disorders in their first trimester of pregnancy. For comparison, data of 22767 deliveries in 2004 year were used, published in "Perinatal outcomes in Republic of Macedonia for year 2004". The following parameters were studied: age, maternal body mass index, diabetes duration, planning of pregnancy, HbA1c values in first, second and third trimester, pre-eclampsia, birth weight, gestational age at delivery, mode of delivery, and pregnancy outcomes (spontaneous abortions, perinatal mortality, and major congenital malformations).

Results: The perinatal mortality rate was 10,9% and congenital malformations rate was 7,3%, in type 1 diabetic pregnancies compared with 1,1% and 1,9%, respectively in the general population. Macrosomic babies were born in 9,1% of type 1 diabetic pregnancies compared with 1,01% in the general population. The caesarean section rate was 61,8% and 16,1%, respectively, and the preterm delivery rate was 25,5% and 6,1%, respectively. Pregnancies with serious adverse outcomes (spontaneous abortion, perinatal mortality and congenital malformations) were characterized by higher values of HbA1c in the first trimester of diabetes type 1 pregnancies

Conclusion: Type 1 diabetic pregnancies have worse outcomes than general population. Planning of pregnancy and rigorous glycaemic control using glucose monitoring before and during early pregnancy are crucial for better pregnancy outcomes.

Key words: pregnancy outcomes, diabetes mellitus type 1, glycosylated haemoglobin, congenital malformations.

Introduction. Diabetes is the most common pre-existing medical condition complicating pregnancy and It is known to have a substantial impact on maternal, fetal and neonatal outcomes. Women with type 1 diabetes have a poor outcome compared with women without diabetes, with increased rates of congenital malformations, pre-eclampsia, premature delivery, perinatal mortality, and risk of delivering a macrosomic baby.¹

Studies suggest that the risk of adverse outcome (malformation and perinatal mortality) is related to poor glycaemic control in early pregnancy. The critical time period for optimal glycaemic control is before 7 weeks' gestation, during early organogenesis. There is a small number of studies which examine the influence of glycaemic control on pregnancy outcomes in the second and third trimester of pregnancy.²

Glycosylated haemoglobin (HbA1c) reflects long-term glycaemic control and is a more accurate and stable measure than fasting and postprandial blood glucose levels.¹

The aim of this study was to examine the pregnancy outcomes between the pregnancies from type 1 diabetes and general population, and also the influence of HbA1c values on the risk of adverse outcome of pregnancy.

Material and methods. The study was conducted from 02.2007 to 02.2009, in the Outpatient department of Endocrinology, Diabetes and Metabolic disorders in Skopje, R. Macedonia. Fifty five consecutive pregnant women with type 1 diabetes and singleton pregnancy who enrolled in first trimester were included in this study. The following parameters were analyzed: patient's age, prepregnancy body mass index (BMI), duration of pregnancy, HbA1c in first, second and third trimester, retinopathy, nephropathy, pre-eclampsia, LGA, gestational age at delivery, mode of delivery, pregnancy outcomes (spontaneous abortion, perinatal mortality, major congenital malformation).

Patients were treated with basal-bolus insulin 4 times per day. According to glycaemic profile and HbA1c every two weeks, the insulin doses were adjusted.

Analyzed parameters were compared with the same from the general population. For that purpose were used information from perinatal results of Clinic for Gynecology and Obstetrics, Skopje, R.M.

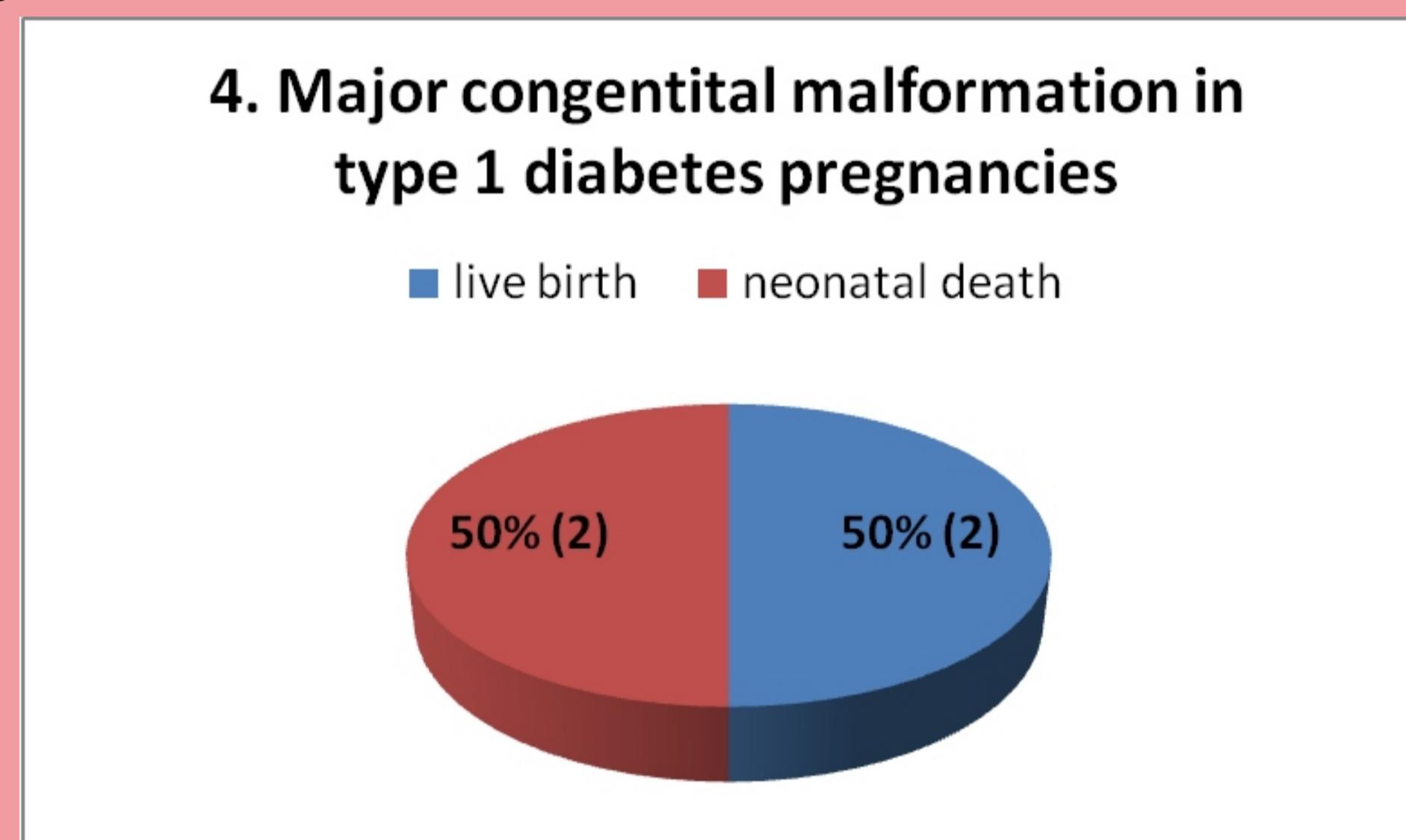
In order to understand the influence of HbA1c on the outcomes of pregnancy in patients with type 1 diabetes, we divided them: patients with adverse and normal outcome of pregnancy, and planned and not planned pregnancy.

Results.

Table 1. Obstetric complication and fetal characteristics in pregnancies with type 1 diabetes and general population

	diabetes type 1	general population	RR (95%CI)
number of patients	55	22767	
premature delivery	14 (25,5%)	1394 (6,1%)	4,2 (2,6-6,6)
sectio caesaria	34 (61,8%)	3674 (16,1%)	3,8 (3,1-4,7)
pre-eclampsia	4 (7,3%)	1115 (4,9%)	1,5 (0,6-3,8)
LGA	5 (9,1%)	231 (1,01%)	8,9 (3,8-20,9)
spontaneous abortion	4 (7,3%)	1013(4,4%)	1,6 (0,6-4,2)
perinatalen mortalitet	6 (10,9%)	253 (1,1%)	9,8 (4,6-21,1)
congenital malformation	4 (7,3%)	83 (1,9%)*	3,8 (1,4-9,9)

*83 were congenital malformation only in capital city in R.M. (from 4315 newborns).

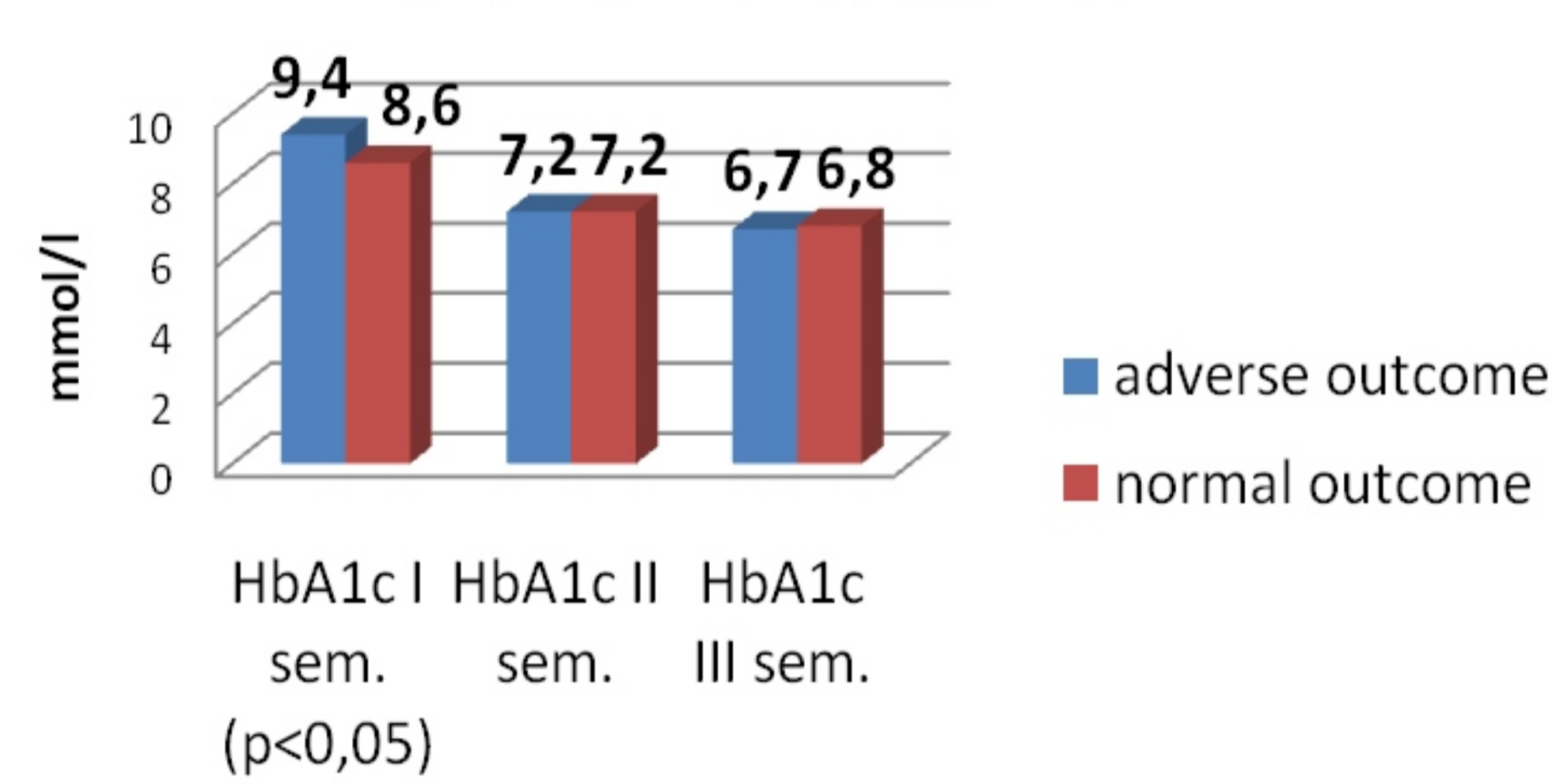


Four neonates were with major congenital malformations, two of them died.

Table 2. Outcomes from adverse and normal type 1 diabetes pregnancy

type 1 diabetes	adverse outcome	normal outcome	p
total number	8	47	
age (years)	27 (21-37)	26 (18-40)	0,47
BMI kg/m ²	23 (22-34)	24,2 (18,5-35)	0,5
diabetes duration (years)	10 (1-22)	9 (1-24)	0,76
planning pregnancy	1 (12,5%)	25 (53,2%)	0,04
HbA1c I trim	9,4 (6,2-14,6)	8,6 (5,4-12,0)	0,04
HbA1c II trim	7,2 (4,3-12,3)	7,2 (4,3-10)	0,13
HbA1c III trim	6,7 (5,7-9,4)	6,8 (4,7-8,4)	0,4
retinopathy	2 (25%)	11 (23,4%)	0,9
nephropathy	1 (12,5%)	3 (6,4%)	0,5
pre-eclampsia	-	4 (8,5%)	0,39
LGA	1 (12,5%)	4 (8,5%)	0,7

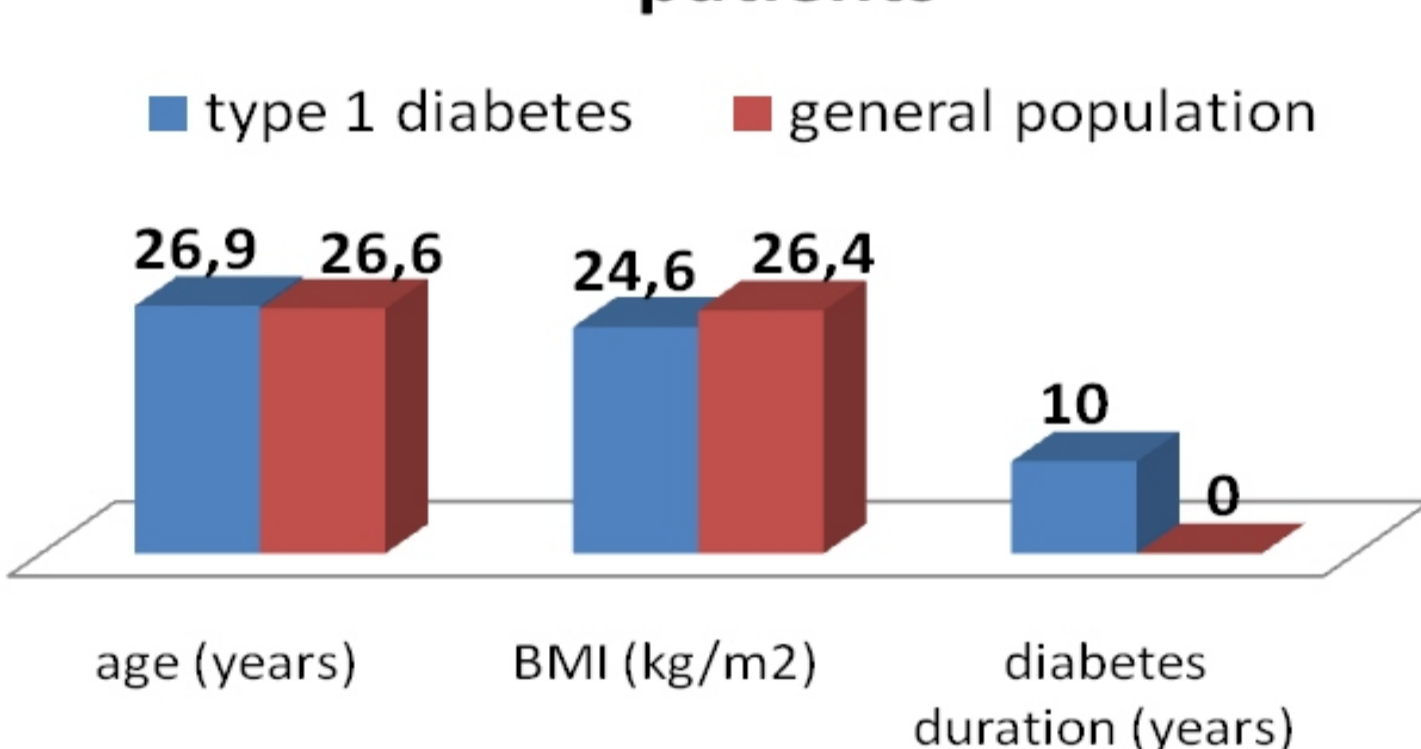
6. HbA1c comparison between type 1 diabetes pregnancies with adverse and normal outcomes



Adverse outcomes of pregnancy were associated with statistically higher values of HbA1c in the first trimester.

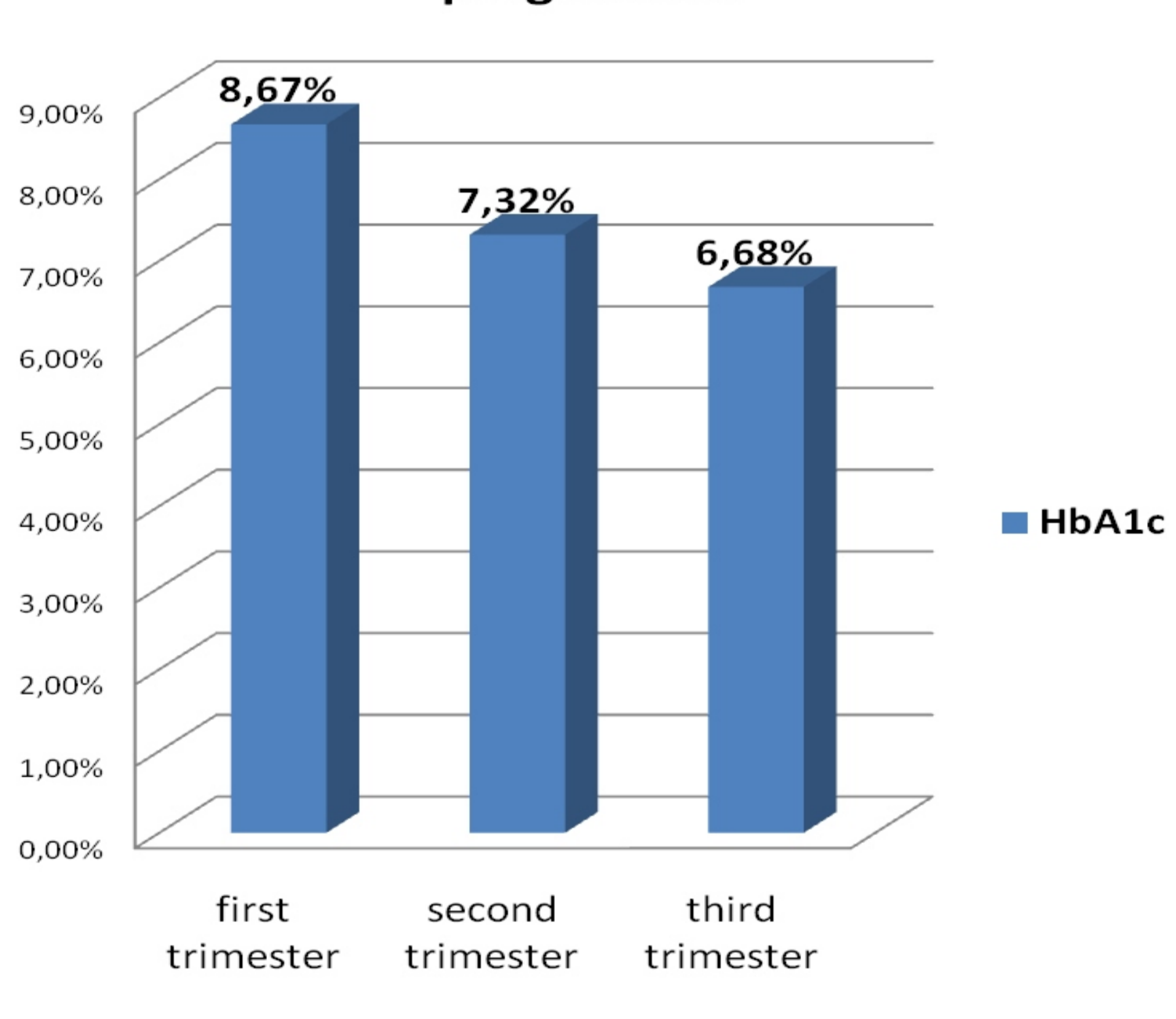
Univariate analysis showed that HbA1c in the first trimester is an independent predictor of adverse outcome of pregnancy in patients with type 1 diabetes.

1. General information for analysed patients

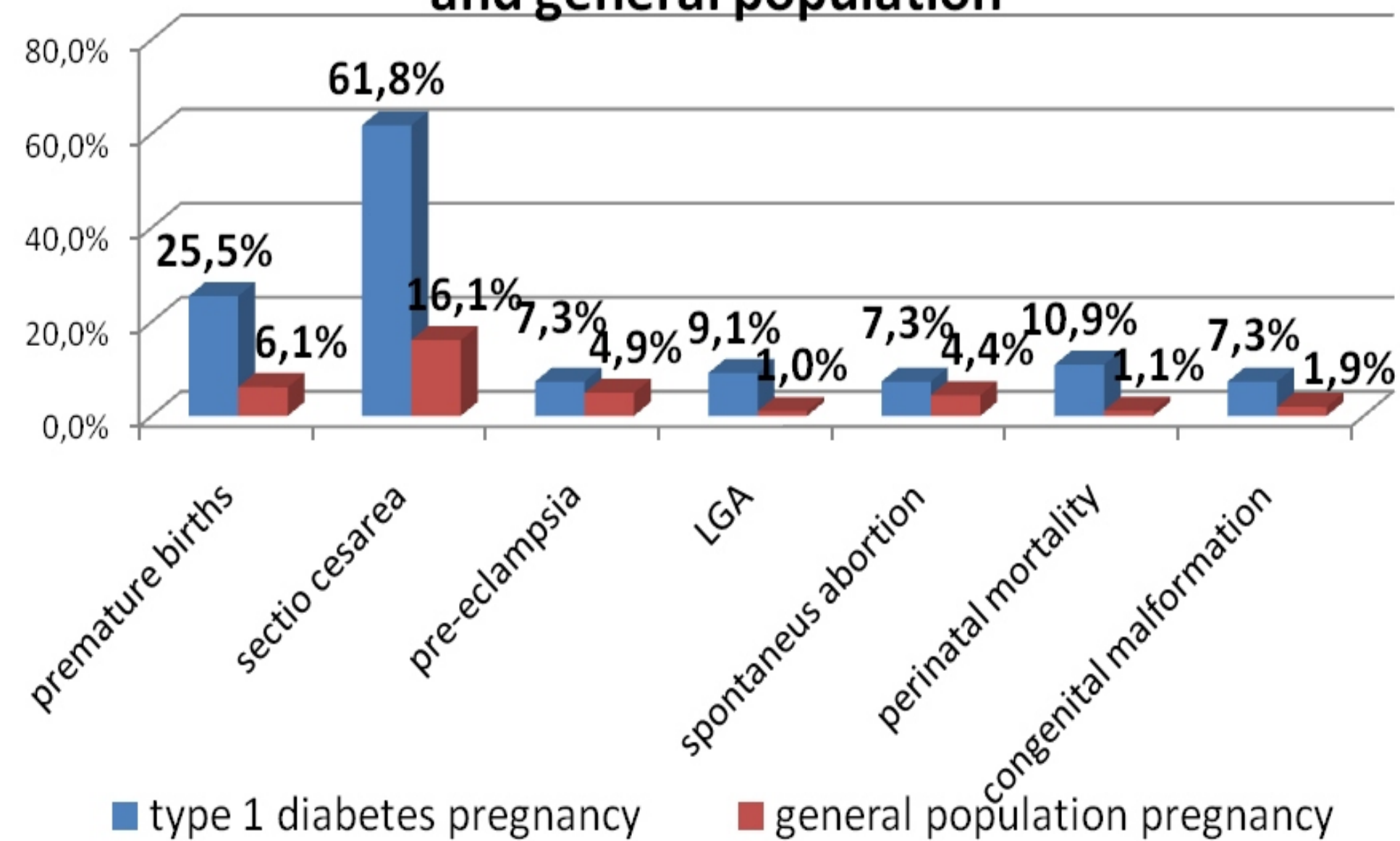


Patients with type 1 diabetes had their first visit at 9th gestational week.

2. Values of HbA1c in type 1 diabetic pregnancies

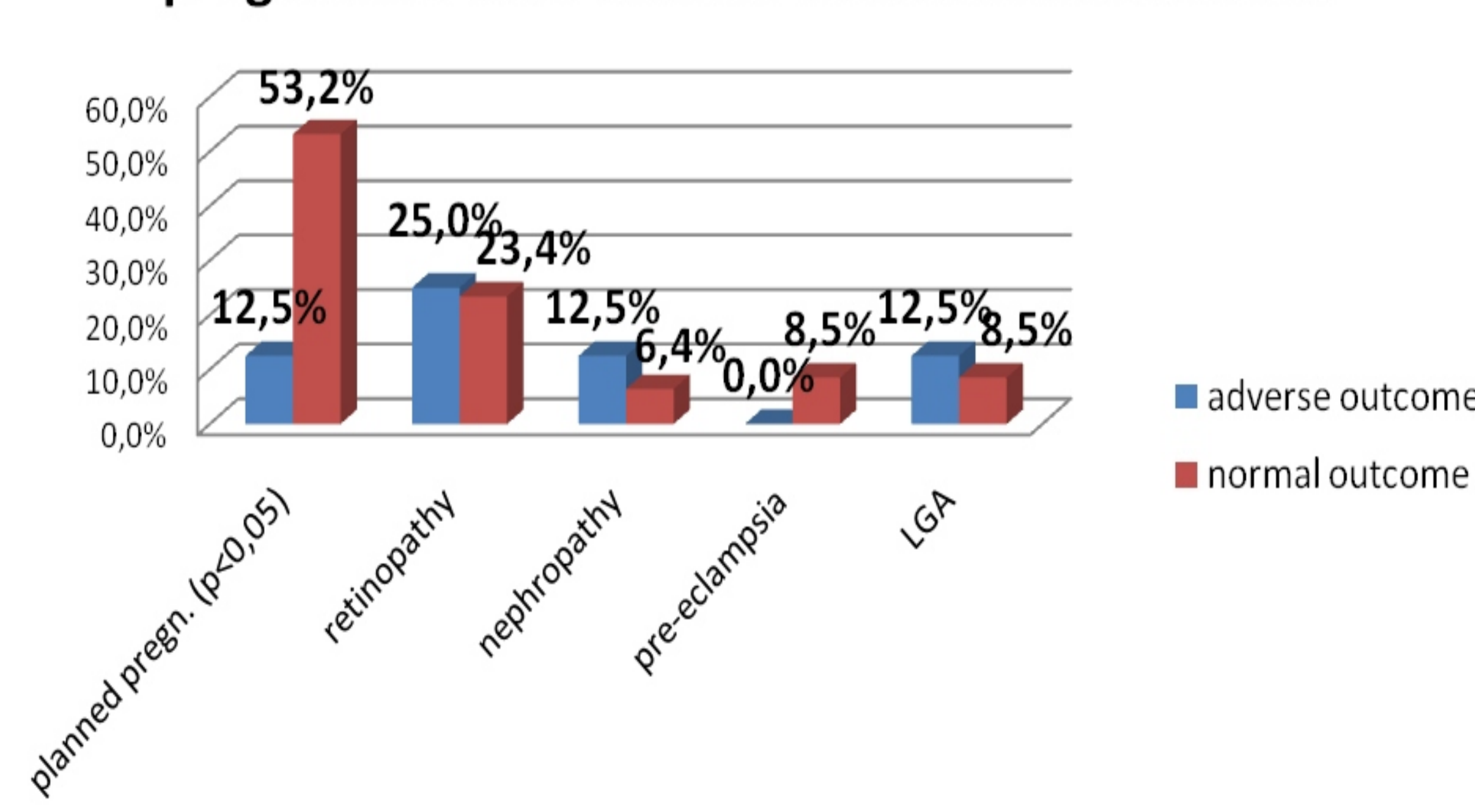


3. Pregnancies outcomes from type 1 diabetes and general population



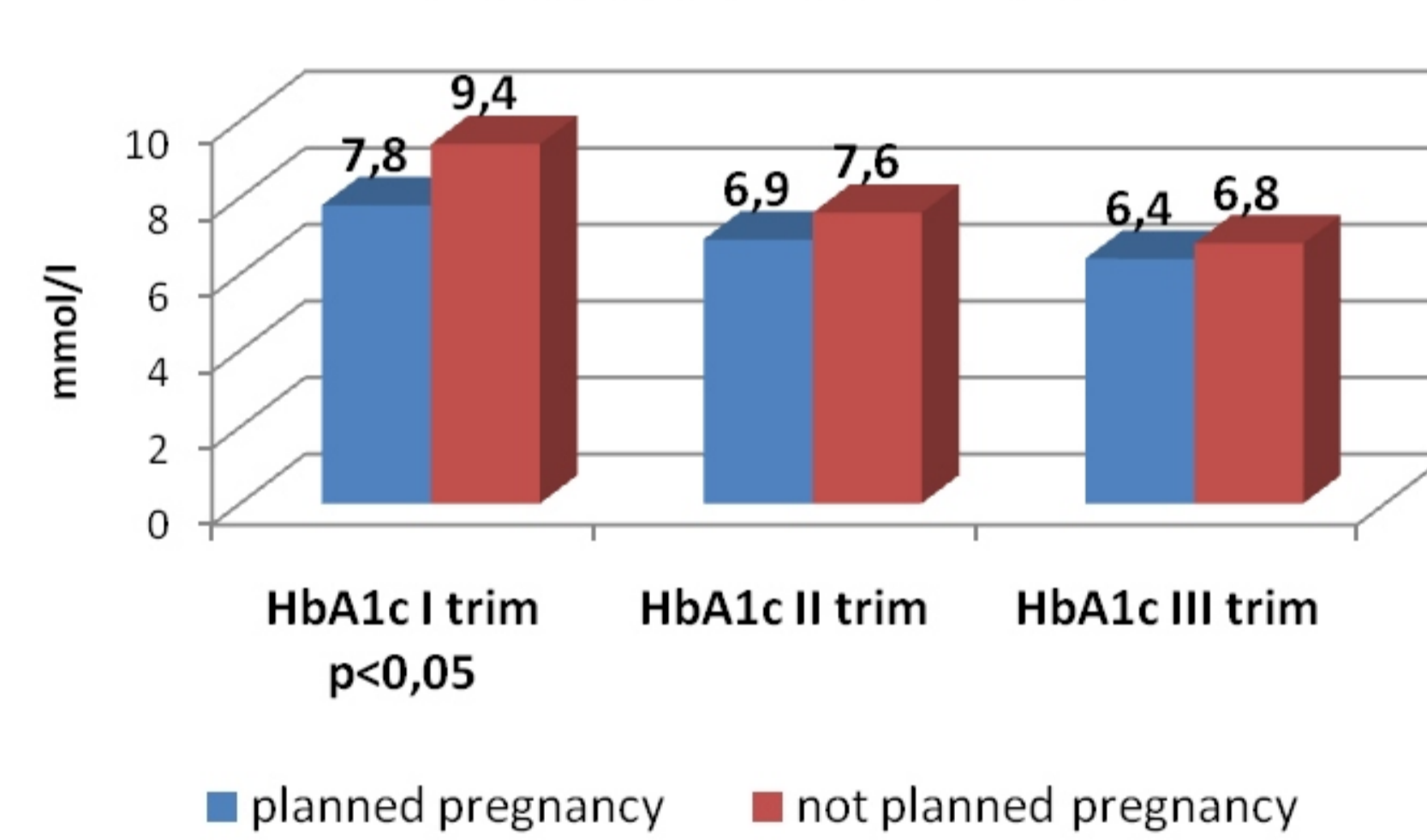
Newborns of patients with type 1 diabetes were born earlier, more often were macrosomic, more pregnancies ended by caesarean section and neonatal mortality was significantly higher than the general population.

5. Comparison between type 1 diabetes pregnancies with adverse and normal outcomes



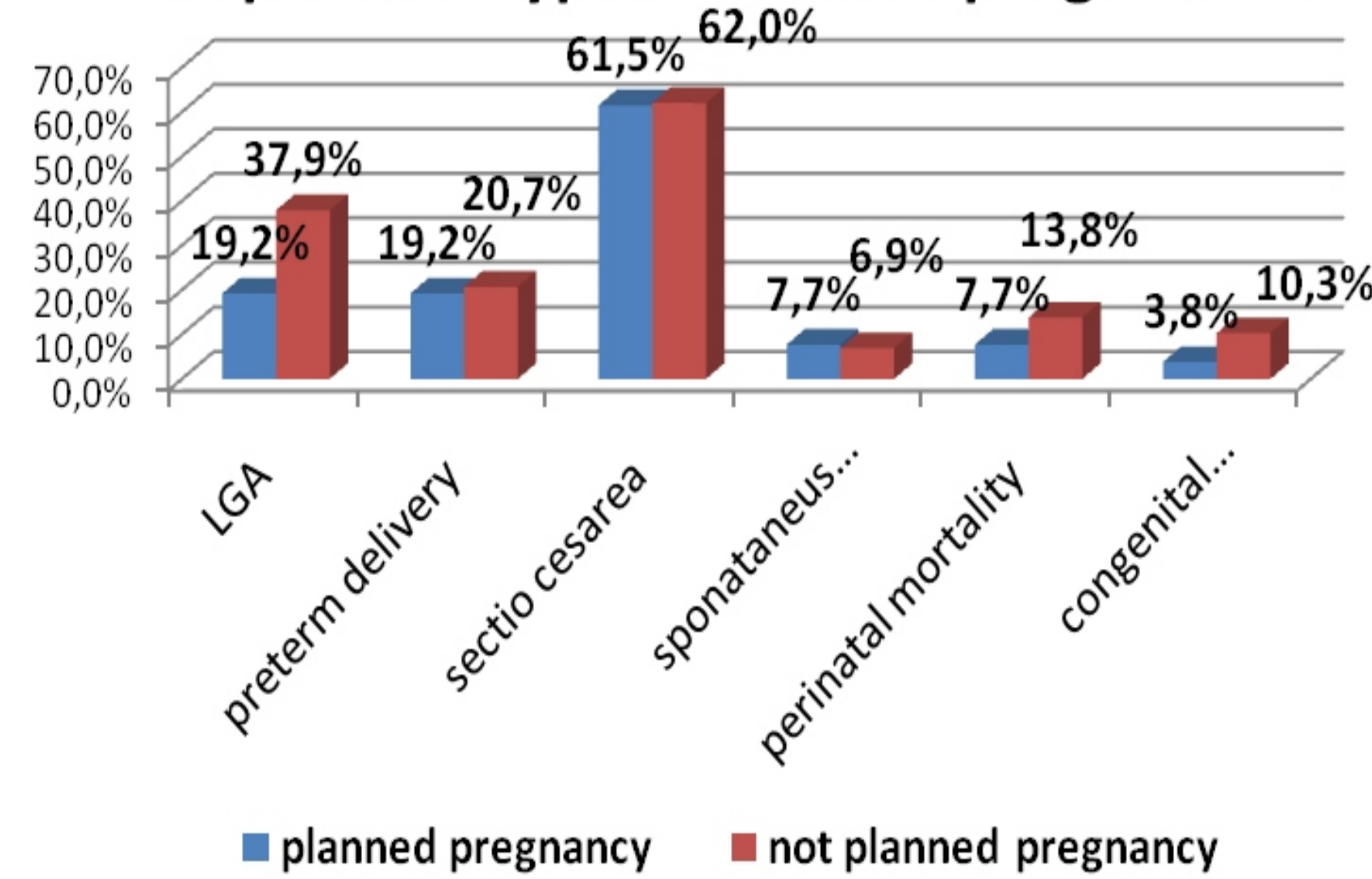
Patients with normal outcome were significantly more among women with planned pregnancy than women with an adverse outcome.

7. Comparison in HbA1c values between planned and not planned type 1 diabetes pregnancies



Women with planned type 1 diabetes pregnancies had statistically significant lower values of HbA1c in the first trimester.

8. Pregnancy outcomes from planned and not planned type 1 diabetes pregnancies



Discussion. This study revealed a high incidence of obstetric complications, spontaneous abortion, perinatal mortality, congenital malformations, preterm delivery and macrosomia compared with the general population. Perinatal mortality in this study is higher than the national Danish³ and U.K. study (10,9% vs. 5,2% and 6,8%, respectively).⁴ The difference is probably due to the small group of women with type 1 diabetes. St. Vincent declaration, as in other countries is not achieved.^{5,6,7}

Adverse outcomes of pregnancy were associated with statistically significant higher values of HbA1c only in the first trimester of pregnancy. Also, women with type 1 diabetes who had planned their pregnancy had statistically significant lower values of HbA1c in the first trimester. These data support the hypothesis that the increase in the incidence of fetal malformations and perinatal mortality among mothers with type 1 diabetes is associated with maternal hyperglycemia during organogenesis and there after, until 16-18 weeks' gestation.² Women with type 1 diabetes who were planning pregnancy had a better outcome than those who did not plan the pregnancy. Planned pregnancy provides an opportunity to correct eventually not optimal glycaemic control and achieve a normal outcome of pregnancy in type 1 diabetes. diabetes who were planning pregnancy provides an opportunity to correct eventually not optimal glycaemic control and achieve a normal outcome of pregnancy in type 1 diabetes.

Conclusion. Type 1 diabetic pregnancies have worse outcomes than the general population. Planning of pregnancy and tight glycaemic control before and during early pregnancy are crucial for better pregnancy outcomes

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