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THE CORRELATION OF IRISIN LEVELS AND SOME TRACE ELEMENT AS A POTENTIAL MARK FOR DIAGNOSIS OF GESTATIONAL DIABETES MELLITOUS

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Abstract

The objective of this project was investigating and comparing changes of serum irisin, and trace levels of the elements (Zn, Cu, Mg) in pregnant women with gestational diabetes mellitus GDM in addition to wholesome pregnant group, examining the correlation among (Zn, Cu, Mg) levels and irisin insulin impedance in GDM pregnant women.

Sixty GDM pregnant women and thirty wholesome pregnant women were examined. The pair groups were matched for age, and maternal serum irisin. Insulin levels and gestational age were calculated by the assay for enzyme-linked immune sorbent kit at gestation at 24-28 weeks. The confederation between clinical and biochemical parameters and maternal serum irisin levels were predestined. Serum levels of glucose, body mass index, insulin, OGTT, HOMA IR, HOMA β , HbA1c,Hb%, irisin, Zn, Cu and Mg were investigated and analyzed for the examined collection as well as control samples.

Pregnant women with GDM disease had noteworthy rising fast blood glucose FBG (p = 0.004), first-hour OGTT glucose (p = 0.001), second-hour OGTT glucose (p = 0.001), fasting insulin FI(p = 0.001) levels , HOMA IR(p = 0.001), HOMA β (p = 0.001), HbA1C(p = 0.001), Hb%(p = 0.017), as contrasted to healthy women. Levels of irisin serum were significantly minimizing (p = 0.001) in women, and sequentially more advanced GDM (mean ± SD =71.65±8.03) than healthy pregnant controls (mean ± SD 136.54±22.56).

Correlation analyses among irisin levels of anthropometric and biochemical values in gestational diabetes patients disclosed that none of the scrupulousness values were remediated with serum irisin level.

The present outcomes indicate that the levels of serum irisin might be presented as an incoming GDM marker with decreased irisin levels being GDM symptomatic.

Keywords: gestational diabetes mellitus, trace elements, irisin, glycemic indices

Introduction

GDM Gestational diabetes mellitus is recognized as a high sensitivity of carbohydrate differing seriousness, by initializing confession through gestation GDM propagation which may ambit domain from (1% - 14%) of each gestational, basing on the calculated inhabitance, and the diagnostic test was conducted(1)The GDM pathogenesis is multifactorial and it comprises environmental and genetic parameters, but the accurate mechanism stays to be completely illustrated (2).GDM women are of increased danger for perinatal morbidity, and deteriorated glucose disparity. The kind of diabetes 2 occurs after years of pregnancy. This condition is for woman who may or may not have diabetes before. It goes away after delivery. When a woman is personated with GDM, there is a risk of having it in the future gestational. Women who had this condition during pregnancy are additionally open to improve diabetes mellitus kind 2 (3). Human pregnancy is described by weight gaining as well as an introductory decrease in the sensitiveness of insulin, which is similar to the fetoplacental growth unity. The insulin impedance of maternity in delayed pregnancy is a paramount mechanism to transfer nutritious substances to the foetus to encourage outgrowth(4).Ordinary pregnancy insulin impedance is furthermore reinforced in pregnancy complexities like those outputs in abnormally foetal outgrowth i.e. intrauterine outgrowth constraint (IUGR) and foetal macrosomia. Neoteric compelling directorv proposes that these gestation disturbances are connected by future evolution of maternal metabolic syndrome. Insulin impedance plays an essential functional role in the GDM pathogenesis. In spite of comprehensive research, the basic mechanisms of insulin impedance are not completely comprehended (3). Insulin impedance in gestation is traditionally observed to raise placental hormones as well as maternal adiposity with diabetogenic effect (5). Although the subsidiary mechanisms are not completely realized, the basic fulfillments have concentrated on diverse modern prospective moderators of pregnancy insulin impedance reckonings (6). It is the massive member in the person age, skeletal muscle reckonings by the glucose plurality absorbed in the insulin answer and, quantitatively, the generality essential position for the insulin impedance Though a past contract, skeletal muscle has been furthermore specified as a secretory member and cytokines as other peptides created and excreted with myocytes and are distributed as myokines (7) .These myokines play a role as endocrine hormones.

Irisin is a novel myokine [1], adipokine [2] and neurokine [3] including 112 amino acids, with remaining 12 587 kDa as a molecular weight. Proteolytical treatment from the outcome of fibronectin kind III field includes gene with 5 (FNDC5) in response to the peroxisome energetic proliferator stimulated receptor g (PPARg), coactivator-1a (PGC-1a), and the hormone of antidiabetic that adjusts the metabolism of glucose and energy consuming via transformation white to brown sebaceous tissue (8).

Lately, it has been specified as a practice encouraged hormone excreted by skeletal muscle and has been suggested as a medium that usefully influences the practice of metabolism (9). A potential danger agent for diabetes mellitus type 2 was sedentary lifestyle. Randomized striped experiments have expounded that physical action evolves glucose toleration and decreases type 2 diabetes mellitus risk (10). For this reason, it has been meditated by physical practice that may usefully influences on the energy through metabolism excreted agents from myocytes such as irisin (7). Later research has shown that widespread irisin amounts are considerably dropping in diabetes type 2 patients in comparison to human without diabetes (11).

Studies on mice have shown that FNDC5 which immediately catalyze the transformations of white greasy tissue (WGT) to brown greasy tissue (BAT), is essential to increase overall energy disbursements; consequently, weight loss, evolved glucose toleration and insulin sensitizing (12). For this reason its metabolic characteristics of irisin have lately been shown of many benefits as a possible modern aim for the treatment of rotundity and its connected disorders. By clinical frames, widespread irisin amounts are ordinarily minimized for patients by rotundity and (DM) diabetes mellitus type 2 (13), signalizing that irisin may have a fundamental function in glucose toleration. After that, widespread irisin is recorded to be contradictorily greater in grown-ups by the metabolic syndrome

(14) indicating that conditions of irisin impedance or toleration may occur (15). Information concerning irisin in human gestation is infrequent. Irisin harbinger has been obviously shown in human placenta through the pregnancy and its serum grades to be greater through the entire gestation, when contrasted with nongravid women. After examining the mass of body index BMI, maternal irisin degrees were examined by the homeostasis sample of assessment predestined insulin impedance, suggesting that irisin may contribute in the ordinary evolution pregnancies insulin impedance (7).

The target of the study is to realize and contrast the concentrations of serum irisin between control pregnant women and GDM pregnant women. Irisin grades may have a possible modern marker for diagnosis, a way to keep track of pregnancy diabetes mellitus, estimation of the correlations between Cu^{2+} , Zn^{2+} and Mg^{2+} , and alteration in the concentrations of serum irisin between healthy pregnant women and pregnant women with GDM.

Materials and Methods

The case-control project was conducted at the Pregnant Care Center, in Najaf, Iraq, between June 2017 and March 2018. The morals committee of the foundation confirmed the project, and all participants provided acquainted consent. The study group comprised 60 women diagnosed with GDM and thirty healthy gravid controls with ordinary glucose toleration test (OGTT) results. All participants were recruited at the screening time for the GDM, utilizing a 75 g, 2-h OGTT between 24 and 28 weeks of pregnancies. GDM was embodied while one or more uncommon amounts of plasma glucose (fasting 92 mg/dL, 1h 180 mg/dL, 2 h 153 mg/dL) were acquired utilizing International Association Criteria of International Association for Diabetes. Also, gestation groups were examined.

The GDM and the groups of control were matched for maternal age, pregnancies age and current (BMI) body mass index. Pregnancies age was determined by the last menstrual interval and assured by ultrasonographic test carried out through the first trimester of pregnancy. BMIs were measured during OGTT screening using the following formula: weight (kg)/height (m2). No patients received medications that interfered with glucose or lipid metabolism before blood sampling.

Patients with doubled gestation, pre- present glucose fanaticism, gestation _ motivate preeclampsia, hypertension, chronic inflammation or acute additionally energetic smokers were not included. The venous blood sample of overnight fasting was acquired from all entrants to estimate Iris in levels as well as other biochemical values on the OGTT screening day. A total of specimens were stocked at 25 C at minimal 30 minutes to let the coagulated blood, followed by (3000 rpm) for 15 minute centrifugation to disconnect serum. The samples specimens of serum were taken aliquots and stocked at (8oC) and Iris levels were analyzed. The levels of glucose during OGTT were calculated with the hexokinase project utilizing a commercially obtainable kit (Bio Maghreb, Tunisian). The levels of insulin were specified using a glycosylated hemoglobin (HbA1c) and chemiluminescent assay (USA), and commercially available kits and highperformance liquid chromatography (BIOLABO, France). Homeostatic sample estimation of insulin impedance (HOMA-IR) was determined by the following formula: fasting glucose (mmol/L) fasting (IU/mL)/22.5. concentrations insulin The of magnesium, zinc, and copper on serum were calculated by colorimetric approach using Randox kit (Randox, UK).

The statistical analysis was carried out utilizing two statistical software programs; the Graphpad Prism ver.5 and Statistical Package of Social Science (SPSS ver. 21). Uninterrupted variables were represented as standard deviation (SD) \pm mean. Significant differences were assessed utilizing double t-test as well as independent t-test for variables with equal and unequal frequencies respectively. Bivariate correlations were assessed using standardized Pearson coefficients. The *p* amounts obtained of little less than 0.05 and 0.01 were considered as statistically and strongly statistically considerable respectively.

Results and discussion

The properties of demography of all participants are shown in Table 1. The total study population was 60 gestational diabetes mellitus, and 30 normal pregnant in each group. The mean of maternal ages, and pregnancies ages of the two collections were not considerable (NS) various. In addition, BMI at the sample collection time varied in both collections. Clinical data comparisons between the two collections are introduced in Table 2. In the OGTT, HOMA-IR, fasting glucose and insulin amounts are (p = 0.001). Furthermore Hb% (p = 0.017) were considerably higher, except HOMA β (p = 0.001) which was considerably lower in the group of GDM in comparison with control at the GDM screening time. Serum irisin amounts were considerably lower (p < 0.001) in women thereafter sophisticated GDM (mean ± SD =71.65±8.03) than in controls (mean ± SD 136.54±22.56).

As shown in Table 3, serum Zn amounts were considerably minimized in GDM women as compared to ordinary pregnancy (p=0.001). However, serum Cu level appeared significantly lower in the healthy pregnant women compared to GDM collection (p=0.001). Conversely, serum Mg levels appeared significantly lower in GDM collection compared to control pregnant women (p=0.001). The relations between serum irisin amounts and other variables analyzed separately at the GDM screening time are in Table 4. In the group of GDM, age significance was (p=0.025) while no significant engagements were observed between serum irisin amounts or any other biochemical or clinical parameters. BMI quantities and irisin amounts were observed in women free of diabetes. However, the similar project likewise observed no connection between irisin represented by BMI and myocytes, fasting blood glucose (FBG), and fasting insulin in diabetic patients. The correlations with positive values between BMI and widespread irisin amounts in human free of diabetes were observed in the studies of (16,17).

Several projects have discovered the correlations of positive values between low-density lipoprotein cholesterol and irisin.(18) uncovered the correlations of positive values between HDL levels and irisin in chronic renal failure patients. Compared to our ouecomes,(19) did not discover any correlation between lipid profile and irisin.

The correlations of negative values between HOMA-IR scores and irisin levels were shown. In our project, although likewise we obtained the correlations of negative values between HOMA-IR scores and irisin levels, they were not statistically significant.

It was elucidated that serum irisin of pregnant women was positively conjugated with insulin, fasting glucose and HOMA-IR. Ebert et al.(20)likewise discovered a positive connection between insulin circulating and irisin; however, only in the GDM subgroup. Otherwise, Yuksel et al. (21), stated that irisin level of serum was negatively conjecated with HOMA-IR. In the current study, the concentration of irisin in the healthy women conjected with OGTT and DI120, utilized as the measurements of the sensitivity of insulin additionally beta cell reparations, and negatively with insulin level and HOMA-IR at 120 minutes for the OGTT. A positive connection of insulin sensitivity with circulating irisin.

Identically, studies on the concentrations of blood irisin in GDM women elucidated conflicting resuts, with some of them showing decreasing irisin levels, suggesting that irisin may have an essential function in glucose intolerance and others elucidating no variations in the irisin levels of maternal between GDM women and control pregnant women (22).

Furthermore stated in tubby Chinese adults, serum irisin was considerably negatively conjecated HbA1c and fasting insulin .On the another hand, Liu et al. discover that widespread irisin was considerably positively conjected with fasting blood glucose (23).futhermore stated that widespread irisin was conjected with positively with fasting glucose as well as homeostasis sample appreciation of insulin impedance (HOMA-IR). Every one was established that irisin amounts were positively conjected with fasting as well as 2 h post-load insulin amounts, additionally were negatively conjected with insulincatalyzed glucose conductance as well as insulin riddance. (24) . did not discover an combination between blood glucose levels as well as serum irisin, but instituted that irisin of serum was positively conjected with insulin amounts.

elucidated that serum irisin in pregnant women was positively conjected with HOMA-IR as well as fasting glucose, insulin. (25) instituted a positive connection between insulin and widespread irisin,but ultimately in the GDM subgroup. In dissimilarity (26)

stated that level of serum irisin was negatively conjected with HOMA-IR. In the sitting project, the outcomes connecting insulin impedance-conjected disorders to irisin are dialectically. Numerous of researchs discover lower widespread circulating irisin amounts in type 2 DM patients . Likely, studies on the concentrations of blood irisin in GDM women elucidated dialectical outcomes , with sundry of them appearing lower irisin amounts, submitting that irisin may take part an essential function in the intolerance of glucose and with another elucidating no variations in maternal irisin amonuts between GDM women as well as control pregnant women.

Several article groups discove that decreased irisin amounts in long-term recently obtained as well as indefinite type 2 DM contrasted with controls with non-diabetic.Decreasing irisin amounts have been free conjected with macrovascular complexities in type 2 DM In disparity Stated no variation in irisin amounts between type 2 diabetic as well as nondiabetic persons. Moreover, irisin amounts were either negatively or positively conjecated with glucose homeostasis- linked values in type 2 DM patients It appears that there should be some other parameters conjected with the irisin levels of blood. initial (27). had discover an reverse conjection between plasma irisin as well as the HbA1c.The appearing variation in HbA1c amounts between normal control pregnant women as well as GDM patients is proportionate with preceding studies aforementioned. But variations of the average of the HbA1c of everyone group among researchs were showen . In addendum, there were variations of severance amount of HbA1c between our project and previous former researchs. We supposed that these contradictions are perform by ethnical variations which have been obtained previously.

relations between the levels of serum irisin and trace element parameters at the patients group sgnificant in Table 5. Negative correlations were obtained between Cu(r=-0.164,p=0.031) but Non Significant positive correlations were obtained between Zn(r=0.151, p=0.735).while obviously positive connections were obtained between Mg(r=0.376, p=0.033) Significant.

The deficiency connections of between rope cord plasma zinc as well as the does of copper not permit to affirm that in every one person case, at submission, a zinc increasing concentration may minimize the copper existent concentration ,as could be anticipated from the recognized antibiosis between the copper and zinc elements (28). Notwithstanding, the evolutionarily directions in

placental transmit of copper as well as zinc were obviously, apparent The outcomes offered feel bad here for the two metals in the mothers plasma as well as rope blood plasma of term toddlers are identical to those stated stated previously (29).Furthermore it was obsreved as the management of magnesium ion concentration to the mother for the tocolysis penetrates the placenta additionally basically equiponderates with foetal, indicating a promulgation incident. The passing neonate hyper magnesemia, subsequently maternal magnesium, remediation is good authenticated.A management of magnesium through action shows to have an extra outcome in connection to the zinc placental transmit. The infromation acquired appear an connection between rope plasma zinc as well as magnesium. It is not obvious whether a impulse in zinc promulgation conjecate to magnesium management, or another velum incident, are implicated in this appreach . The recognized gestation hypercupremia (30). Obsreves to be a lot of remarkable in those women who transported precocious. Synchronous, maternal ceruloplasmin resorts to diminish as GA increasing. This is proportionate with the decline inclination of the copper plasma from mother to bantling, which is additional remarkable in 24-28-week GA newborns than in the more overripe bantling. The outcomes we gained appear that the concentration of rope plasma ceruloplasmin is much little than the particular maternal amounts .A preceding study in the previous researchs furthermore appeared a sundry -fold variation between rope blood plasma as well as maternalcopper (31).

However although, the project utilized highly than three contract ago as well as the ultimate amounts educe questions concerning thoroughness. The parsimonious of copper conveyance of to the foetus is proportionate with its disability to composition highly qunatities of ceruloplasmin, or, as alternative, a physiologically outcome of the largly zinc inflow into the foetus chamber, which prevents copper transmission by an increasing of placental metallothionein. This prospect is corroboratived by the discovering of minimum copper concentrations in the fetuses liver of rats fed with largly zinc nourishment than in ordinary fed controls (32) The ceruloplasmin test for ultizing this project is based on the so-called (GDM)Gestational diabetes mellitus is the metabolic disorder through gestation leading to acute and chronic complications in both mother and newborn. Thus, GDM patients have an increasing danger of co-morbidities through pregnancies, e.g. pregnancy-induced hypertension, preeclampsia, as well as houlder dystocia with d hindered submission. Moreover, inveterate complexities might happened after transmission contained cardiovascular disease as well as (T2DM) type 2 diabetes mellitus (33).

For this reason, premature prosopopoeia and suitable GDM remediation of is beneficial in decreasing the inverse maternal as well as foetal consequences additionaaly in conserving mothers as well as pickaninny from long-term. complexities consequently, preceding researchs have attempted to locate the oracular amount of maternal or placental biofactors before the GDM evlution, a swell as these specified in a lot of biological approach containing insulin resistance, oxidative stress, additionally inflammation ,carbohydrate metabolism (27). To the good of present knowing, this outcome are the initial to utilize a state-control project to caluclate the serum irisin of GDM patients as well as healthy controls in Iraqi population . Moreover in the current lead to this analyses to appreciate the widespread irisin between healthy control pregnant well as GDM as patients.Harmonious with these findings, this study assured that GDM pregnant have lower widespread irisin. Involved in the disturbances of the maternal metabolic conjected with foetal abnormal evolution. Gestation is connected fundamental with maternal metabolism changes, which supply adequate energy as well as nutrients to the foetus (34). In this situation, mothers improve a status of insulin impedance thought mid pregnancy, that advances the third trimester, leading to reduced consumption of glucose by maternal tissues and increased during gluconeo genesis (13).whilst, in a essential ratio of pregnancies, the resistant of insulin- status is extremely excessed product to inverse the condition of maternal metabolic as well as foetal outgrowth aberrations (3).

Irisin is a modern adipokine as well as myokine which encouraged an increasing in overall energy of body disbursements meliorative glucose tolerance as well as insulin sensibility in empirical animals. In the current project showed that the levels of serum

irisin were largely lower in the GDM patients than in the healthy control pregnant women, the current outcomes are agreement with the findings of .who futher more communicated a lower in widespread irisin in GDM women that lead to increase in serum irisinwith largely amount in pregnant women, but this increasing was largely lowering in objects with GDM(35). The irisin increased largely concentration from colostrum to transmission additionally overripe milk, the plasma irisin as well excessed in lactating GDM women as well as without GDM as comparsion with non-lactating women (26). In GDM, there is enhanced ability of glucose to cross the placenta, with resultant fetal hyperglycaemia, hyperinsulinaemia and macrosomia. This may lead to a variety of fetal pathologies postpartum and pregnancy associated morbidity, such as preeclampsia susceptibility (36). and to development of GD in subsequent pregnancies. Up to 90% of GDM afflicted women develop type 2 diabetes (37). GDM may therefore, serve to unmask women who are predisposed and destined to improve diabetes type 2 last in life (38).give no variation in widespread irisin between gravid women without as well as with GDM, although however after the birth with 4 years irisin levels were geartly extremely in patients with preceding gestational diabetes mellitus than in the women with normal glucose tolerance. reciprocally (39). additionall other studies (25).

showed lower serum irisin in GDM lactating women as comparing with healthy contoal lactating women. No greatly variations in serum irisin between obese, non-obese as well as GDM objects at interval were lately recorded (40)., additional studies uncovered that after the regulating for lipids,BMI,glucose as well as irisin levels were geartly lower in pregnant women with non-obese state as comparsion with the obese as well as GDM groups. Our results showed that the irisin levels were markedly minimize than healthy control pregnant, disagreement with other studies that may propose a reparations for a physiologic increasing in insulin impedance or a activating influence of high levels of the estrogens (10). or its probably extra excretion by the placenta, though the placental tissue influence to widespread irisin shows Unintentionally (41). The researchers introduced that these returns may reason irisin impedance evolving with each other with insulin impedance.

The connotation of irisin impedance resistance with compensative hyper irisinemia was too suggested (42).who appeared that great irisin levels were conjected with an increasing of the metabolic additionally syndrome danger cardiovascular diseases. However, a connection between insulin impedance as well as irisin in specially through pregnancy, appears as yet unclear. (43). confirmed that in serum irisin of pregnant women was positively conjecated with HOMA-IR, insulin as well as fasting blood glucose (23). Introduced that the level of serum irisin was negatively conjecated with HOMA-IR.In persons with diverse obesity degree.Further, we showen that in the entire group of serum irisin concentration of pregnant women conjecated negatively with the glucose level at 120 min for the OGTT, that is proportionate with the outcomes (44). who discover that the glucose of 2 h plasma was an separate negative foreteller for the concentration of irisin in the patients with recently diagnosed diabetes type 2.Every one these contradictions may outcome from variations in clinical properties of the objects intended as well as diverse gauges; As though, the potential effect of weight earning or BMI through gestational week as well as pregnancy at specimen taken appears controversial since a positive conjection between body mass index as well as the level of irisin at the final weeks in third gestation trimester . were studied by various researchers . In the current study, no conjections between BMI as well as circulating irisin were showen .Furthermore, dialectical outcomes, i.e. largely the concentration of irisin in pregnant than in women with nonpregnant (45). or no largely variations through as well as after pregnancy have been establish in various researchs.

in the present study suggest that this element also contributes at some level to the pathogenesis of GDM and pregnancy in diabetes. This is consistent with the role of this metal as a organizer of carbohydrate metabolism in pregnancy (46). The diabetes influence in pregnancy may arise through two related mechanisms, namely, the direct effect of trace elements and oxidative stress on immune regulation (47). A significant lowering in Zn concentration was appeared in the diet-treated diabetic group relative to healthy pregnancy which supports the hypothesis that Zn and Cu may perform a funcation in the mechanisms regulating the immune response (48).Another study found that deficiency of Mg++ is associated with immunosuppression in athletes, suggesting that Mg++ has a role in immune regulation (49).

did not discover a relation between the levels of magnesium, zinc as well as copper in serum with the gestational hypertension, for this reason , they suggested that thes metals might not clinically take part in the gestational hypertension pathogenesis (**50**). The average of serum amounts of copper ,magnesium as well as zinc between the two groups were largely various. For realizing, the function of the electrolytes in serum in GDM highly is project indispensable. The outcomes of the cuerent project appeared that these metals did take a outstanding function in the GDM pathogenesis.

Conclusions

The patients with maternal serum irisin amounts with GDM are largely minimizing likened as matched with healthy control pregnants, while, The present outcomes give that serum irisin amountts might presented as a modern of GDM marker , with minimizied amounts of irisin being GDM symptomatic ,and revealed that these trace elements Cu,Zn,Mg did play a conspicuous funcation in the GDM pathogenesis The essential issues of the combinations between future danger of the metabolic syndrome in mother as well as maternal insulin resistance during pregnancy, necessity to be furthermore classified in future possible projects.

References

- 1. Dawonauth L, Rademacher L, L'Omelette AD, Jankee S, Yan MY, Jeeawoody RB, Rademacher TW. Urinary inositol phosphoglycan-P type: near patient test to detect preeclampsia prior to clinical onset of the disease. A study on 416 pregnant Mauritian women. Journal of reproductive immunology. 2014 Mar 1;101:148-52.
- Diaz SO, Pinto J, Graça G, Duarte IF, Barros AS, Galhano E, Pita C, Almeida MD, Goodfellow BJ, Carreira IM, Gil AM. Metabolic biomarkers of prenatal disorders: an exploratory NMR metabonomics study of

second trimester maternal urine and blood plasma. Journal of proteome research. 2011 Jun 30;10(8):3732-42.

- 3. Newman J. To Siri, With Love: A mother, her autistic son, and the kindness of a machine. Hachette UK; 2017 Aug 24.
- Stoeckel LE, Arvanitakis Z, Gandy S, Small D, Kahn CR, Pascual-Leone A, Pawlyk A, Sherwin R, Smith P. Complex mechanisms linking neurocognitive dysfunction to insulin resistance and other metabolic dysfunction. F1000Research. 2016;5.
- 5. Koski KG, Burns DH, inventors; McGill University, assignee. Method and apparatus for analyzing amniotic fluid. United States patent US 8,165,661. 2012 Apr 24.
- 6. Perfetti C. Reading ability: Lexical quality to comprehension. Scientific studies of reading. 2007 Sep 26;11(4):357-83.
- Nederveen JP, Joanisse S, Snijders T, Parise G. The influence and delivery of cytokines and their mediating effect on muscle satellite cells. Current Stem Cell Reports. 2017 Sep 1;3(3):192-201.
- 8. Kuipers F, Bloks VW, Groen AK. Beyond intestinal soap—bile acids in metabolic control. Nature Reviews Endocrinology. 2014 Aug;10(8):488.
- 9. Vij K. Textbook of Forensic Medicine & Toxicology: Principles & Practice-e-book. Elsevier Health Sciences; 2014 Feb 10.
- 10. Norman RA, Paul SP. The Last Natural Man: Where Have We Been and Where Are We Going?. Springer; 2017 Mar 20.
- 11. Preethi DM, Jayanthi VE. Ocular disease diagnosis based on LBP and gabor filter. Int J Sci Eng Res. 2014;5:297-304.
- 12. DeBrabander J, Shay JW, Wang W, Nijhawan D, Theodoropoulos P, inventors; University of Texas System, assignee. Targeting emopamil binding protein (ebp) with small molecules that induce an abnormal feedback response by lowering endogenous cholesterol biosynthesis. United States patent application US 15/201,667. 2016 Oct 27.
- 13. Epstein EB. The Experience of Recovery from Food Addiction. Michigan School of Professional Psychology; 2014.

- 14. Hackett GI. Sexual health and wellbeing. Diabetes in Old Age. 2017 Feb 13:148.
- 15. Wahlqvist ML, Krawetz SA, Rizzo NS, Dominguez-Bello MG, Szymanski LM, Barkin S, Yatkine A, Waterland RA, Mennella JA, Desai M, Ross MG. Early-life influences on obesity: from preconception to adolescence. Annals of the New York Academy of Sciences. 2015 Jul 1;1347(1):1-28.
- Hofmann T, Elbelt U, Stengel A. Irisin as a muscle-derived hormone stimulating thermogenesis–a critical update. Peptides. 2014 Apr 1;54:89-100.
- 17. Bakker L, Sleddering MA, Schoones JW, Meinders AE, Jazet I. Pathogenesis of type 2 diabetes in South Asians. European journal of endocrinology. 2013 Aug 12:EJE-13.
- 18. de la Iglesia R, Lopez-Legarrea P, Crujeiras AB, Pardo M, Casanueva FF, Zulet MA, Martinez JA. Plasma irisin depletion under energy restriction is associated with improvements in lipid profile in metabolic syndrome patients. Clinical endocrinology. 2014 Aug;81(2):306-11.
- 19. liuber O. Complex problem solving as multistage decision making. Complex problem solving: The European perspective. 2014 Apr 4:151.
- 20. Galhardo, M.S., 2015. INTEGRATED ANALYSIS OF TRANSCRIPT-LEVEL REGULATION OF HUMAN ADIPOGENESIS AND CELL TYPE-SELECTIVE DISEASE ASSOCIATION OF HIGH REGULATORY LOAD GENES(Doctoral dissertation, University of Luxembourg, Luxembourg, Luxembourg).
- Karras SN, Koufakis T, Fakhoury H, Kotsa K. Deconvoluting the Biological Roles of vitamin D-Binding Protein During Pregnancy: A Both Clinical and Theoretical Challenge. Frontiers in endocrinology. 2018;9.
- 22. Crume TL, Shapiro AL, Brinton JT, Glueck DH, Martinez M, Kohn M, Harrod C, Friedman JE, Dabelea D. Maternal fuels and metabolic measures during pregnancy and neonatal body composition: the healthy start study. The Journal of Clinical Endocrinology & Metabolism. 2015 Apr 1;100(4):1672-80.

- 23. Lam SK. The health of the elderly in Hong Kong. Hong Kong University Press; 1997 Jun 1.
- 24. Nadeem M, Li J, Wang M, Shah L, Lu S, Wang X, Ma C. Unraveling Field Crops Sensitivity to Heat Stress: Mechanisms, Approaches, and Future Prospects. Agronomy. 2018 Jul 23;8(7):128.
- 25. Ebert T, Stepan H, Schrey S, Kralisch S, Hindricks J, Hopf L, Platz M, Lossner U, Jessnitzer B, Drewlo S, Blüher M. Serum levels of irisin in gestational diabetes mellitus during pregnancy and after delivery. Cytokine. 2014 Feb 1;65(2):153-8.
- 26. Lal M. Women's psychosomatic health promotion and the biopsychosociocultural nexus. Clinical Psychosomatic Obstetrics and Gynaecology: A Patient-centred Biopsychosocial Practice. 2017 Jun 9:199.
- 27. Blei F. Update August 2018. Lymphatic research and biology. 2018 Aug 1;16(4):397-417.
- 28. Bhutta ZA, Das JK, Rizvi A, Gaffey MF, Walker N, Horton S, Webb P, Lartey A, Black RE, Group TL, Maternal and Child Nutrition Study Group. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost?. The lancet. 2013 Aug 3;382(9890):452-77.
- 29. Premalatha M, Tabassum-Abbasi, Abbasi T, Abbasi SA. The generation, impact, and management of e-waste: State of the art. Critical Reviews in Environmental Science and Technology. 2014 Jul 18;44(14):1577-678.
- 30. Goulding R. Handbook of dental pharmacology and therapeutics. Elsevier; 2013 Oct 22.
- 31. Mather, L.E., 2015. Stereopharmacological research in anaesthesiology.
- 32. Heaney RP. Nutrition and risk for osteoporosis. InOsteoporosis (Fourth Edition) 2013 (pp. 645-681).
- 33. Hu FB, Malik VS. Sugar-sweetened beverages and risk of obesity and type 2 diabetes: epidemiologic evidence. Physiology & behavior. 2010 Apr 26;100(1):47-54.

- 34. Leddy MA, Power ML, Schulkin J. The impact of maternal obesity on maternal and fetal health. Reviews in obstetrics and gynecology. 2008;1(4):170.
- 35. Agudelo, L.Z., 2017. Skeletal muscle PGC-1α1 and KAT enzymes at the intersection between depression and metabolic disease.
- 36. Spong CY, Mercer BM, D'Alton M, Kilpatrick S, Blackwell S, Saade G. Timing of indicated late-preterm and early-term birth. Obstetrics and gynecology. 2011 Aug;118(2 Pt 1):323.
- 37. Mahmoud F, Abul H, Dashti A, Al-Jassar W, Omu A. Trace elements and cell-mediated immunity in gestational and pre-gestational diabetes mellitus at third trimester of pregnancy. Acta medica academica. 2012 Nov 16;41(2):175-85.
- 38. Carolan M, Gill GK, Steele C. Women's experiences of factors that facilitate or inhibit gestational diabetes selfmanagement. BMC pregnancy and childbirth. 2012 Dec;12(1):99.
- Buchanan TA, Xiang A, Kjos SL, Watanabe R. What is gestational diabetes?. Diabetes care. 2007 Jul 1;30(Supplement 2):S105-11.
- 40. Dubuc-Messier G, Caro SP, Perrier C, van Oers K, Réale D, Charmantier A. Gene flow does not prevent personality and morphological differentiation between two blue tit populations. Journal of evolutionary biology. 2018 May 23.
- 41. Houser CM. Neonatal Topics. InPediatric Development and Neonatology 2014 (pp. 35-141). Springer, New York, NY.
- 42. Pajari, J., 2016. Correlation of endogenous secretory receptor for advanced glycation end product (esRAGE) with metabolic health related biomarkers of skeletal muscle.
- 43. Rahimi R, Karimi J, Khodadadi I, Tayebinia H, Kheiripour N, Hashemnia M, Goli F. Silymarin ameliorates expression of urotensin II (U-II) and its receptor (UTR) and attenuates toxic oxidative stress in the heart of rats with type 2 diabetes. Biomedicine & Pharmacotherapy. 2018 May 31;101:244-50.
- 44. O'brien MD, Rhoads RP, Sanders SR, Duff GC, Baumgard LH. Metabolic adaptations to heat stress in growing cattle. Domestic

animal endocrinology. 2010 Feb 1;38(2):86-94-

- 45. Wawrusiewicz-Kurylonek N, Telejko B, Kuzmicki M, Sobota A, Lipinska D, Pliszka J, Raczkowska B, Kuc P, Urban R, Szamatowicz J, Kretowski A. Increased maternal and cord blood betatrophin in gestational diabetes. PloS one. 2015 Jun 26;10(6):e0131171.
- 46. Jenkins A, Lengyel I, Rutter GA, Lowe N, Shai I, Tirosh A, Petro T, Khamaisi M, Andrews S, Zmora N, Gross A. Obesity, Diabetes and Zinc: A Workshop Promoting Knowledge and Collaboration Between the UK and Israel, November 28-30, 2016–Israel.
- 47. Drutel A, Archambeaud F, Caron P. Selenium and the thyroid gland: more good news for clinicians. Clinical endocrinology. 2013 Feb;78(2):155-64.
- 48. Prasad AS. Discovery of Human Zinc Deficiency: Its Impact on Human Health and Disease–. Advances in nutrition. 2013 Mar 6;4(2):176-90.
- 49. Laires MJ, Monteiro C. Exercise, magnesium and immune function. Magnesium research. 2008 Jun 1;21(2):92-6.
- 50. Jain S, Sharma P, Kulshreshtha S, Mohan G, Singh S. The role of calcium, magnesium, and zinc in pre-eclampsia. Biological trace element research. 2010 Feb 1;133(2):162-70.

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Variables	GDM	Control	P value
Mother's age (Years)	26.33±3.21	26.07±3.58	0.772 NS
BMI Kg/m ² at sampling	34.39±2.00	31.04±1.82	0.000**
Gestational age (weeks) at sampling	28.47±0.96	28.07±0.98	0.069NS

Table1: The Demographics characterizes of the study population

BMI: body mass index, GDM: Gestational diabetic mellitus

Parameters	GDM Mean ± SD	Control Mean±SD	P value
Glucose(mg/dl)	115.35±11.82	99.00±15.37	0.000**
OGTT(mg/dl) 1h	182.04±4.23	133.23±5.22	0.000**
OGTT(mg/dl) 2h	149.38±8.19	103.11±2.15	0.000**
Isulin(µlu/ml)	15.32±2.70	8.63±1.20	0.000**
HOMA IR	2.51±0.22	1.97±0.21	0.000**
ΗΟΜΑ β%	103.00±23.86	84.70±6.92	0.000**
HbA1C%	5.08±0.23	4.47±0.19	0.000**
Hb %	11.70±0.77	11.27±0.81	0.017*
Irisin(ng/ml)	71.65±8.03	136.54±22.56	0.000**

HbA1c: Glycated heamoglobin A₁c ,OGTT: oral glucose tolerance test, Hb: Hemoglobin, HOMA: Homeostatic Model Assessment

 Table 3. Comparisons of trace Elements in gestational diabetes mellitus patients as well as healthy group

Parameters	Groups	Mean±SD	P value
(ua/dl)	GDM	109.00±14.62	0.001**
Cu(µg/dl)	Control	85.43±5.06	0.001**
Zn(µg/dl)	GDM	79.27±6.87	0.004**
	Control	101.30±7.20	0.001**
	GDM	1.99±0.07	
Mg(mg/dl)	Control	2.35±0.07	0.001**

Cu:copper, Zn:zinc, Mg: magnesium, **=significant differences at 1%.

 Table 4. Engagements Correlations between irisin amount with another biochemical parameters in control objects and in women with GDM diagnosed.

Parameters	R	P-value
Age	-0.289	0.025*
Glucose(mg/dl)	-0.240	0.065NS
OGTT(mg/dl)1hr.	-0.232	0.074NS
OGTT(mg/dl)2hr.	-0.321	0.060NS
Insulin(µlu/ml)	-0.038	0.774NS
HOMA IR	-0.154	0.241NS
ΗΟΜΑ β	0.044	0.740NS
HbA1C(%)	-0.077	0.558NS
Hb(%)	0.038	0.773NS

HbA1c: Glycated heamoglobin A1c,OGTT: oral glucose tolerance test,Hb: Hemoglobin, HOMA: Homeostatic Model Assessment

Table 5. The relevance of irisin with concentrations of trace element parameters in the patients group

Parameter	R	Р
Cu(µg/dl)	-0.164	0.031*
Zn(µg/dl)	0.151	0.735NS
Mg(mg/dl)	0.376	0.033*

Cu:copper, Zn:zinc, Mg: magnesium, **=significant differences at 1%.