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Pregnant women may be sweeter in the summer: Seasonal changes in glucose challenge tests results. A population-based study

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ABSTRACT

Aims: A 1-hour, 50-gram glucose challenge test (GCT) is the first step in the diagnosis of gestational diabetes mellitus (GDM). Seasonal fluctuations in fasting glucose levels and GCT results were previously described. We sought to investigate seasonal changes in GCT results in a large cohort.

Methods: GCT results were analyzed of all women insured at the Central District of Clalit Health Services (the largest health maintenance organization in Israel), between the years 2005 and 2016.

Results: A total of 101,359 GCT results were analyzed. Mean GCT was 110 ± 28.9 mg/dL, and 14.5% (n = 14,652) were pathological. Both the mean and the incidence of pathological GCT were lowest in the winter, followed by spring, fall, and summer, (*p for trend* < 0.001). The difference in mean GCT between winter and summer was 7.82 ± 0.24 mg/dL (95% CI, 7.35–8.29). After adjustment for BMI and age, having a GCT in the winter was independently associated with the lowest risk for pathological GCT, as compared to all other seasons.

Conclusions: Seasonal changes in GCT results should be studied further in additional regions, and if found, the cutoff threshold for abnormal GCT should be re-examined and adapted to local weather conditions and seasonal variability.

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1. Introduction

A 1-hour, 50-gram glucose challenge test (GCT) is performed between 24 and 28 gestational weeks, as a screening tool preceding the decisive 100-g glucose tolerance test (OGTT) for the diagnosis of gestational diabetes mellitus (GDM) [1,2]. As of today, one abnormal result in OGTT is defined as an impaired OGTT and two or more abnormal results, as GDM.

GDM is strongly associated with short- and long-term health risks for the mother, developing fetus, and offspring. Women with GDM are at higher risk for developing metabolic and cardiovascular diseases later in life [3], female malignancies [4] and ophthalmic diseases [5]. GDM also carries significant long-term risks for offspring, such as diabetes [6] and respiratory diseases [7].

Although GCT is used as a screening test only, recent studies have found an association between an abnormal result

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(>140 mg/dl, 7.8 mmol/L) and future type-2 diabetes and cardiovascular diseases [8]. Even glucose levels within the *high-normal* GCT range were found to be associated with future dysglycemia [9]. Some, but not all studies, have shown seasonal variations in mean GCT results, with a significantly higher mean GCT during summer as compared to winter [10,11]. The aim of this study was to evaluate the seasonality of GCT results in a large population-based cohort of pregnant women, over a 11-year period, and additionally address seasonality in OGTT results.

2. Subjects

This population-based retrospective cohort study included all pregnant women who underwent GCT between the years 2005 and 2016 at the Central District of Clalit Health Services, the largest health maintenance organization in Israel.

The study was approved by the Clalit Health Services Ethical Board (Approval No.0142-17, August 2017).

3. Methods

Data on age, pre-pregnancy body-mass index (BMI), GCT and OGTT results were obtained from the District's computerized database. GCT and OGTT results were subjected to both continuous and dichotomous analyses, defining a GCT cutoff value of 140 mg/dL as the screening threshold preparatory to subsequent OGTT. The OGTT cutoff values were defined as follow: fasting glucose <95 mg/dL, at 60′ <180; at 120′ <155; at 180 < 140 mg/dL. OGTT results were categorized as abnormal if 2 or more results were above the cutoff values. Dates of tests results were recorded according to calendric months. The months were categorized into 4 seasons, according to the local weather, as follows: winter (November to March), spring (April and May), summer (June to August), and autumn (September to October). Dummy variables were used for seasonal comparisons, with winter defined as the reference season. Additionally, the hot seasons were combined (summer and spring) and compared to the cold seasons (winter and autumn). Lastly, multivariable Generalized Estimating Equation binary logistic and linear models were used to study the seasonality effect while adjusting for maternal BMI and age.

4. Results

A total of 101,359 GCT results (of 59,882 women) were analyzed. The mean GCT was 110 ± 28.9 (range 38–374) mg/dL, and in 14.5% (*n* = 14,652) of the cohort the result was pathological. Mean women's age was 29.4 ± 51, and their BMI categories were as follow: 4864 (8.1%) were with BMI < 18.5; 35,863 (59.8%) were with normal BMI (18.5–24.99) and 19,212 (32.0%) were overweight or obese (BMI ≥ 25).

Both the mean value and the incidence of pathological GCT varied depending on the season in which the test was performed, and were lowest in the winter (Fig. 1), followed by spring, fall, and summer, (*p for trend* < 0.001). The difference in mean GCT between winter and summer was 7.82 ± 0.24 mg/dL (95% CI, 7.35–8.29). In multivariable models (presented in the Table 1), after adjustment for BMI and age, having a GCT in the winter was independently associated with the lowest risk for pathological GCT, as compared to the other seasons, e.g., in the summer as compared to the winter: adj. OR = 1.58; 95%CI 1.51–1.66. Results remained similar when comparing warm seasons (summer and spring) to the cold seasons (winter and fall): 16.2% and 13.1% GCTs were pathological in the warm and cold seasons, respectively (OR = 1.28; 1.23–1.32, p < 0.001; age and BMI adj. OR = 1.27; 1.23–1.31, p < 0.001).

Out of the women performing the GCT, 15,893 performed OGTT. Of them, 1801 (11.3%) had two pathological tests: 491 (10.8%) of winter tests were pathological, and 295 (11.6%), 566 (12.0%), 449 (11.0%) were pathological in the spring, summer and fall respectively. There were no significant differences in rates of pathological tests results between the seasons (p = 0.24). Results remained similar when comparing warm seasons (summer and spring) to the cold seasons (winter and fall): 11.3% and 11.2% were pathological in the warm and cold seasons, respectively (OR = 1.1; 0.97–1.24, p = 0.15, age and BMI adj. OR = 1.09; 0.97–1.24, p = 0.16).

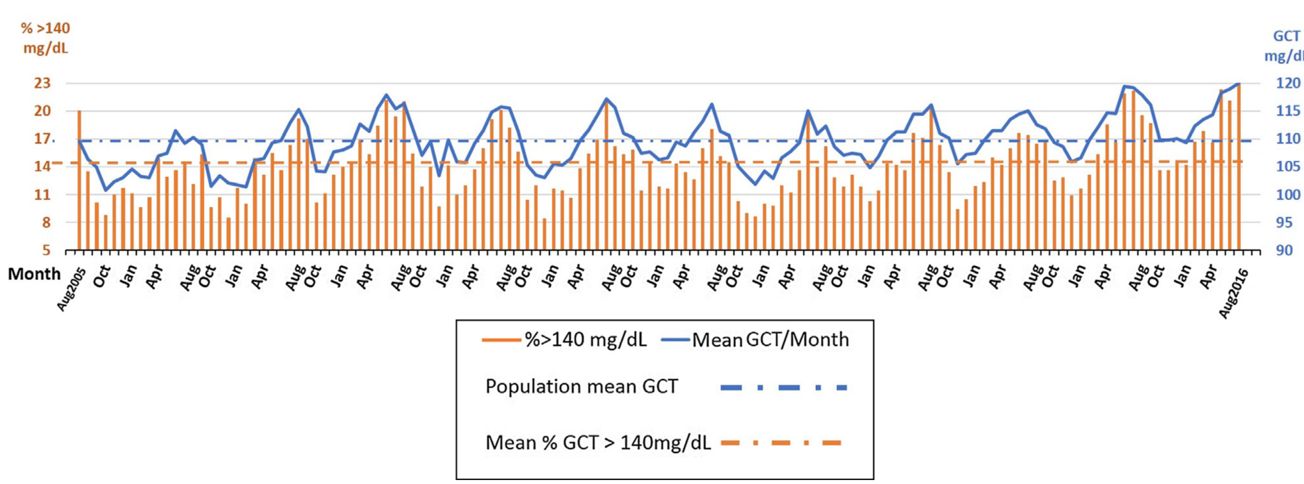

Fig. 1 – Monthly mean GCT and the incidence of abnormal GCT. GCT results and the percent of abnormal GCT were significantly higher when performed in the summer as compared to tests performed in the winter.

Table 1 – Mean glucose challenge test results and incidence of abnormal results by seasons.

	GCT mg/dL		>140 mg/dL		
	Mean ± SD	Beta; p	*n* (%)	OR; 95%CI	Adjusted OR; 95%CI
Winter	106.28 ± 28.46	1 (Reference)	3704 (11.8)	1 (Reference)	1 (Reference)
Spring	109.72 ± 28.76	0.045; <0.001	2522 (14.2)	1.244; 1.178–1.314	1.22; 1.14–1.30
Summer	114.11 ± 29.17	0.12; <0.001	4691 (17.4)	1.582; 1.511–1.658	1.59; 1.51–1.68
Fall	110.42 ± 28.79	0.065; <0.001	3735 (14.8)	1.296; 1.235–1.361	1.31; 1.24–1.39
BMI		<−0.001; 0.83			1.066; 1.061–1.070
Age		0.181; <0.001			1.069; 1.064–1.073

GCT, glucose challenge test: OR, odds ratio; SD, standard deviation.

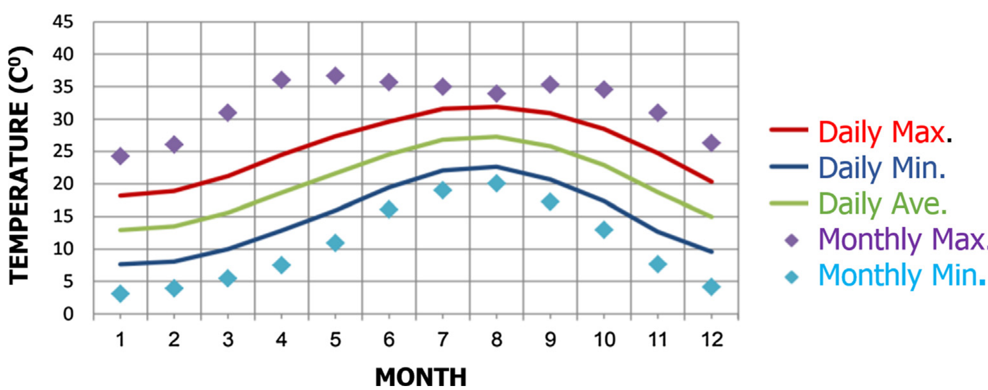

Fig 2 – Average monthly temperature in the central district of Israel. In November-March, temperatures were notably lower than in June-August and were in direct correlation to monthly GCT results.

5. Discussion

In this large cohort of low risk pregnant women, mean GCT results during the winter were significantly lower than in the other seasons (mean difference of 7.8 ± 0.2 mg/dL between the summer and winter), with an age- and BMI-adjusted odds ratio of 1.58 for obtaining a pathological GCT result in the summer as compared to the winter. Seasonal fluctuations were not found in abnormal OGTT results. The fluctuating seasonal results found in the current study correspond with the average monthly ambient temperature in the central district of Israel [12] (Fig. 2), which support the possible correlation between the tests results and the temperature. Our findings regarding the seasonality in GCT results, suggest different cutoff points should be applied according to seasonal changes. Although OGTT results seem to be unaffected by seasonality, applying different GCT cutoff points based on the season may prevent unnecessary OGTT testing, with its financial and maternal emotional burden.

Seasonal trends have been noted regarding other obstetrical complications such as preterm delivery [13], placental abruption [14] and preeclampsia [15,16].

Seasonal changes in fasting glucose and in type 1 Diabetes mellitus [17,18] have been previously reported. The exact mechanism by which cold or hot ambient temperature changes glucose and insulin metabolism, remained unclear. Several theories have been suggested: relative dehydration causing hemoconcentration in the summer, difference in hormones release based on ambient temperature, vasodilatation due to hot temperature causing changes in insulin resistance, seasonal changes in gut microbiome [19], and more. Another possible mechanism might be the activation of brown adipose tissue at low temperatures and its role in whole-body glucose homeostasis, energy expenditure and insulin sensitivity [20]. Body exposure to cold temperature has been shown to result in increased glucose disposal in brown adipose tissue, decreased plasma glucose levels and improved insulin sensitivity [21].

Our study has several limitations: The study results, although being of a large cohort, represent only the population of one district in Israel with a relatively similar socioeconomic status, and we do not have nationwide GCT results. Perinatal outcomes, as well as long term maternal health status were unavailable, therefore the clinical significance of the seasonal changes in GCT results is unclear.

Whether seasonal changes in GCT results are present in other countries need to be investigated. If indeed found, in order to preserve the traditionally established specificity and sensitivity of GCT, it seems that the cutoff threshold for abnormal GCT should be re-examined and, if necessary, adapted to local weather conditions and seasonal variability.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2018.11.020.

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