



Glucose metabolism in gestational diabetes and their relationship with fat mass / muscle mass index

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ABSTRACT

Introduction: During pregnancy, women experience metabolic changes that may induce insulin resistance, which can be traced to the blood glucose levels. A number of factors may intervene in the metabolism of glucose in pregnant women; one of them is body composition. This factor is useful for studying metabolic diseases, for which the identification of the fat mass/muscle mass index (FMMMI) considered an especially relevant factor. Owing to their nature, techniques such as bioimpedance have been sparsely used for analysis during pregnancy. **Aim:** This study aimed to identify the relationship between fat mass / muscle mass index and glucose metabolism in pregnant women.

Methods: This descriptive cross-sectional study included 231 women between the ages of 18 and 35 years and 24–28 weeks of gestation, who attended a state hospital for regular check-ups and exhibited risk factors for the development of gestational diabetes (GD) according to the Current Practice Guidelines in Primary Care. The participants underwent a physical examination, anthropometric measurements, bioimpedance were obtained, and oral glucose tolerance curves were constructed. FMMMI was calculated.

Results: The prevalence of gestational diabetes was observed to be 13.4%. Women with a GD diagnosis had a significantly higher FMMMI than in those with no GD (0.746 ± 0.168 vs 0.567 ± 0.167 ; $p < 0.005$). The assessment of the FMMMI tertiles revealed that GD prevalence was higher in tertile 3 than in tertiles 1 and 2 (tertile 1: 2.6%; tertile 2: 9.1%; tertile 3: 24%).

Conclusion: FMMMI is associated with glucose tolerance test response in pregnant women and a higher prevalence of GD.

1. Introduction

Gestational diabetes (GD) is associated with insulin resistance that occurs during pregnancy. Factors related to insulin resistance, such as overweight or obesity, family history of type 2 diabetes mellitus, and high-risk ethnicity (Hispanic, African, native American, Asian, Pacific islander, indigenous Australian), can significantly increase the incidence of GD [1–4].

The oral glucose tolerance test (OGTT) allows the diagnosis of GD and is recommended between 24 and 28 weeks of gestation [5,6]. In recent years, the prevalence of GD has increased owing to the

aggravation of triggering factors such as overweight and obesity [7]. Non-invasive complementary techniques such as body composition measurements have been used to identify at-risk women such as skinfold thickness, bioelectrical impedance, BMI, healthy weight gain, fat mass, fat free mass, among others [8–11]. Body composition and the amount of lean mass may be involved in the development of GD, newborn health [12,13], and breast milk quality [14,15]. Moreover, decreased muscle mass is associated with an increased risk of insulin resistance and cardiovascular disease [16,17]. Although the relationship between muscle and fat mass has not been thoroughly studied in pregnant patients, previous studies have described the use of bioimpedance during

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pregnancy and its usefulness in identifying glucose disorders [18,19].

This study aimed to identify the relationship between fat mass/muscle mass index (FMMMI) and glucose metabolism in pregnant women at risk of GD development.

2. Materials and methods

2.1. Study design and population

This was a descriptive cross-sectional study. The study included women aged between 18–40 years and between the 24th–28th week of gestation with any risk factors for the development of GD and who agreed to participate in this project [21].

Women with a history of smoking or alcoholism, known type 2 diabetes mellitus, cancer, autoimmune diseases, or consumption of glucose metabolism-modifying drugs such as steroids were excluded.

2.2. Procedures

All participants were asked to visit the hospital for evaluation. Medical history and personal data were recorded, and anthropometric and physical examinations were performed. Weight, fat mass, and muscle mass were measured using electrical bioimpedance (Tanita BC-533, Tokyo, Japan); the subjects were measured in underwear, standing barefoot on toe and heel electrodes with arms hanging down a few centimetres from the hip, according to manufacturer recommendations. The FMMMI was obtained for each patient [15,16]. The height was measured using a stadiometer (Seca, Serial No. 57001). To measure blood pressure, a calibrated manual sphygmomanometer and a stethoscope were used.

2.2.1. Diagnostic criteria for gestational diabetes

Three hundred millilitres of liquid containing 75 g of glucose was offered to the participants within 5 min after the first blood sample was taken on an empty stomach; two other blood samples were taken 1 and 2 h after taking glucose.

GD was defined following the American Diabetes Association (ADA) criteria, which considers cut-off values as those exceeding one of the following points: fasting glucose level as 5.1 mmol/L (92 mg/dL), 10.0 mmol/L (180 mg/dL) at 1 h, and 8.5 mmol/L (153 mg/dL) at 2 h [22].

The serum glucose concentration was determined using the glucose oxidase method (Randox reagents, Vitalab Selectra E, Vital Scientific). The area under the curve was calculated using the trapezoid rule [23].

2.3. Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki [20], and informed consent was obtained from all participants. This research was approved by the Research Committee and Ethics Research Committee of "Mónica Pretelini Saénz" Maternal Perinatal Hospital (2017–06-529).

2.4. Statistical analysis

The results were analysed with SPSS V. 22 software (International Business Machines Corporation, New York: USA), considering a statistical significance of p values ≤ 0.05 . Quantitative variables are expressed as average – standard deviation (SD), and prevalence as a percentage. The distribution of variables was determined using the Kolmogorov-Smirnov test. For the comparison of quantitative variables, the Mann-Whitney u -test or t -test was used according to the distribution. A one-way analysis of variance was used to compare more than two groups. The difference between the prevalence values was determined using the chi-square test.

3. Results

The study included 231 pregnant women, 30 of whom were diagnosed with GD, according to the ADA criteria. The prevalence was observed to be 13.4%. During the evaluation of overall characteristics based on a positive diagnosis of GD, statistically significant differences were found between women with GD and healthy women in terms of weight ($p = 0.001$) and other markers like fat mass ($p = 0.001$), fat mass percentage ($p = 0.001$) and muscle mass ($p = 0.001$) (Table 1).

When analysing FMMMI, patients with a positive GD diagnosis had a significantly higher value than in with healthy individuals (0.746 ± 0.168 vs. 0.567 ± 0.167 ; $p < 0.05$) (Fig. 1). To assess the impact of body composition on GD prevalence, the population was divided into tertiles according to the FMMMI; GD prevalence was found to be different depending on the tertile, with much higher values in tertile 3 (tertile 1, 2.6%; tertile 2, 9.1%; tertile 3, 24.6%) ($p < 0.05$). In the assessment of the response to the oral glucose tolerance curve in the total population, a larger area under the curve was observed in patients in the highest FMMMI tertile (Fig. 2). The same assessment in healthy patients produced similar results for the area under the curve for the entire oral glucose tolerance test (Fig. 3).

4. Discussion

This study describes the relationship between the body composition of pregnant women and their responses to the oral glucose tolerance curve. FMMMI is a determining factor in the metabolic response during the test, not only due to the increasing prevalence of the disease between tertiles, but also by displaying a different metabolic response among women without a GD diagnosis based on FMMMI.

Total body water, protein levels, mineral levels, bone mineral content, lean soft mass, fat-free mass, skeletal muscle mass, and basal metabolic rate are considered protective factors against GD development. Previous research found that the body composition-related indicators were independently associated with the onset of GDM [24].

GD is usually underdiagnosed, since the various reported prevalence values depend on the studied population and method used; furthermore GD diagnosis often depend on the population or geographical area and evidence to support the diagnostic process [25–28].

Early identification of risk factors allows patients with DG to have better glucose control, and reduce the risks and development of perinatal complications directly related to the disease [29]. Some studies have considered that measurements of aspects such as waist-to-hip ratio, excess gestational weight gain, and fat mass may be of assistance to set up interventions or strategies to prevent GD [24]. Shaofang mentioned that a multidisciplinary intervention, in which patients are given

Table 1
General characteristics of the population by groups.

Variables (n = 231)	With GD (n = 31)	Without GD (n = 200)	p
Age (years)	28.77 ± 6.4	25.68 ± 6.77	0.018
Gestation weeks	26.39 ± 3.04	26.86 ± 2.76	0.382
Type 2 diabetes family history (%)	45.16	25.5	0.024
Fat mass (kg)	33.53 ± 10.09	23.53 ± 8.51	0.001*
Fat mass percentage	40.95 ± 5.67	34.29 ± 6.85	0.001*
Muscle mass (kg)	44.08 ± 4.08	40.72 ± 3.76	0.001*
Systolic pressure (mmHg)	110.61 ± 11.77	104.58 ± 9.00	0.001*
Diastolic pressure (mmHg)	68.23 ± 10.84	64.62 ± 8.63	0.038
Weight (kg)	79.83 ± 14.03	66.43 ± 11.97	0.001*
Height (cm)	154.77 ± 6.22	154.89 ± 6.28	0.924

Values calculated with T-Students for independent samples $p \leq 0.05$

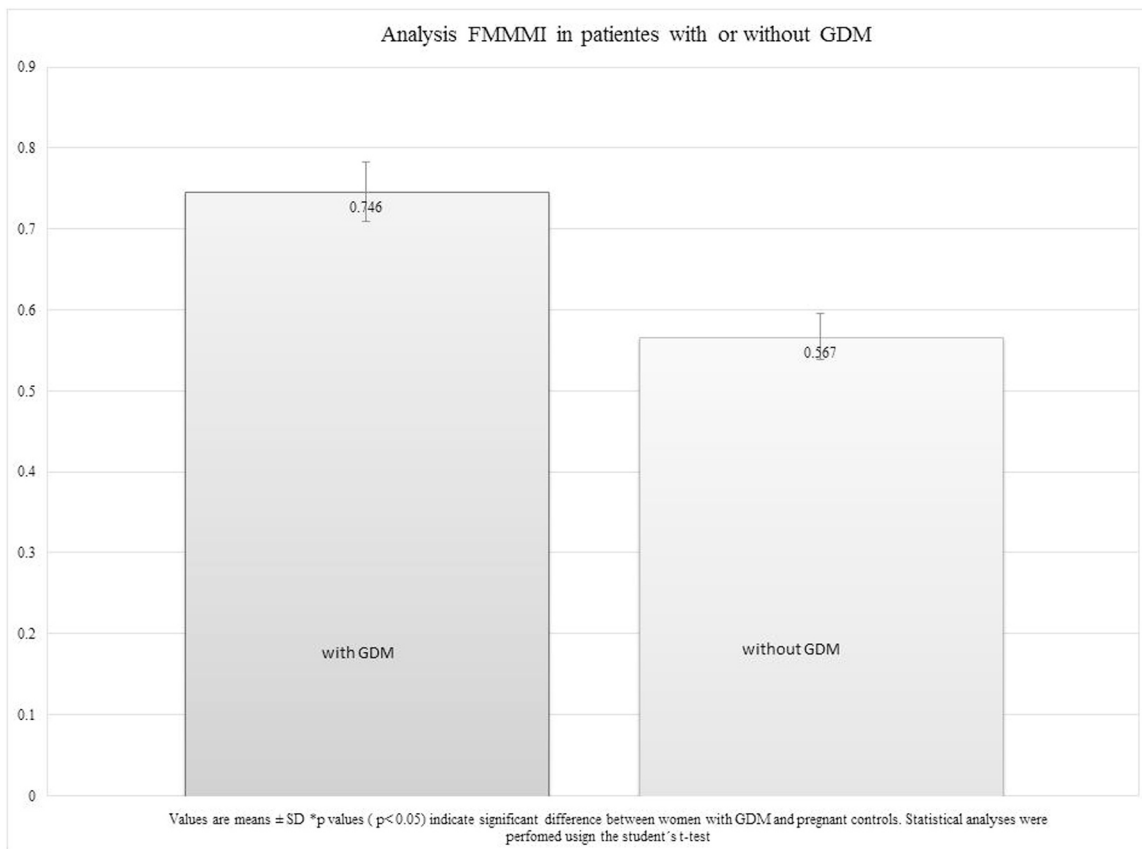


Fig. 1. Analysis FMMMI in pacientes with or without GDM, -Methods should expand on how electrical bioimpedance is performed (line 56).

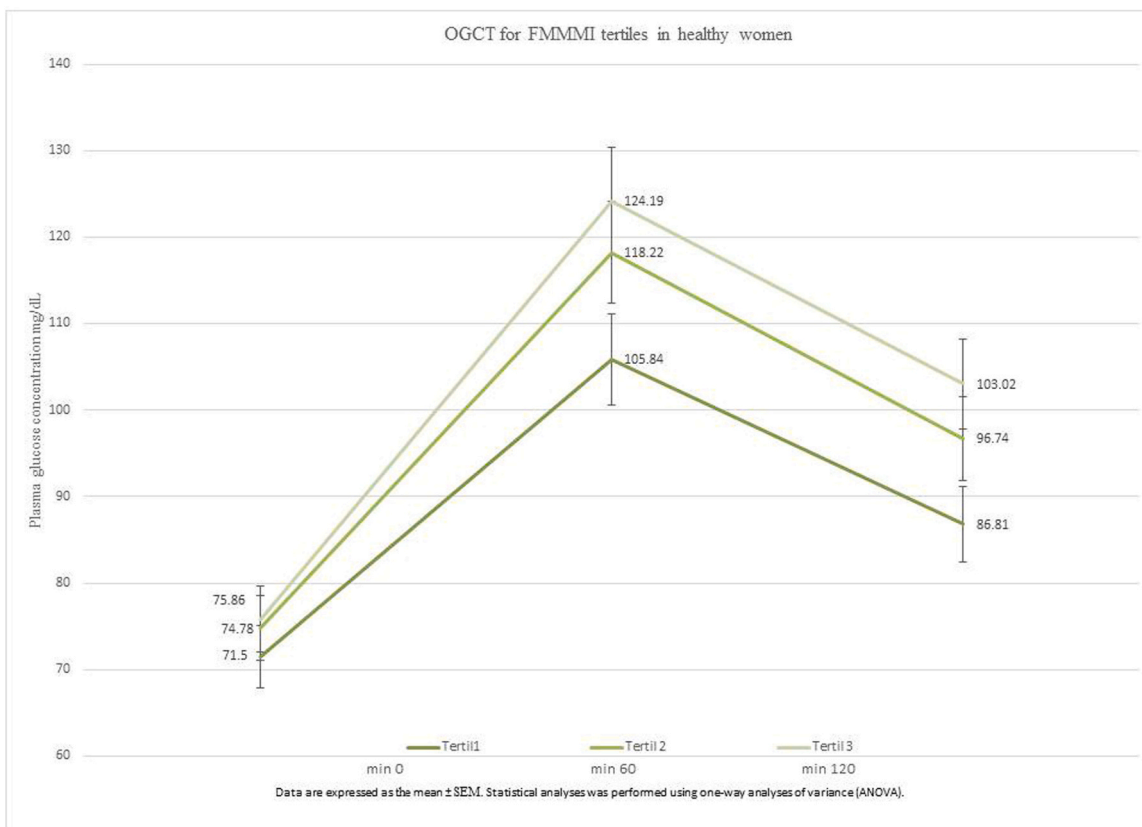


Fig. 2. OGCT for tertiles FMMMI in general.

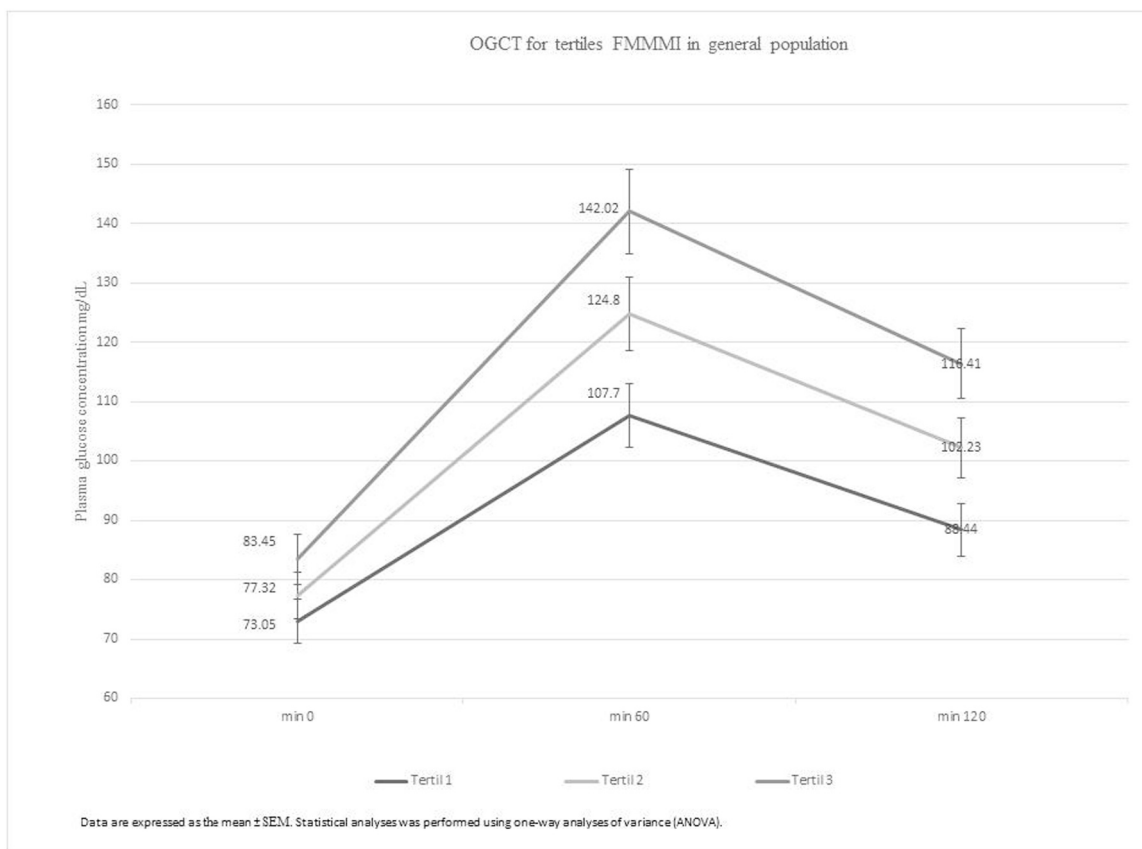


Fig. 3. OGCT for FMMMI tertiles in healthy women.

relevant information regarding the disease and its complications, can help lower glucose levels as they become aware of their condition and decide to take care of themselves, which was verified in our study, since most of the patients reported not being aware of the disease or the risks until they started their treatments.

Devising new, easy-to-obtain, and low-cost parameters relevant to the identification of higher risk could help improve early diagnoses and consequently lead to timely interventions [30]. Measuring body composition using bioimpedance has been helpful in research on various metabolic diseases [31]. Much emphasis has been placed on establishing an association between body fat distribution and the onset of metabolic diseases; therefore, in recent years, muscle tissue and fat proportion measurement have become increasingly relevant [32,33].

Recent research has focused on the muscle fat association in various diseases, including metabolic syndrome [34]; the index should be made available to the general population and not just to the young and active populations, as previously suggested [32]. As reported by Xu, a decrease in muscle mass is associated with insulin resistance based on the FMMMI; nevertheless, the study used or compared results between metabolic syndrome patients and middle-aged people. Similarly, Ramirez et al. conducted studies using this index and reported that the FMMMI may be a good predictive indicator of metabolic syndrome in adolescents and is a useful, practical, and economical tool for diagnosing metabolic diseases.

Little information is available on the use of bioimpedance during pregnancy. While it is true that a woman's metabolism and body composition change over the pregnancy period, the use of this method is an accessible and practical auxiliary in the control and care of patients, as it would produce an overview to help set up primary-care strategies to avoid complications in pregnancy and the subsequent stages [35,36]. The evaluation of body composition using bioelectrical impedance is a simple, inexpensive, and minimally invasive method that allows the

measurement of muscle, fat, and bone mass; this could be a useful tool to find people at risk of developing gestational hypertension and pre-eclampsia. [24,37,38]. Studies similar to those by Loehr et al. [39] have attempted to establish strategies to diagnose GD before the 24th week of pregnancy [40]. Proper control of fat mass percentage and previous- and during-pregnancy muscle mass seems to be more feasible for preventing the development of GD [41,42].

5. Conclusions

Measurement of fat and muscle mass between weeks 24 and 28 of gestation using bioimpedance may be an adjuvant for predicting the diagnosis of GD. The FMMMI makes the OGTT response different in pregnant women, even in patients with no GD.

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Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationship that may be construed as a potential conflict of interest.

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References

- [1] Alfadhli EM, Osman EN, Basri TH, Mansuri NS, Youssef MH, Assaaedi SA, et al. Gestational diabetes among Saudi women: Prevalence, risk factors and pregnancy outcomes. *Ann Saudi Med* 2015;35(3):222–30.
- [2] Huerta-Chagoya A, Vázquez-Cárdenas P, Moreno-Macías H, Tapia-Maruri L, Rodríguez-Guillén R, López-Vite E, et al. Genetic determinants for gestational diabetes mellitus and related metabolic traits in Mexican women. *PLoS One* 2015; 10(5):1–17.
- [3] Ozgu-Erdinc AS, Sert UY, Buyuk GN, Engin-Ustun Y. Prevalence of gestational diabetes mellitus and results of the screening tests at a tertiary referral center: A cross-sectional study. *Diabetes Metab Syndr: Clin Res Rev* 2019;13(1):74–7.
- [4] Shaofang L, Shanlan Y, Rongxiang C, Dongmei W. Effects of nutritional nursing intervention based on glycemic load in patients with gestational diabetes mellitus. *Ginekol Pol* 2019;90(1):46–9.
- [5] International Diabetes Federation. *Diabetes Atlas de la FID*. Vol. 8, Diabetes India and Jaslok Hospital President-Elect International Diabetes Federation. 2017. 150 p.
- [6] American Diabetes Association. 14. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes d 2019. *Diabetes Care*. 2019;42(Supplem (January)):S165–72.
- [7] Wang C, Guelfi KJ, Yang HX. Exercise and its role in gestational diabetes mellitus. *Chronic Dis Transl Med [Internet]* 2016;2(4):208–14. Available from: (<https://www.ncbi.nlm.nih.gov/pubmed/29063044>).
- [8] Jiménez Cruz A, Ortega Cisneros A, Bacardí Gascón M. Efecto de la diabetes gestacional sobre los indicadores de adiposidad en los primeros 18 años; revisión sistemática. *Nutr Hosp* 2014;29(2):397–401.
- [9] Wang Y, Mao J, Wang W, Qiou J, Yang L, Chen S. Maternal fat free mass during pregnancy is associated with birth weight. *Reprod Health* 2017;14(1):1–7.
- [10] Most J, Marlatt KL, Altazan AD, Redman LM. Advances in assessing body composition during pregnancy. *Eur J Clin Nutr* 2018;72(5):645–56.
- [11] Piuri G, Ferrazzi E, Bulfoni C, Mastricci L, Di Martino D, Speciani AF. Longitudinal changes and correlations of bioimpedance and anthropometric measurements in pregnancy: Simple possible bed-side tools to assess pregnancy evolution. *J Matern-Fetal Neonatal Med* 2017;30(23):2824–30.
- [12] Herrera E, Ortega-Senovilla H. Implications of Lipids in Neonatal Body Weight and Fat Mass in Gestational Diabetic Mothers and Non-Diabetic Controls. *Curr Diab Rep* 2018;18(2).
- [13] Grotenfelt NE, Wasenius N, Eriksson JG, Huvinen E, Stach-Lempinen B, Koivusalo SB, et al. Effect of maternal lifestyle intervention on metabolic health and adiposity of offspring: Findings from the Finnish Gestational Diabetes Prevention Study (RADIEL). *Diabetes Metab* 2019;8.
- [14] Zhao P, Liu E, Qiao Yijuan, Katzarzyk PT, Chaput J philippe, Johnson WD, et al. Maternal gestational diabetes and childhood obesity at age 9–11: Results of a Multinational Study. *Diabetology* 2017;59(11):2339–48.
- [15] Ramírez-Vélez R, Carrillo HA, Correa-Bautista JE, Schmidt-Riovalle J, González-Jiménez E, Correa-Rodríguez M, et al. Fat-to-muscle ratio: a new anthropometric indicator as a screening tool for metabolic syndrome in young colombian people. *Nutrients* 2018;10(8).
- [16] Ke X.U., Juan Z.H.U.H., Shi C., Lu C., Xin W., Yuan Z.L. Fat-to-muscle Ratio: A New Anthropometric Indicator for. 2018;31(2012):261–71.
- [17] Kawanabe S, Nagai Y, Nakamura Y, Nishine A, Nakagawa T, Tanaka Y. Association of the muscle/fat mass ratio with insulin resistance in gestational diabetes mellitus. *Endocr J* 2018;28(66):75–88.
- [18] Balani J, Hyer SL, Shehata H, Mohareb F. Visceral fat mass as a novel risk factor for predicting gestational diabetes in obese pregnant women. *Obstet Med* 2018;11(3): 121–5.
- [19] Guillemette L, Allard C, Lacroix M, Patenaude J, Battista MC, Doyon M, et al. Genetics of Glucose regulation in Gestation and Growth (Gen3G): a prospective prebirth cohort of mother-child pairs in Sherbrooke, Canada. *BMJ Open* 2016;6(2): 1–13.
- [20] Asociación Medica Mundial. Declaración de Helsinki de la AMM - Principios éticos para las investigaciones médicas en seres humanos. Fortaleza, Brazil, October 2013. *Acta bioeth.* 2013;1–9.
- [21] Assaf-Balut C, García de la Torre N, Rubio MA, Bordiú E, Calle-Pascual AL. Change in postpartum insulin resistance syndrome in women with prior GDM identified by Carpenter–Coustan and IADPSG criteria. *Endocrinol Diabetes Nutr* 2017;64(7): 400–3.
- [22] American Diabetes Association. 15. Diabetes Care in the Hospital: Standards of Medical Care in Diabetes d 2019. *Diabetes Care*. 2019;42(Supplem(January)): S173–81.
- [23] Tai MM. A mathematical model for the determination of total area under glucose tolerance and other metabolic curves. *Diabetes Care* 1994;17(2):152–4.
- [24] Xintong L, Dongmei X, Li Z, Ruimin C, Yide H, Lingling C, et al. Correlation of body composition in early pregnancy on gestational diabetes mellitus under different body weights before pregnancy. *Front Endocrinol (Lausanne)* 2022 28;13.
- [25] Jr W.L.L., Lowe L.P., Kuang A., Catalano P.M., Nodzenski M., Talbot O., et al. Maternal glucose levels during pregnancy and childhood adiposity in the Hyperglycemia and Adverse Pregnancy Outcome Follow-up Study. 2019;
- [26] Reyes-Muñoz E, Sandoval-Osuna NL, Reyes-Mayoral C, Ortega-González C, Martínez-Cruz N, Ramírez-Torres MA, et al. Sensitivity of fasting glucose for gestational diabetes mellitus screening in Mexican adolescents based on International Association of Diabetes and Pregnancy Study Groups criteria: a diagnostic accuracy study based on retrospective data analysis. *BMJ Open* 2018;8 (4):1–8.
- [27] Martínez-Cruz N, Rapisarda AMC, Soriano-Ortega KP, Arce-Sánchez L, Cianci A, Ortega-Gonzalez C, et al. Perinatal outcomes in Mexican women with untreated mild gestational diabetes mellitus diagnosed by the international association of diabetes and pregnancy study groups criteria. *Diabetes Metab Syndr Obes* 2019;12: 2667–74.
- [28] Dainelli L, Prieto-Patron A, Silva-Zolezzi I, Sosa-Rubi SG, Espino Y Sosa S, Reyes-Muñoz E, et al. Diabetes, metabolic syndrome and obesity: targets and therapy doypress screening and management of gestational diabetes in Mexico: results from a survey of multilocation, multi-health care institution practitioners (Available from:) *Diabetes Metab Syndr Obes [Internet]* 2018;11:105. <https://doi.org/10.2147/DMSO.S160658>.
- [29] Borgen I, Garnweidner-Holme LM, Jacobsen AF, Bjerkan K, Fayyad S, Joranger P, et al. Smartphone application for women with gestational diabetes mellitus: a study protocol for a multicentre randomised controlled trial. *BMJ Open* 2017;7(3).
- [30] Naranjo-Hernández D, Reina-Tosina J, Roa LM, Barbarov-Rostán G, Aresté-Fosalba N, Lara-Ruiz A, et al. Smart bioimpedance spectroscopy device for body composition estimation. *Sensors (Switzerland)* 2020;20(1):1–27.
- [31] Myers J, Kokkinos P, Nyelin E. Physical activity, cardiorespiratory fitness, and the metabolic syndrome. *Nutrients* 2019;11(7):1–18.
- [32] Rodríguez-Rodríguez F, Cristi-Montero C, González-Ruiz K, Correa-Bautista JE, Ramírez-Vélez R. Bioelectrical impedance vector analysis and muscular fitness in healthy men. *Nutrients* 2016;8(7):1–9.
- [33] Mizuno N, Seko Y, Kataoka S, Okuda K, Furuta M, Takemura M, et al. Increase in the skeletal muscle mass to body fat mass ratio predicts the decline in transaminase in patients with nonalcoholic fatty liver disease. *J Gastroenterol* 2019;54(2): 160–70.
- [34] Kurinami N, Sugiyama S, Yoshida A, Hieshima K, Miyamoto F, Kajiwara K, et al. Correlation of body muscle/fat ratio with insulin sensitivity using hyperinsulinemic-euglycemic clamp in treatment-naïve type 2 diabetes mellitus. *Diabetes Res Clin Pr* 2016;120:65–72.
- [35] Chiou YL, Hung CH, Liao HY. The impact of prepregnancy body mass index and gestational weight gain on perinatal outcomes for women with gestational diabetes mellitus. *World Evid Based Nurs* 2018;15(4):313–22.
- [36] Bosaeus M, Andersson-hall U, Andersson L, Karlsson T, Ellegård L, Holmång A, et al. Body composition during pregnancy: longitudinal changes and method comparisons. *Reprod Sci* 2020.
- [37] Obuchowska A., Standylo A., Kimber-Trojnar Ż., Leszczyńska-Gorzela B. The possibility of using bioelectrical impedance analysis in pregnant and postpartum women. Vol. 11, *Diagnostics*. MDPI; 2021.
- [38] Wang N, Sun Y, Zhang H, Chen C, Wang Y, Zhang J, et al. Total and regional fat-to-muscle mass ratio measured by bioelectrical impedance and risk of incident type 2 diabetes. *J Cachex– Sarcopenia Muscle* 2021;12(6):2154–62. Dec 1.
- [39] Loehr FW, Mackeen AD, Paglia MJ, Nordberg C. Establishing New Diagnostic Criteria for Early Gestational Diabetes Screening [30N]. *Obstet Gynecol* 2019;133.
- [40] Brown FM, Wyckoff J. Application of One-Step IADPSG versus two-step diagnostic criteria for gestational diabetes in the real world: impact on health services, clinical care, and outcomes. *Curr Diab Rep* 2017;17(10):1–13.
- [41] Sommer C, Mørkrid K, Jenum AK, Sletner L, Mosdøl A, Birkeland KI. Weight gain, total fat gain and regional fat gain during pregnancy and the association with gestational diabetes: a population-based cohort study. *Int J Obes* 2014;38(1): 76–81.
- [42] Voerman E, Santos S, Patro Golab B, Amiano P, Ballester F, Barros H, et al. Maternal body mass index, gestational weight gain, and the risk of overweight and obesity across childhood: an individual participant data meta-analysis. *PLoS Med* 2019;16(2):e1002744.