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The Relationship between Metabolic Indicators in the First Trimester of Pregnancy and Gestational Diabetes: the Lipid Accumulation Products and Visceral Adiposity Index

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Abstract: ***Objective: The aim of this study was to research the place of lipid accumulation product (LAP; includes waist circumference (WC) and triglycerides) and visceral adiposity index (VAI; includes WC, triglycerides, and high-density lipoprotein), which are calculated in the first trimester for prediction of gestational diabetes mellitus (GDM). Methods: The LAP and VAI values of 134 women were calculated during the first prenatal visit, and they were followed until the 24th week of pregnancy. Comparisons were performed with regard to these values between women with a diagnosis of GDM (GDM group) and women in whom GDM was not detected (group with normal glucose metabolism). The correlations of these indices with metabolic parameters, anthropometric measurements, and demographic data were evaluated. Results: There were no differences in VAI or LAP index between the groups (p=0.12). VAI had positive correlation with weight gain, hip circumference (HC), insulin, and HOMA-IR. LAP exhibited positive correlation with age, body mass index, HC, total cholesterol, low-density lipoprotein, pregnancy, weight gain, parity, and HOMA-IR. Conclusion: A relationship between GDM development and VAI and LAP indices calculated in the first trimester could not be determined. Thus, these metabolic indices might not be a good indicator for GDM.***

Keywords: Pregnancy, Diabetes, Lipid Accumulation Product

1. Introduction

Gestational diabetes mellitus (GDM) is a major health problem that causes maternal and fetal risks. High body mass index (BMI), previous macrosomic baby, previous GDM, family history of diabetes, and origin family with a high prevalence of diabetes are defined as risk factors for GDM. The use of these risk factors is recommended when determining which pregnant women to test for GDM in the early weeks of pregnancy (1). However, this association does not mean that pregnant patients who not have these risk factors are protected against GDM. Parous women with a negative history of GDM and nulliparous women could still be at risk for GDM. In these pregnancies, it is important to be able to predict GDM with a simple, easily accessible, inexpensive, and comfortable test that can provide an early diagnosis without waiting until the 24th week (2).

Obesity is a significant risk factor for diabetes mellitus and metabolic disorders (3). It has been shown that adipose tissue deposited in the visceral compartment is mainly responsible for metabolic side effects. By provoking inflammation, cytokines released from visceral adipose tissue lead to increased oxidative stress followed by endothelial damage (4). Lipid accumulation product (LAP), an index of central lipid accumulation, is composed of waist circumference (WC) and fasting triglyceride (TG) concentration (5). It has been suggested that elevated LAP value is associated with cardiovascular risk factors (5) and metabolic conditions such as diabetes (6). Because LAP index is especially a useful risk marker for identifying young women with abnormal glucose regulation (7), it is suggested that it might also be a reliable marker for GDM in pregnant patients.

The AlkaMeSy Study Group identified visceral adiposity index (VAI) as an indicator of visceral fat function. They claimed that VAI is significantly correlated with all metabolic syndrome factors, such as altered production of adipocytokines, increased lipolysis, and plasma free fatty acids, which are not signified by BMI, WC, TG, or high-density lipoprotein (HDL) separately (8). Therefore, VAI might be a valuable index of fat distribution and function, as well as a good predictor of diabetes and cardiometabolic risk (8, 9).

Simple screening tests/indicators that allow the early identification of the greatest possible population of pregnant women who might have deteriorating glucose regulation is needed in order to reduce the incidence of GDM and associated metabolic disorders without waiting until the 24th week of pregnancy and without exposure to an irritating test (10). I also aimed to research the relationship between and the place of LAP and VAI measurements, which are simple, cheap, and comfortable methods for predicting GDM in the early stages of gestation.

2. Materials and Methods

Study design

This prospective study was carried out in Merkezefendi State Hospital with approval from the Ethical Committee of Celal Bayar University. One hundred thirty-four patients, 16–39 years of age, with singleton pregnancies at 6–13 weeks gestation were included in the study. Informed consent was obtained from all patients before being including in the study. Exclusion criteria were diagnosis of Type 1 or Type 2 diabetes mellitus, hypertension,

hyperlipidemia, any other metabolic disease, and chronic drug use. At the first prenatal examination, a one-hour 50-g oral glucose challenge test (GCT) was administered to patients with fasting blood glucose (FBG) levels ≥105 mg/dL, patients with BMIs ≥30, patients with GDM and/or history of macrosomic baby delivery (≥4000 gr), and patients whose mother or father had a history of diabetes mellitus. A three-hour 100-g oral glucose tolerance test (OGTT) was administered to patients with GCT≥140 mg/dL. Patients with high 2 values on the OGTT were considered to have Type 2 diabetes mellitus and excluded from the study.

Measurements

Weights and heights were measured with the patient wearing light clothing and without shoes. BMI was calculated using the formula weight (kg) / height $(m)^2$. WC was measured from the middle point of the border of the iliac crest and the last costa after normal expiration with the patient in a straight position. Hip circumference (HC) was measured where it protruded the most. Using an automated sphygmomanometric procedure, blood pressure was determined with two measurements taken five minutes apart after resting in a seated position for at least five minutes. The average of the two measurements was taken.

FBG, total cholesterol (TC), TG, HDL, low-density lipoprotein (LDL), and insulin levels were obtained from morning preprandial blood. To evaluate insulin resistance, homeostatic model assessment of insulin resistance (HOMA-IR) was calculated using the formula [FBG (mg/dl)/18 x fasting serum insulin (mU/L)]/22.5.

The GCT was performed in the 24th gestational week regardless of whether or not the patient had fasted. Participants with GCT <140 mg/dL were considered to have normal glucose metabolism. The OGTT was administered to patients with GCT ≥140 mg/dL between 8:00 and 9:00 AM, after fasting for eight hours. After obtaining the FBG, glucose levels at the first, second, and third hour were determined. Cutoff values were accepted as FBG ≥105 mg/dL, first hour ≥190 mg/dL, second hour ≥165 mg/dL, and third hour ≥145 mg/dL. Patients with two high results were diagnosed as GDM.

LAP index was determined using the formula (WC –58) × TG (5). VAI was determined using the formula [WC/36.58 + (1.89 × BMI)] × (TG/0.81) × (1.52/HDL) (8). TG and HDL levels as mmol/L and WC as cm were introduced in the formulas.

Statistical Analysis:

Statistical package SPSS for Windows 16.0 (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL) was used to analyze the data. The Mann–Whitney U test was used for comparisons between the GDM and normal glucose metabolism groups. Mean and standard deviations were used to describe data. Pearson's correlation coefficient was used to evaluate the relationships between metabolic and anthropometric measurements and between LAP and VAI. A *p* value of 0.05 was considered to be statistically significant.

3. Results

Four of the 134 pregnant women included in the study were excluded due to spontaneous abortion, and 16 patients were excluded when they left gestational follow up before the 24th week. In addition, 19 patients who reached the 24th gestational week did not pass the GCT.

Seven (7.36 %) of the final 95 pregnant women included in the study were diagnosed with GDM and comprised the GDM group. The other 88 women comprised the normal glucose metabolism group. The flow chart of the study is presented in Figure 1.

One patient was determined to have metabolic syndrome according to the classification system established in 2005 by the International Diabetes Federation, and consequently, she was not diagnosed with GDM.

There was no difference between the groups in terms of gestational weeks at the first prenatal visit (p=0.19). Age, pregnancy, and parity were significantly higher in the GDM group than in the group with normal glucose metabolism (p=0.006, p=0.03, and p=0.01, respectively). There were no differences in blood chemistry analysis, anthropometric measurements, or blood pressure levels between the groups. There was no statistically significant difference in VAI and LAP indices between the groups (p=0.12). The baseline characteristics and VAI and LAP index of the normal glucose metabolism and GDM groups are presented in Table 1.

VAI exhibited a positive correlation with the parameters that constitutes the formula (p<0.001) and with weight gain (p=0.002), HC (p<0.001), insulin (p=0.03), and HOMA-IR (p=0.01). LAP index exhibited a positive correlation with age, BMI, HC, TC, LDL, and the parameters that constitute the formula (p<0.001), as well as pregnancy, weight gain (p=0.01), parity (p=0.02), and HOMA-IR (p=0.03). There was a positive correlation between LAP and VAI (r=0.790, p<0.001). The correlations of the indices with the metabolic parameters, anthropometric measurements, and demographic data are presented in Table 2.

4. Discussion

To my knowledge, this is the first study to investigate the possibility of using the VAI and LAP indices to predict GDM at the first prenatal visit. The likelihood of GDM was increased by higher age, gravidity, and parity. Although I found a positive correlation between these three parameters and LAP index, and between LAP index and VAI index, we could not detect any significant correlation between the two indices and GDM.

Weight at the beginning of pregnancy and weight gain seriously influences maternal metabolism during pregnancy (11-12). Recent research has shown that pre-pregnancy obesity and excessive gestational weight gain are risk factors for GDM (13,14). Increased adipose tissue in obese people has been recognized not only as a storage compartment for unconsumed energy, but also as a contributor of several factors involved in endocrine regulation (15). A recent study

claimed that the part of fat tissue that has endocrine function is visceral fat tissue. Cytokines released from visceral fatty tissue lead to metabolic disorders (4). In the present study, the GDM group exhibited no statistically significant increase in LAP, which has been defined as "an index of central lipid accumulation" (5), or in VAI, which has been defined as "are presentation marker of adipose tissue dysfunction" (8). However, it has recently been reported that WC, which is a component of both indices, is not able to assess visceral fat tissue, the principal mediator of endocrinological functions, specifically, as is the case with BMI. WC measures not only visceral adipose tissue, but also subcutaneous adipose tissue, which is another component of abdominal fat mass (16). In other words, visceral fat tissue measurements can be significantly different among women with the same WC value (17). Failure to assess the visceral component specifically when measuring WC and BMI could be a reason for the lack of any correlation between these two metabolic indices and GDM.

It is known that TG level is significantly elevated in patients with GDM compared with patients without insulin resistance. This difference in TG level continues throughout the three trimesters of pregnancy. In addition, HDL levels are lower in patients with GDM compared patients without GDM in the second and third trimesters of pregnancy. There are no differences in TC or LDL levels between patients with GDM and patients without insulin resistance (18). Gür et al. (19) reported that the group that developed GDM later in pregnancy only had elevated triglyceride levels among all the biochemical markers studied in the first trimester. They found no differences in TC, HDL, or LDL. Despite the similar number and characteristics of the pregnant subjects in that study compared with our participants, that study had a greater percentage of patients with metabolic syndrome. Studying a lower risk group might have led to the failure to detect a difference in TG level between the groups.

A study performed in 2810 Korean non-pregnant women aged 18–39 years showed that the LAP index could be useful for identifying young Korean women with abnormal glucose regulation (7). Another study was conducted on the basis of the hypothesis that LAP might be related to glucose dysregulation in pregnancy, as it is a reliable marker of glucose regulation in young people. It was concluded that the LAP index determined at the first prenatal visit was correlated with insulin resistance and subsequent gestational hyperglycemia in the second trimester. However, that study did not assess the relationship between clinical hyperglycemia/GDM and LAP (20). As for VAI, a study was conducted to answer the question of whether GDM could be predicted in a subsequent pregnancy by VAI index during the preconception period; unfortunately, that study failed to show any statistically significant correlation (21). My study did not attempt to assess the correlation of these two indices with glucose levels in the second trimester, but it aimed to investigate whether they were sufficient enough to predict GDM. While these numerical markers might be correlated with increased insulin resistance or elevated glucose levels, they might not have sufficient power to determine women with glucose levels exceeding the cutoff levels, and thus who will have GDM.

Especially in the LAP index, a very different result that leads to high standard deviation levels were obtained from participants similar to the study of Harville et al. (21). This situation may be another factor which prevents statistical significance. In addition, higher LAP levels were obtained in our study compared to study of Harville et al. (21). I believe that it may be caused by racial differences.

The power of the study is that it is a prospective study in which data was collected until the 24th–28th week of pregnancy. The main limitation is the relatively small number of participants and the small number of patients with GDM, which might be another reason for the failure to establish a correlation between these two indices and GDM.

5. Conclusion

In conclusion, among women at low risk for GDM development, this study failed to show any correlation between GDM development and VAI and LAP indices, which are simple, inexpensive, and easy to compute metabolic indicators among others. It is essential to understand in finer detail the metabolic factors affecting these two markers. There is a need for prospective studies with larger sample sizes to determine simple screening tests that are beneficial for predicting GDM early in pregnancy.

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References

[1] The Guideline Development Group. Management of diabetes from preconception to the postnatal period: summary of NICE guidance. BMJ 2008;336:714–717.
[2] American Diabetes Association. Standards of medical care in diabetes--2009. Diabetes Care 2009;32:13-61.
[3] Ehrenberg HM, Mercer BM, Catalano PM. The influence of obesity and diabetes on the prevalence of macrosomia. Am J Obstet Gynecol 2004191: 964–968.
[4] Berg AH, Scherer PE. Adipose tissue, inflammation, and cardiovascular disease. Circulation Research 2005;96:939–949.
[5] Kahn HS. The ''lipid accumulation product'' performs beter than the body mass index for recognizing cardiovascular risk: a population-based comparison. BMC Cardiovasc Disord 2005;5:26.
[6] Kahn HS. The lipid accumulation product is better than BMI for identifying diabetes: a population-based comparison. Diabetes Care 2006;29:151–153.
[7] Oh JY, Sung YA, Lee HJ. The lipid accumulation product as a useful index for identifying abnormal glucose regulation in young Korean women. Diabet Med 2013;30:436-442.
[8] Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, Galluzzo A; AlkaMeSy Study Group. Visceral Adiposity Index: a reliable indicator of visceral fat function associated with cardiometabolic risk. Diabetes Care 2010;33:920–922.

[9] Bozorgmanesh M, Hadaegh F, Azizi F. Predictive performance of the visceral adiposity index for a visceral adiposity-related risk: type 2 diabetes. Lipids Health Dis 2011;10:88.
[10] Lindsay RS. Gestational diabetes: costs and consequences. Diabetologia 2011;54:227–229.
[11] Zhang S, Rattanatray L, MacLaughlin SM, Cropley JE, Suter CM, Molloy L, Kleemann D, Walker SK, Muhlhausler BS, Morrison JL, McMillen IC. Periconceptional undernutrition in normal and overweight ewes leads to increased adrenal growth and epigenetic changes in adrenal IGF2/H19 gene in offspring. FASEB J 2010; 24: 2772–2782.
[12] Dodd JM, Turnbull D, McPhee AJ, Deussen AR, Grivell RM, Yelland LN, Crowther CA, Wittert G, Owens JA, Robinson JS; LIMIT Randomised Trial Group. Antenatal lifestyle advice for women who are overweight or obese: LIMIT randomised trial. BMJ 2014; 348: g1285.
[13] Li N, Liu E, Guo J, Pan L, Li B, Wang P, Liu J, Wang Y, Liu G, Baccarelli AA, Hou L, Hu G. Maternal prepregnancy body mass index and gestational weight gain on pregnancy outcomes. PLoS One 2013; 8: e82310.
[14] Alberico S, Montico M, Barresi V, Monasta L, Businelli C, Soini V, Erenbourg A, Ronfani L, Maso G; Multicentre Study Group on Mode of Delivery in Friuli Venezia Giulia. The role of gestational diabetes, pre-pregnancy body mass index and gestational weight gain on the risk of newborn macrosomia: results from a prospective multicentre study. BMC Pregnancy Childbirth 2014;14:23.
[15] Galic S, Oakhill JS, Steinberg GR. Adipose tissue as an endocrine organ. Mol Cell Endocrinol 2010;316:129-139
[16] Warming L, Ravn P, Christiansen C. Visceral fat is more important than peripheral fat for endometrial thickness and bone mass in healthy postmenopausal women. Am J Obstet Gynecol 2003;188:349-353
[17] Fernández Muñoz MJ, Basurto Acevedo L, Córdova Pérez N, Vázquez Martínez AL,Tepach Gutiérrez N, Vega García S, Rocha Cruz A, Díaz Martínez A, Saucedo García R, Zárate Treviño A, González Escudero EA, Degollado Córdova JA. Epicardial adipose tissue is associated with visceral fat, metabolic syndrome, and insulin resistance in menopausal women. Rev Esp Cardiol 2014;67:436-441.
[18] Ryckman KK, Spracklen CN, Smith CJ, Robinson JG, Saftlas AF. Maternal lipid levels during pregnancy and gestational diabetes: a systematic review and meta-analysis. BJOG 2015;122:643-651.
[19] Gur EB, Ince O, Turan GA, Karadeniz M, Tatar S, Celik E, Yalcin M, Guclu S. Ultrasonographic visceral fat thickness in the first trimester can predict metabolic syndrome and gestational diabetes mellitus. Endocrine 2014;47:478-484.
[20] Brisson D, Perron P, Kahn HS, Gaudet D, Bouchard L. The lipid accumulation product for the early prediction of gestational insulin resistance and glucose dysregulation. J Womens Health (Larchmt) 2013;22:362-367.
[21] Harville EW, Juonala M, Viikari JS, Raitakari OT. Preconception metabolic indicators predict gestational diabetes and offspring birthweight. Gynecol Endocrinol 2014;30:840-844.

Table 1: Baseline characteristics, VAI (visceral adiposity index) and LAP (lipid accumulation product) index of pregnancies in GDM and normal glucose metabolism groups. Values are presented as mean±SD (Standard Deviation). $p<0.05$ was considered statistically significant

	GDM (n=88) %92,64 mean±SD	Normal Glucose Metabolism (n=7) %7,36 mean±SD	*P*
Age (years)	32.71±5.85	26.97±5.02	**0.006**
Pregnancy	2.85±1.34	2.06±1.10	**0.03**
Parity	1.57±0.97	0.82±0.70	**0.01**
Pregnancy week	8.42±2.22	9.27±2.58	0.19
BMI (kg/m2)	29.21±5.61	26.01±4.76	0.07
Weight gain (kg)	5.76±2.77	6.51±2.83	0.28
Waist circumference (cm)	83.85±11.81	78.56±9.81	0.12
Hip circumference (cm)	107.29±8.75	102.06±9.19	0.05
Systolic blood pressure (mmHg)	111.43±10.69	107.55±11.22	0.18
Dyastolic blood pressure (mmHg)	71.42±8.99	69.88±7.42	0.30
Blood Chemistry Analysis			
FBG (mg/dL)	87.71±8.22	85.34±8.81	0.20
TC (mg/dL)	176.57±19.04	158.47±33.66	0.06
TG (mg/dL)	128.29±74.41	99.61±40.08	0.17
HDL (mg/dL)	52.14±5.08	55.36±12.66	0.25
LDL (mg/dL)	98.71±10.12	85.25±27.68	0.05
İnsulin (mU/L)	10.28±5.18	12.99±11.52	0.33
HOMA-IR	2.28±1.28	2.48±2.56	0.41
Metaboic Indexes			
VAI	1.84±1.03	1.45±0.77	0.12
LAP	42.66±41.00	24.70±18.30	0.12

Table 2: The correlations of indexes with metabolic parameters, anthropometric measurements and demographic data . *r*= Pearson correlation coefficient. $p<0.05$ was considered statistically significant

	VAI ***r***	***P***	**LAP** ***r***	***P***	**WC** ***r***	***p***	**BMI** ***R***	***P***
Age (years)	0.156	0.10	0.338	**<0.001**	0.457	**<0.001**	0.459	**<0.001**
Pregnancy	0.163	0.09	0.243	**0.01**	0.236	**0.01**	**0.234**	**0.01**
Parity	0.143	0.14	0.212	**0.02**	0.273	**0.004**	0.316	**0.001**
Pregnancy week	0.172	0.08	0.192	0.05	0.066	0.51	0.001	0.99
BMI (kg/m2)	0.455	**<0.001**	0.769	**<0.001**	0.906	**<0.001**	-	-
Weight gain (kg)	0.396	**0.002**	0.311	**0.01**	-0.205	0.12	-0.218	0.10
Waist circumference (cm)	0.470	**<0.001**	0.807	**<0.001**	-	-	0.906	**<0.001**
Hip circumference (cm)	0.357	**<0.001**	0.688	**<0.001**	0.839	<0.001	0.881	**<0.001**
Systolic blood pressure (mm Hg)	0.125	0.19	0.091	0.35	0.093	0.34	0.103	0.29
Diastolic blood pressure (mmHg)	0.113	0.24	0.148	0.12	0.186	0.05	0.187	0.05
Blood Chemistry Analysis								
FBG (mg/dL)	0.035	0.71	0.086	0.36	0.120	0.20	0.062	0.51
TC (mg/dL)	0.153	0.10	0.395	**<0.001**	0.308	**0.001**	0.288	**0.002**
TG (mg/dL)	0.885	**<0.001**	0.817	**<0.001**	0.395	**<0.001**	0.392	**<0.001**
HDL (mg/dL)	-0.544	**<0.001**	-0.213	**0.02**	-0.233	**0.01**	-0.249	**0.008**
LDL (mg/dL)	0.148	0.12	0.325	**<0.001**	0.361	<0.001	0.291	**0.002**
İnsulin (mU/L)	0.211	**0.03**	0.172	0.08	0.128	0.20	0.143	0.15
HOMA-IR	0.232	**0.01**	0.199	**0.03**	0.129	0.17	0.167	0.08
Metabolic Indexes								
VAI	-	-	-	-	-	-	-	-
LAP	0.790	**<0.001**	-	-	-	-	-	-

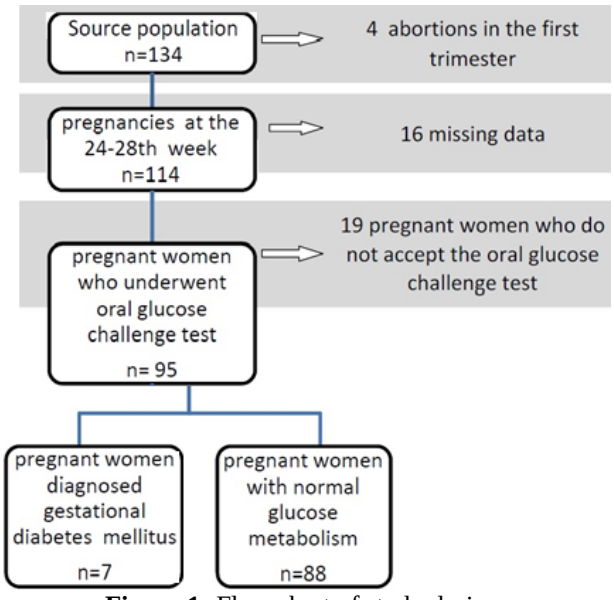

Figure 1: Flow chart of study design