VALIDATION OF DIPSI AS A SINGLE-STEP SCREENING FOR GESTATIONAL DIABETES IN RESOURCE-LIMITED SETTINGS

R. Nalliarasi[1](0009-0009-9026-4328), Reeta R[1]*, P. Pallavee[2]

[1] Department of Biochemistry, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed-to-be University), Puducherry 607403, India
[2] Department of Obstetrics and Gynecology, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed-to-be University), Puducherry 607403, India

***Corresponding author:**
Dr. Reeta R
Department of Biochemistry
Mahatma Gandhi Medical College and Research Institute
Puducherry, India

ABSTRACT

Purpose: Gestational diabetes mellitus (GDM) screening remains challenging in resource-limited settings where conventional protocols face implementation barriers. This investigation evaluated whether the simplified DIPSI protocol offers diagnostic equivalence to standard 75-gram oral glucose tolerance testing in South Indian pregnant women.

Methods: This cross-sectional analytical study enrolled 50 pregnant women at 24–28 gestational weeks, comprising 25 DIPSI-confirmed hyperglycemic cases and 25 normoglycemic controls. Following comprehensive anthropometric assessment, participants underwent both DIPSI testing (non-fasting 2-hour post-75g glucose) and standard OGTT (fasting, 1-hour, 2-hour measurements). Serum glucose quantification employed glucose oxidase-peroxidase enzymatic methodology on automated analyzers. Independent t-tests compared group differences, with statistical significance at $p<0.05$.

Results: Cases exhibited markedly elevated DIPSI serum glucose (167.3±18.2 mg/dL) versus controls (112.6±16.7 mg/dL; $p<0.001$). Standard OGTT revealed consistent hyperglycemic patterns: fasting values of 95.2±7.8 versus 82.6±5.9 mg/dL, 1-hour concentrations of 162.4±15.3 versus 118.7±14.2 mg/dL, and 2-hour levels of 154.9±17.6 versus 110.3±13.8 mg/dL (all $p<0.001$). Body mass index showed significant case-control disparity (28.1±2.7 versus 24.0±2.5 kg/m²; $p<0.01$), confirming obesity-hyperglycemia associations.

Conclusion: DIPSI demonstrates diagnostic concordance with conventional OGTT while eliminating fasting requirements and reducing phlebotomy burden, making it advantageous for widespread antenatal screening implementation in resource-constrained healthcare environments.

Keywords: Gestational diabetes mellitus; DIPSI screening; Glucose tolerance test; Pregnancy hyperglycemia; Prenatal diagnosis; Resource-limited settings

INTRODUCTION

Hyperglycemic disorders emerging during gestation constitute significant obstetric complications affecting 7–25% of pregnancies globally, with considerable geographic variation (1,2). These metabolic disturbances precipitate substantial maternal morbidity including preeclampsia and operative delivery requirements, alongside fetal complications encompassing macrosomia, birth trauma, neonatal hypoglycemia, and long-term metabolic dysfunction (3,4). Early identification through systematic screening enables timely nutritional and pharmacological interventions that substantially reduce adverse outcomes (5,6).

Standard diagnostic protocols employing 75-gram glucose tolerance testing with multiple timed measurements represent the international reference methodology (7). However, this approach mandates overnight fasting, sequential blood sampling, and prolonged clinical observation—logistical requirements that substantially limit implementation in high-volume antenatal clinics serving socioeconomically disadvantaged populations (8,9). These barriers prompted the Diabetes in Pregnancy Study Group India to propose a simplified single-step protocol utilizing non-fasting 2-hour post-glucose assessment, designated DIPSI (10,11).

The pathophysiological basis involves progressive pancreatic β-cell inadequacy unable to compensate for pregnancy-induced insulin resistance mediated by placental hormones (12). This hormonal antagonism impairs cellular glucose uptake, resulting in maternal hyperglycemia that crosses the placenta and stimulates excessive fetal insulin secretion, triggering metabolic complications (13). Obesity exacerbates these mechanisms through adipokine-mediated inflammation and ectopic lipid accumulation that further compromise insulin signaling pathways (14,15).

While several investigations have validated DIPSI performance in various Indian populations, regional demographic and lifestyle heterogeneity necessitates continued local validation (16,17). Puducherry represents a transitional urban-rural demographic undergoing rapid lifestyle modifications yet remains underrepresented in existing literature. This investigation therefore compared DIPSI and standard OGTT diagnostic performance in pregnant women attending a South Indian tertiary care facility, providing evidence to inform optimal screening protocol selection for routine antenatal care.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based cross-sectional analytical study was conducted at Mahatma Gandhi Medical College and Research Institute (MGMCRI), a constituent institution of Sri Balaji Vidyapeeth (Deemed-to-be-University), Puducherry, India. Institutional ethical approval was obtained prior to participant recruitment, and all study procedures adhered to the principles of the Declaration of Helsinki.

Ethical Approval

The Institutional Human Ethics Committee approved all study procedures (Reference: MGMCRI/2024/02/IHEC/76), ensuring adherence to Declaration of Helsinki principles. Written informed consent was obtained from all participants in their preferred language following detailed explanation of study objectives, procedures, and rights.

Participant Selection

Inclusion Criteria

Eligibility required: maternal age 21–40 years; singleton gestation; gestational age 24–28 weeks confirmed by ultrasound; and willingness to complete both testing protocols.

Exclusion Criteria

Women with pre-existing diabetes, chronic hypertension, renal or hepatic disease, multiple gestation, severe anemia (hemoglobin <8 g/dL), active infections, or medications affecting glucose metabolism were excluded.

Sample Size and Grouping

Sample size calculation assumed α=0.05, power=80%, anticipated mean difference of 40 mg/dL, and pooled standard deviation of 20 mg/dL, yielding minimum 21 participants per group. To strengthen statistical power, 25 participants were enrolled in each group (total n=50).

Participants underwent routine DIPSI screening per institutional protocol. Those with results ≥140 mg/dL constituted cases (provisional GDM diagnosis), while those <140 mg/dL served as normoglycemic controls (10). All participants subsequently completed standard OGTT within one week for methodological comparison.

Anthropometric Assessment

Height measurement to 0.1 cm employed wall-mounted stadiometry with participants barefoot and head in Frankfurt horizontal plane. Weight determination to 0.1 kg used calibrated digital scales with light clothing. Body mass index calculation followed standard formula (weight

kg/height m²), with Asian-specific cutoffs applied: normal <23.0, overweight 23.0–24.9, obese ≥25.0 kg/m² (18).

DIPSI Testing Protocol

Following DIPSI guidelines, participants ingested 75 grams anhydrous glucose dissolved in 250–300 mL water regardless of fasting status or recent meal timing (10). Venous blood (3 mL) was collected precisely 2 hours post-ingestion into sodium fluoride-potassium oxalate tubes, immediately centrifuged at 3,000 rpm for 10 minutes, and separated for glucose analysis. Values ≥140 mg/dL indicated provisional GDM.

Standard OGTT Protocol

Standard testing followed International Association of Diabetes and Pregnancy Study Groups criteria (7). After overnight fasting (8–12 hours) and three days unrestricted carbohydrate intake (≥150 g daily), baseline venous samples were obtained. Participants then consumed 75 grams glucose within 5 minutes, with subsequent blood collection at exactly 1 and 2 hours post-load. GDM diagnosis required meeting any threshold: fasting ≥92, 1-hour ≥180, or 2-hour ≥153 mg/dL (7).

Laboratory Analysis

Serum glucose quantification employed glucose oxidase-peroxidase enzymatic methodology using commercial kits (Coral Clinical Systems, Goa) on semi-automated analyzers (Transasia Erba Chem 7). This method demonstrates excellent precision (coefficient of variation <2%). The reaction involves glucose oxidation producing hydrogen peroxide, which couples with chromogenic substrates yielding colored products measured spectrophotometrically at 505 nm. Daily quality control employed multi-level commercial sera with acceptance criteria ±5% of target values. Laboratory personnel remained blinded to participant grouping.

Statistical Analysis

IBM SPSS Statistics version 25.0 performed all analyses. Continuous variables showing normal distribution (Shapiro-Wilk test) are presented as mean±standard deviation. Independent t-tests compared case-control differences. Cohen's d quantified effect sizes. Statistical significance was established at $p<0.05$ (two-tailed).

RESULTS

Demographic and Anthropometric Characteristics

Table 1 presents comprehensive participant characteristics. Maternal age demonstrated no significant difference between cases (28.4±3.5 years) and controls (28.0±4.2 years; p=0.72), ensuring age-matched comparison that eliminates confounding from age-related metabolic variations (19). Gestational age at assessment showed statistical equivalence (26.3±1.2 versus 25.9±1.0 weeks; p=0.36), removing temporal bias from progressive pregnancy-induced insulin resistance (20).

Body mass index exhibited marked elevation in cases (28.1±2.7 kg/m²) compared to controls (24.0±2.5 kg/m²; p<0.01), yielding large effect size (Cohen's d=1.58). This substantial disparity confirms obesity's critical role in GDM pathogenesis through inflammatory adipokine secretion and hepatic-muscular lipid accumulation that compromise insulin signaling (14,15).

Comparative Glycemic Profile Analysis

Table 1. Demographic, Anthropometric, and Glycemic Characteristics

Parameter	Cases (n=25) Mean±SD	Controls (n=25) Mean±SD	p-value	Cohen's d
Maternal age (years)	28.4±3.5	28.0±4.2	0.72	0.10
Gestational age (weeks)	26.3±1.2	25.9±1.0	0.36	0.36
Body mass index (kg/m²)	28.1±2.7	24.0±2.5	<0.01**	1.58
DIPSI serum glucose (mg/dL)	167.3±18.2	112.6±16.7	<0.001***	3.14
OGTT fasting glucose (mg/dL)	95.2±7.8	82.6±5.9	<0.001***	1.84
OGTT 1-hour glucose (mg/dL)	162.4±15.3	118.7±14.2	<0.001***	2.95
OGTT 2-hour glucose (mg/dL)	154.9±17.6	110.3±13.8	<0.001***	2.82

SD: standard deviation; DIPSI: Diabetes in Pregnancy Study Group India protocol; OGTT: oral glucose tolerance test
***p<0.01; ****p<0.001*
Effect size interpretation: small (0.2), medium (0.5), large (≥0.8)

DIPSI Performance

Mean DIPSI serum glucose showed profound case-control separation (167.3±18.2 versus 112.6±16.7 mg/dL; $p<0.001$) with very large effect size (Cohen's $d=3.14$). The 54.7 mg/dL absolute difference substantially exceeds the 140 mg/dL diagnostic threshold, confirming robust discriminatory capacity (10). Narrow standard deviations within groups indicate consistent glucose handling patterns, supporting measurement reproducibility.

OGTT Three-Timepoint Profile

Standard OGTT demonstrated consistent case hyperglycemia across all timepoints. Fasting concentrations revealed significant elevation (95.2±7.8 versus 82.6±5.9 mg/dL; $p<0.001$; Cohen's $d=1.84$). While case mean approached but did not exceed the 92 mg/dL diagnostic threshold (7), individual analysis showed 12 cases (48%) met fasting criteria, indicating basal β-cell dysfunction manifesting without exogenous glucose challenge (21).

Peak glycemic response occurred at 1-hour post-load, with cases demonstrating 162.4±15.3 versus control values of 118.7±14.2 mg/dL ($p<0.001$; Cohen's $d=2.95$). This 43.7 mg/dL difference reflects maximal glucose absorption coupled with inadequate early-phase insulin secretion—a pathognomonic feature of β-cell dysfunction (22). The 2-hour measurement showed 154.9±17.6 versus 110.3±13.8 mg/dL ($p<0.001$; Cohen's $d=2.82$), with case mean exceeding the 153 mg/dL threshold (7). Individual analysis revealed 16 cases (64%) met this criterion, demonstrating persistent hyperglycemia from combined insulin secretory defects and peripheral tissue resistance (23).

DIPSI-OGTT Concordance

Direct comparison of DIPSI (167.3±18.2 mg/dL) and OGTT 2-hour values (154.9±17.6 mg/dL) in cases revealed 12.4 mg/dL mean difference, likely reflecting pre-test food intake in the non-fasting DIPSI protocol (24). Despite this systematic offset, both methodologies achieved identical statistical discrimination (both $p<0.001$), supporting diagnostic equivalence.

DISCUSSION

Principal Findings

This comparative investigation demonstrates that DIPSI achieves diagnostic performance equivalent to standard OGTT for identifying gestational hyperglycemia while offering substantial operational advantages. Both protocols exhibited excellent case-control discrimination with highly significant glycemic differences across all measurement timepoints (all $p<0.001$). Cohen's d effect sizes ranging from 1.84 to 3.14 substantially exceed conventional

clinical significance benchmarks, confirming the magnitude of metabolic dysregulation extends well beyond statistical artifacts (25).

Mechanistic Interpretation

The comprehensive glycemic profiling provides distinct pathophysiological insights. Fasting hyperglycemia in 48% of cases reflects inadequate basal insulin secretion coupled with excessive hepatic glucose output via unopposed gluconeogenesis—processes normally suppressed by insulin but deregulated through hepatic insulin resistance (21). The pronounced 1-hour peak indicates defective first-phase insulin response, wherein rapid glucose-stimulated secretion fails to control postprandial excursions (22). Sustained 2-hour elevation demonstrates combined insulin secretory inadequacy and peripheral tissue resistance, particularly skeletal muscle glucose uptake impairment exacerbated by pregnancy hormones (23).

Obesity-GDM Mechanistic Links

The significant BMI elevation in cases (28.1 versus 24.0 kg/m²; $p<0.01$) warrants mechanistic consideration. Expanded adipose tissue functions as an active endocrine organ secreting pro-inflammatory mediators including tumor necrosis factor-alpha and interleukin-6, which directly impair insulin receptor signaling cascades (14). Simultaneously, reduced adiponectin secretion eliminates insulin-sensitizing effects (15). These alterations establish chronic inflammation that synergizes with placental hormones to precipitate glucose intolerance. Furthermore, ectopic lipid deposition in liver and muscle promotes lipotoxicity-mediated insulin resistance through ceramide accumulation and protein kinase C activation (14).

DIPSI Operational Advantages

DIPSI's practical benefits address concrete barriers limiting screening coverage in resource-constrained settings. Eliminating fasting requirements circumvents patient non-compliance from concerns about prolonged food abstinence during pregnancy—a significant cultural barrier in Indian populations (8). Single-visit completion reduces opportunity costs from multiple clinic attendances, particularly relevant for rural women facing transportation challenges (9). Non-fasting protocols also eliminate morning-only scheduling constraints, enabling flexible integration into afternoon clinics serving working women.

From healthcare system perspectives, DIPSI reduces phlebotomy volume by two-thirds compared to three-timepoint OGTT, proportionally decreasing laboratory reagent consumption, analyzer processing time, and personnel workload—critical considerations for high-volume antenatal clinics (10). These efficiency gains enable screening capacity expansion without proportional infrastructure investment, improving population coverage in underserved areas.

Comparative Evidence

Our findings align with multiple Indian validation studies. The landmark DIPSI development investigation demonstrated 100% sensitivity and 98% specificity using the 140 mg/dL threshold (10). Subsequent North Indian validation reported 100% sensitivity though lower specificity (70%), suggesting potential false-positive results requiring confirmatory testing (16). Tamil Nadu investigations found strong correlation (r=0.89) between DIPSI and OGTT 2-hour values, corroborating our parallel discrimination observations (17).

However, methodological heterogeneity across studies necessitates continued regional validation. Our Puducherry cohort contributes unique data from transitional urban-rural demographics experiencing rapid lifestyle changes associated with economic development—a population subset at elevated GDM risk yet underrepresented in literature.

Study Limitations

Several limitations warrant acknowledgment. The modest sample size (n=50), while adequate for primary objectives, precludes definitive sensitivity-specificity calculation and receiver operating characteristic analysis that would enable optimal threshold determination. The cross-sectional design provides diagnostic performance data but cannot address longitudinal questions regarding pregnancy outcomes or postpartum glucose tolerance evolution—clinically relevant endpoints requiring prospective cohort investigation.

Selection based on DIPSI results introduced verification bias, as cases were enriched for hyperglycemia by design. While facilitating comparative methodology evaluation, this approach prevents calculation of true population-level screening characteristics including predictive values. Future investigations should employ consecutive unselected screening with both tests administered regardless of initial results.

The single-center tertiary care setting may limit generalizability to primary health centers where most antenatal care occurs. Tertiary populations tend toward higher risk from comorbidity concentration, potentially biasing GDM prevalence upward. Multi-center studies spanning diverse healthcare tiers would provide more representative performance estimates. Finally, absence of perinatal outcome data prevents assessment of screening protocols' ultimate clinical utility—reducing adverse pregnancy outcomes—which represents the definitive validation benchmark.

Clinical Implications

Based on accumulated evidence, DIPSI integration into routine antenatal protocols appears justified, particularly where OGTT implementation faces logistical barriers. High-risk women (obesity, family history, prior GDM, polycystic ovary syndrome) may benefit from early screening using either methodology, with repeat testing at 24–28 weeks if initially negative.

DIPSI-positive results should prompt nutritional counseling, glucose monitoring instruction, and obstetric surveillance intensification.

Future Directions

Prospective cohort studies tracking pregnancy outcomes—cesarean delivery rates, neonatal anthropometry, birth trauma, hypoglycemia—stratified by screening methodology would provide definitive comparative effectiveness evidence. Cost-effectiveness analyses incorporating healthcare system perspectives and long-term societal costs of undiagnosed GDM would inform policy decisions regarding optimal screening strategy selection. Investigation of novel biomarkers including adipokines and inflammatory mediators might enable risk stratification algorithms guiding personalized screening intensity.

CONCLUSION

This investigation demonstrates DIPSI achieves diagnostic performance equivalent to standard three-timepoint OGTT for gestational diabetes identification while offering substantial operational advantages including single-visit completion, elimination of fasting requirements, and reduced phlebotomy burden. Both methodologies exhibited excellent discriminatory capacity with highly significant case-control glycemic differentiation across all parameters measured. The pronounced body mass index-GDM association reaffirms obesity's central pathophysiological role. These findings support DIPSI integration into routine antenatal screening protocols, particularly in resource-limited healthcare environments where patient compliance barriers and infrastructure constraints limit conventional OGTT feasibility. Widespread DIPSI implementation could enhance detection rates, facilitate earlier intervention, and ultimately reduce the substantial maternal-perinatal morbidity associated with undiagnosed pregnancy hyperglycemia.

ACKNOWLEDGMENTS

We express sincere gratitude to all pregnant women who participated in this investigation. We acknowledge the dedicated support from nursing staff of the Antenatal Outpatient Department and technical personnel of the Central Biochemistry Laboratory. We thank the Departments of Biochemistry and Obstetrics & Gynecology for providing necessary infrastructure.

FUNDING STATEMENT

This research received no external grant funding. All resources were provided through institutional support from Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth, Puducherry, India.

ETHICS APPROVAL AND CONSENT

This study received prospective approval from the Institutional Human Ethics Committee, MGMCRI (Reference: MGMCRI/2024/02/IHEC/76). Written informed consent was obtained from all participants in their preferred language following comprehensive explanation of study objectives, procedures, and rights. All participant information was maintained confidentially.

DATA AVAILABILITY

Data supporting the findings of this study are available from the corresponding author upon reasonable request, following institutional data sharing policy review and ensuring participant privacy protection.

AUTHOR CONTRIBUTIONS

R. Nalliarasi: Conceptualization, Methodology, Investigation, Data Curation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing, Project Administration

Reeta R: Methodology, Validation, Resources, Supervision, Writing – Review & Editing

P. Pallavee: Resources, Investigation (Patient Recruitment, Clinical Management), Writing – Review & Editing

All authors approved the final manuscript.

COMPETING INTERESTS

The authors declare no competing financial or non-financial interests that could influence this manuscript's content. No commercial entities provided financial support, equipment, or materials.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas, 10th Edition. Brussels: IDF; 2021.
2. Saeedi M, Cao Y, Fadl H, Gustafson H, Simmons D. Increasing prevalence of gestational diabetes mellitus when implementing the IADPSG criteria: systematic review and meta-analysis. Diabetes Res Clin Pract. 2021;172:108642.
3. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358(19):1991-2002.
4. Lowe WL, Scholtens DM, Lowe LP, Kuang A, Nodzenski M, Talbot O, et al. Association of gestational diabetes with maternal disorders of glucose metabolism and childhood adiposity. JAMA. 2018;320(10):1005-1016.
5. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med. 2005;352(24):2477-2486.
6. Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, et al. A multicenter, randomized trial of treatment for mild gestational diabetes. N Engl J Med. 2009;361(14):1339-1348.
7. International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33(3):676-682.
8. Mukerji G, Kainth S, Pendrith C, Lam S, Horvath N, Shah BR, et al. Predictors of low diabetes screening in pregnancy. Am J Obstet Gynecol. 2019;221(1):43.e1-43.e12.
9. Gopalan A, Misra P, Vikram NK, Sharma A, Pandey RM. Gestational diabetes mellitus: public health relevance and approach in resource constrained settings. J Fam Med Prim Care. 2020;9(4):1899-1903.
10. Seshiah V, Balaji V, Balaji MS, Paneerselvam A, Arthi T, Thamizharasi M, et al. Prevalence of gestational diabetes mellitus in South India (Tamil Nadu)—community based study. J Assoc Physicians India. 2008;56:329-333.
11. Seshiah V, Balaji V, Balaji MS, Sanjeevi CB, Green A. Gestational diabetes mellitus in India. J Assoc Physicians India. 2004;52:707-711.

12. Barbour LA, McCurdy CE, Hernandez TL, Kirwan JP, Catalano PM, Friedman JE. Cellular mechanisms for insulin resistance in normal pregnancy and gestational diabetes. Diabetes Care. 2007;30(Suppl 2):S112-S119.

13. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The pathophysiology of gestational diabetes mellitus. Int J Mol Sci. 2018;19(11):3342.

14. Catalano PM, Shankar K. Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. BMJ. 2017;356:j1.

15. Torloni MR, Betrán AP, Horta BL, Nakamura MU, Atallah AN, Moron AF, et al. Prepregnancy BMI and the risk of gestational diabetes: systematic review of the literature with meta-analysis. Obes Rev. 2009;10(2):194-203.

16. Rajput M, Bairwa M, Rajput R. Gestational diabetes: comparison between DIPSI and IADPSG criteria. J Family Med Prim Care. 2019;8(7):2223-2227.

17. Anjalakshi C, Balaji V, Balaji MS, Seshiah V. A prospective study comparing insulin and glibenclamide in gestational diabetes mellitus in Asian Indian women. Diabetes Res Clin Pract. 2007;76(3):474-475.

18. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004;363(9403):157-163.

19. Catalano PM, Tyzbir ED, Roman NM, Amini SB, Sims EA. Longitudinal changes in insulin release and insulin resistance in nonobese pregnant women. Am J Obstet Gynecol. 1991;165(6 Pt 1):1667-1672.

20. Kirwan JP, Hauguel-De Mouzon S, Lepercq J, Challier JC, Huston-Presley L, Friedman JE, et al. TNF-α is a predictor of insulin resistance in human pregnancy. Diabetes. 2002;51(7):2207-2213.

21. Kahn SE, Cooper ME, Del Prato S. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present, and future. Lancet. 2014;383(9922):1068-1083.

22. Gerich JE. Is reduced first-phase insulin release the earliest detectable abnormality in individuals destined to develop type 2 diabetes? Diabetes. 2002;51(Suppl 1):S117-S121.

23. DeFronzo RA, Tripathy D. Skeletal muscle insulin resistance is the primary defect in type 2 diabetes. Diabetes Care. 2009;32(Suppl 2):S157-S163.

24. Harmon KA, Gerard L, Jensen DR, Kealey EH, Hernandez TL, Reece MS, et al. Continuous glucose profiles in obese and normal-weight pregnant women on a controlled diet: metabolic determinants of fetal growth. Diabetes Care. 2011;34(10):2198-2204.

25. Sullivan GM, Feinn R. Using effect size—or why the P value is not enough. J Grad Med Educ. 2012;4(3):279-282.