ORIGINAL ARTICLE

Annals of Agricultural and Environmental Medicine 2025, Vol 32, No 1, 111–115
www.aaem.pl

Diagnostic values of trimethylamine (TMA) and trimethylamine N-oxide (TMAO) in the prediction of gestational diabetes mellitus – a systematic review and meta-analysis

Monika Tomaszewska[1,A-F], Michal Pruc[1,B-F], Damian Swieczkowski[1,2,B,E-F], Stepan Feduniw[3,4,E-F], Zuzanna Gaca[1,E-F], Lukasz Jankowski[5,C,E-F], Magdalena Florek-Luszczki[6,E-F], Lukasz Szarpak[7,8,1,A-F]✉, Halla Kaminska[9,E-F]

[1] *Department of Clinical Research and Development, LUXMED Group, Poland*
[2] *Department of Toxicology, Faculty of Pharmacy, Medical University, Gdańsk, Poland*
[3] *Department of Gynaecology, University Hospital, Zurich, Switzerland*
[4] *Department of Obstetrics, University Hospital, Zurich, Switzerland*
[5] *Department of Transplantation Medicine, Nephrology and Internal Diseases, Medical University, Warsaw, Poland*
[6] *Department of Medical Anthropology, Institute of Rural Health, Lublin, Poland*
[7] *Henry JN Taub Department of Emergency Medicine, Baylor College of Medicine, United States*
[8] *Institute of Medical Science, Collegium Medicum, The John Paul II Catholic University of Lublin, Poland*
[9] *Department of Children's Diabetology, School of Medicine, Katowice, Medical University of Silesia, Poland*
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Tomaszewska M, Pruc M, Swieczkowski D, Feduniw S, Gaca Z, Jankowski L, Florek-Luszczki M, Szarpak L, Kaminska H. Diagnostic values of trimethylamine (TMA) and trimethylamine N-oxide (TMAO) in the prediction of gestational diabetes mellitus: a systematic review and meta-analysis. Ann Agric Environ Med. 2025; 32(1): 111–115. doi:?

Abstract

Introduction and Objective. Gestational diabetes mellitus (GDM) is a growing concern for public health, affecting approximately 20% of pregnancies globally. This underscores an urgent need for improved diagnostic and management strategies. This study examines the relationship between trimethylamine N-oxide (TMAO) and its precursor trimethylamine (TMA) levels and GDM, aiming to deepen our understanding of GDM's pathophysiology and identify novel therapeutic targets.

Materials and Method. The meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. The PubMed, Scopus, Web of Science, and the Cochrane Library electronic databases were comprehensively searched up to 11 July 2024.

Results. The analysis included five studies, encompassing a total of 1,726 participants. The studies reported TMAO levels among GDM and non-GDM patients. The reported TMAO levels among GDM and non-GDM patients were 57.66 ± 42.2 and 47.94 ± 30.86, respectively (SMD = -0.49; 95%CI: -2.69 to 1.71; p = 0.66). However, TMA levels in the GDM group (224.28 ± 39.88) were statistically higher than in the non-GDM group (124.05 ± 21.93; SMD = 3.11; 95%CI: 2.84 to 3.37; p<0.001).

Conclusions. The best available evidence indicates that while TMA levels are significantly increased in GDM, TMAO does not seem to have a diagnostic role in gestational diabetes mellitus. More prospective trials evaluating TMA and TMAO values among pregnant women with gestational diabetes mellitus are required.

Key words

gestational diabetes mellitus, trimethylamine N-oxide, trimethyloxamine, TMA, TMAO

INTRODUCTION

Gestational diabetes mellitus (GDM), characterised by decreased insulin sensitivity and impaired glucose tolerance, poses a significant challenge for public health [1]. Recent studies estimated that GDM affects around 20% of pregnancies worldwide, with the prevalence showing an upward trend [2] and the highest incidence rates occurring in industrialized countries [3].

The impact of GDM extends beyond gestational complications, including gestational hypertension, polyhydramnios, and foetal growth abnormalities. Furthermore, GDM increases the risk of maternal and neonatal injuries, necessitates more frequent surgical interventions during delivery, and is associated with a range of neonatal complications, including cardiomyopathy, respiratory distress, and metabolic disorders that may persist into adulthood [4]. Given these risks, there is a pressing need to refine diagnostic strategies for GDM and develop effective preventive measures. While dietary management remains crucial in GDM management, additional interventions are required to mitigate the risk of GDM-related complications [5]. Although diet modification alone can be sufficient to control blood glucose levels in some cases, approximately 50% of those affected require pharmacological interventions. Although glucose metabolism generally returns to normal

✉ Address for correspondence: Lukasz Szarpak, Henry JN Taub Department of Emergency Medicine, Baylor College of Medicine, Houston (TX), United States
E-mail: lukasz.szarpak@gmail.com

Received: 17.10.2024; accepted: 07.12.2024; first published: 10.02.2025

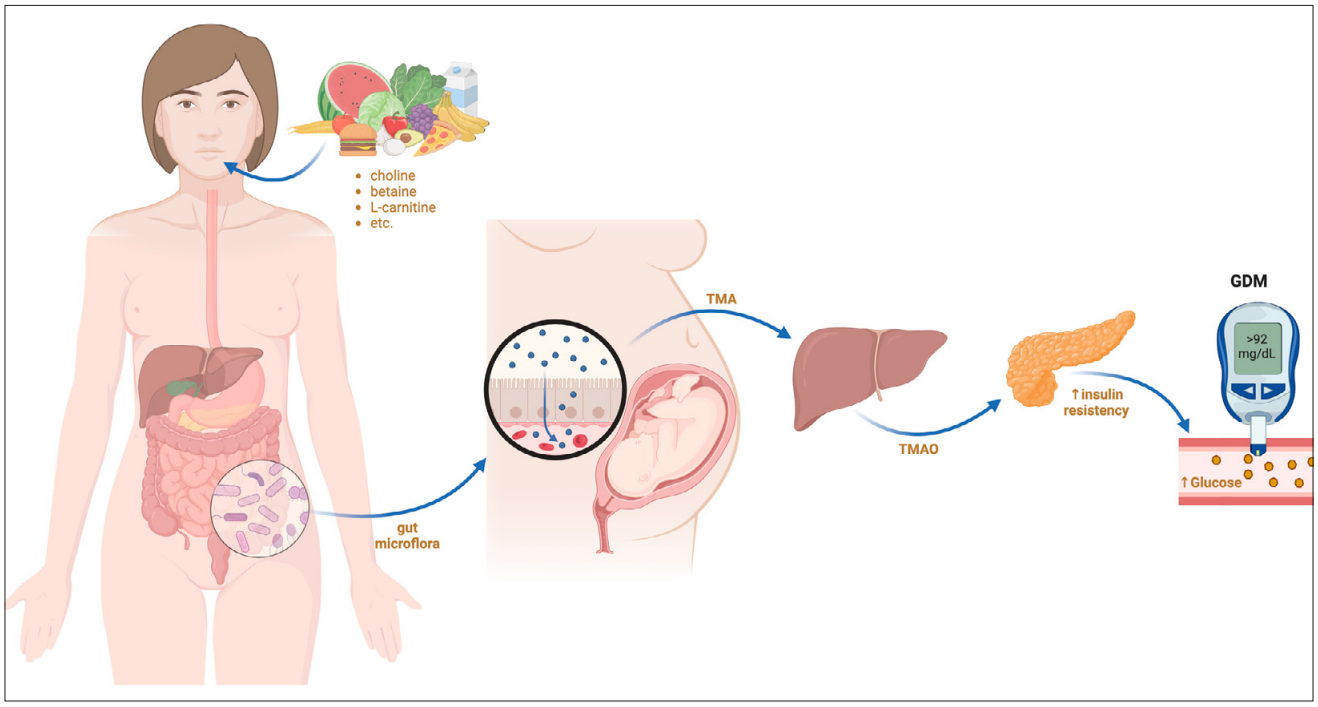

Figure 1. Biochemical pathways involved in the formation of TMA and TMAO

in the postpartum period, the women who developed GDM remain at an increased risk of developing type 2 diabetes later in life [6].

Recent advancements in identifying biochemical biomarkers offer a promising path to enhancing the diagnosis and management of GDM. Specifically, trimethylamine N-oxide (TMAO), along with its precursor trimethylamine (TMA), have gained attention due to their link to metabolic syndrome, cardiovascular diseases, and other chronic conditions [7] (Fig. 1). Their association with Type 2 Diabetes Mellitus and GDM, mainly through the mediation of pathological metabolic changes, is becoming more evident and substantiated [8–10].

The relevance of TMAO in GDM is highlighted by its role in the metabolic and inflammatory pathways that are fundamental to the pathogenesis of the disease. TMA-induced intracellular calcium mobilization from endoplasmic reticulum stores has been implicated in cellular stress responses, increasingly recognized as a central mechanism in the development of GDM [11]. This stress on the endoplasmic reticulum may trigger a series of adverse cellular events, including dysregulated transcription, changes in gene expression, ion channel dysfunction, metabolic disturbances, oxidative stress, and inflammation.

Diet significantly affects the gut microbiota [12]. TMAO is mainly produced in the liver, where TMA – a byproduct of gut microbial metabolism of certain nutrients, such as choline, betaine, and L-carnitine, are oxidized [17, 18]. High levels of TMAO have been linked to insulin resistance and impaired glucose metabolism – both indicative of GDM [10]. Additionally, there is growing interest in modulating gut microbiota through probiotic interventions as an innovative approach to potentially predict or manage GDM [13].

The aim of the study is to clarify the relationship between TMAO and TMA levels and the incidence of GDM, and thereby contribute to the existing body of knowledge on the pathophysiological underpinnings of GDM, and to identify potential targets for novel therapeutic intervention.

MATERIALS AND METHOD

Protocol and registration. The presented systematic review and meta-analysis was conducted in accordance with recommendations from the Cochrane Collaboration, and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [14]. The study protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (Registration No. CRD42024510672).

Search strategy. A comprehensive systematic review was performed by two authors (MP and MT) who conducted a literature search encompassing all publications cited on PubMed, Scopus, Web of Science, and the Cochrane Library for studies published up to 11 July 2024. The literature search utilized specific key words, such as 'gestational diabetes mellitus', 'gestational diabetes', 'trimethyloxamine', 'trimethylamine-n-oxide', 'trimethylamine-n-oxide', 'TMA', and 'TMAO'. Additionally, to ensure that all related articles were included in the study, reference lists of relevant studies were manually reviewed. Only articles published in English were included. The search results were then exported to EndNote X6 (Clarivate, London, United Kingdom; http://www.endnote.com) to remove duplicates.

Eligibility criteria. Two reviewers (MT and MP) independently assessed the eligibility of studies for inclusion, and any discrepancies between reviewers were resolved via consensus with a third reviewer (LS or HK). The inclusion criteria specified that the eligible studies had to be: 1) original peer-reviewed articles measuring TMA or TMAO; 2) include

adult participants only (≥18 years old); 3) report biomarker concentrations measured in both GDM and non-GDM groups.

Studies were excluded if they were: (A) review articles, letters, editorials, case reports, or series; (B) animal studies; (C) not published in English. In cases where multiple studies had been conducted on the same cohort or the same threshold, preference was given to the most recent or comprehensive study, and the duplicates were excluded.

Study selection and data extraction. Three reviewers (MT, MP, and LS) independently performed data extraction into a structured template in an Excel spreadsheet. The identified studies were screened against the inclusion and exclusion criteria, based on the study title and abstract. Full manuscripts of selected studies were then comprehensively reviewed for eligibility. For records from the same study with overlapping populations and study endpoints, preference was given to those with larger participant numbers and longer follow-up periods.

A secondary review of the extracted data was carried out by another investigator (either LS or HK) to ensure accuracy. For each study, the following information was extracted: study characteristics (author, country, study design, sample sizes), patient demographics (baseline characteristics), and TMA and TMAO values.

Quality of the included studies. The quality of the included studies was rigorously evaluated using the Newcastle-Ottawa Scale (NOS) [15] independentl by two authors (MT and MP). Any discrepancies were resolved through discussion until consensus was attained among all reviewers. The NOS is based on a star scoring system, where a maximum of nine (for prospective and cross-sectional studies) and ten scores (for case-control studies) can be awarded to each study. It consists of eight questions across three domains – selection, comparability, and exposure – each graded with a maximum score of one point, with the exception of comparability, which allowed for two points. Studies scoring ≥7 points were considered high quality.

Data synthesis and statistical analysis. Statistical analysis was conducted using STATA version 14 (Stata Corp., College Station, TX, USA) and Review Manager software (version 5.4, Nordic Cochrane Centre, Cochrane Collaboration, Denmark). All statistical tests were two-sided, and p-values <0.05 were considered statistically significant. The concentrations of inflammatory markers were collated as the mean and standard deviations (SDs). When the continuous outcome was reported as medians with ranges and interquartile ranges, means and standard deviations were estimated using the formula described by Hozo et al. [16]. Heterogeneity among studies was assessed using the I^2 index and the Cochrane Q test, with I^2 values <25%, 25%–75%, and >75%, indicating low, moderate, and high heterogeneity, respectively. The significance threshold for the Cochrane Q test was set at p<0.1. The DerSimonian and Laird methods were used for random-effect meta-analysis. To assess publication bias, funnel plots and Egger's test were employed for analyses including more than ten studies. Finally, sensitivity analyses were performed using a leave-one-out approach.

RESULTS

The initial search yielded 277 publications (after removal of duplicates), of which 258 were excluded after screening titles and abstracts, leaving 19 studies for the full-text review. Manual reference list checks did not identify any additional relevant studies. After full text evaluation, a further 33 studies were excluded for reasons listed in Figure 2. Finally, 5 studies comprising a total of 1726 participants were included in the review [8, 9, 17–19]. The process of study selection is visually represented in a PRISMA flow diagram (Fig. 2).

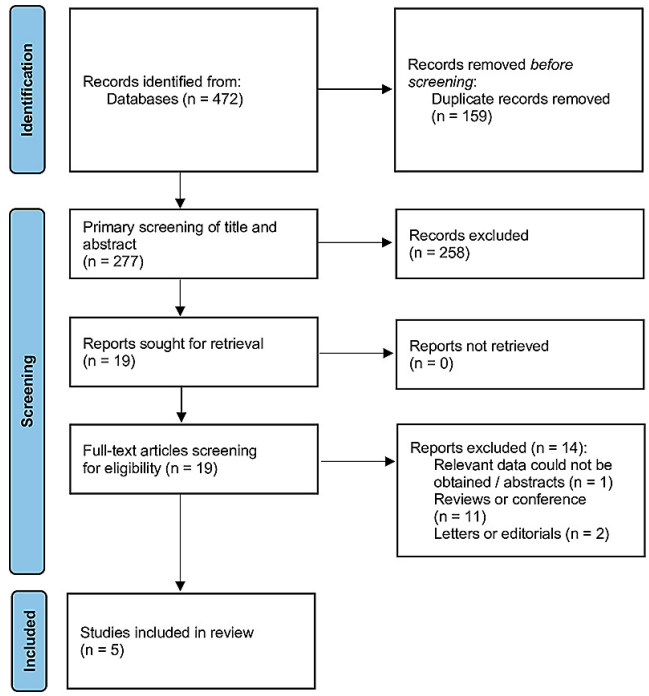

Figure 2. PRISMA Diagram Resembling Electronic Database Search and Inclusion/Exclusion Process of the Review

Study characteristics. The characteristics of the five included studies are shown in Table 1. The studies together involved 1,726 participants, divided into 819 individuals in the GDM group and 907 in the non-GDM (control) group. These studies, ranging in sample size from 48 – 866 participants, were published between 2018 – 2022, and conducted in China

Table 1. Baseline characteristics of included trials

Study	Country	Study design	Study group	No. of patients	Age	NOS score
Gao et al., 2022	China	Cross-sectional study	GDM	24	30.54 (4.67)	8
			non-GDM	24	28.61 (2.81)	
Gong et al., 2021	China	Hospital-based cohort	GDM	57	NS	7
			non-GDM	130	NS	
Huo et al., 2019	China	Prospective cohort study	GDM	243	29.2 (2.7)	8
			non-GDM	243	29.2 (3.3)	
Li et al., 2018	China	case-control study	GDM	433	29.81 (4.05)	8
			non-GDM	433	29.43 (3.72)	
Spanou et al., 2022	Greece	Prospective cohort study	GDM	62	34.27 (5.07)	8
			non-GDM	77	32.69 (4.72)	

Legends: NOS = Newcastle Ottawa scale; NS = not specified

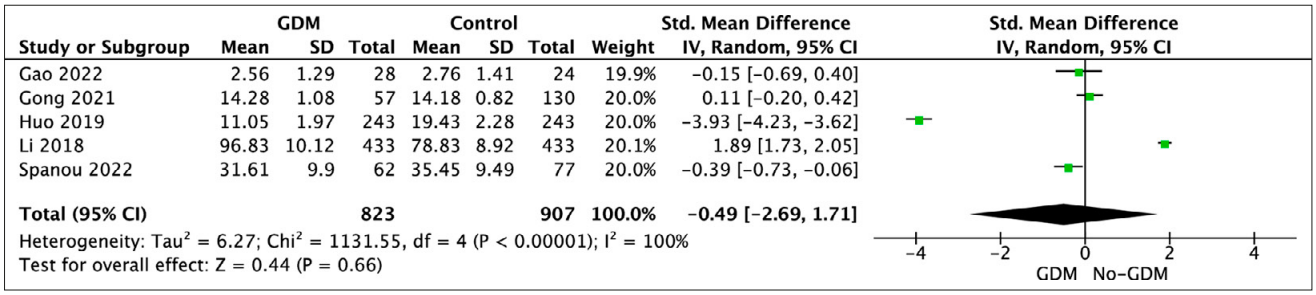

Figure 3. Forest plot of TMAO levels in GDM vs. non-GDM group. The centre of each square represents the weighted standardized mean differences for individual trials, and the corresponding horizontal line indicates a 95% confidence interval. The diamonds represent pooled results.
GDM – gestational diabetes mellitus; CI – Confidence Interval

and Greece. Quality assessment using the Newcastle-Ottawa Scale (NOS) rated all included studies as high quality (Tab. 1).

Meta-analysis. All five studies reported on TMAO levels in both GDM and non-GDM groups. The TMAO levels differed between the groups – 57.66 ± 42.2 in the GDM group versus 47.94 ± 30.86 in the non-GDM group, which was not statistically significant (SMD = -0.49; 95%CI: -2.69 to 1.71; p = 0.66 (Fig. 3). Only one study by Huo et al. reported on TMA levels in GDM and non-GDM groups. In the GDM group, TMA levels were at the level of 224.28 ± 39.88, and were statistically significantly higher than in the non-GDM group (124.05 ± 21.93; SMD = 3.11; 95%CI: 2.84 – 3.37; p<0.001).

DISCUSSION

The presented meta-analysis found no significant difference in TMAO levels between gestational diabetes mellitus (GDM) and non-GDM groups. Results were based on observational studies, to a significant degree based on nested case-control studies derived from prospective cohort studies, typical for this kind of epidemiological inquiry. In terms of TMA, only one study identified a statistically significant difference between GDM and non-GDM groups. Given the limited number of studies identified, especially concerning TMA, the findings of this study primarily serve as a basis for future discussions or could assist in the design of forthcoming studies.

A significant limitation of the studies included in the systematic review and meta-analysis is the fact that they were conducted among populations with specific dietary patterns, such as restricted meat consumption in Chinese patients, which may not be representative of broader dietary habits. Moreover, there is no detailed information on the actions following GDM diagnosis, including dietary adjustments and lifestyle modifications, which are typically recommended to manage the condition. The absence of detailed descriptions of these interventions limits the ability to fully understand the potential impact of TMA and TMAO levels on GDM, and further research is still needed.

Various biomarkers have been evaluated in the context of the diagnostic and predictive properties of biomarkers in GDM. Lorenzo-Almorós et al. divided the potential prognostic biomarkers used to assess the risk of GDM into three groups: 1) adipose tissue-derived factors, 2) placenta-secreted factors, and 3) urine biomarkers [20]. Since GDM is associated with the development of insulin resistance and inflammation, reducing the level of substances with anti-inflammatory effects and anti-oxidative properties may also be a predictive biomarker of GDM. Notably, adiponectin and leptin, derived from adipose tissue, emerge as critical indicators, with the former typically decreased and the latter increased in GDM patients. This suggests that an imbalance between substances with anti-inflammatory or antioxidant properties and substances with pro-inflammatory properties may contribute to the development of GDM. Moreover, these substances can be used to predict the risk of GDM and serve as biomarkers [19]. Further research is gravitating towards combining two biomarkers to refine predictive accuracy. For instance, the ficolin-3/adiponectin ratio has shown promising results, as Yuan et al. managed to obtain 90.9% sensitivity and 96.5% specificity in the prediction of GDM [21]. Additionally, urine-based biomarkers like serotonin and its metabolites (especially tryptophan) show significant differences between GDM and non-GDM individuals, underscoring their potential as diagnostic tools [17, 21].

More advanced biomarkers, the so-called placental proteins, have also emerged as potential GDM diagnostic biomarkers. Among these, pentraxin 3 (PTX3) and soluble fms-like tyrosine kinase-1 (sFlt-1) are notable examples. Zhao et al. showed that measuring these biomarkers between the 16th and 20th week of pregnancy can predict GDM risk [21]. Another group of placental biomarkers are the so-called non-coding RNAs, e.g., micro-RNAs (miR). Research suggests a correlation between specific micro-RNA levels and GDM, especially in obese women or those carrying male foetuses, While this may significantly limit the applicability of some of these biomarkers; it is important to note that final conclusions cannot be based on a single study, underlining the need for further investigation [22].

In one of the studies, a prospective cohort study, the analysis of repeated measurements – haemoglobin, haematocrit, fasting blood sugar, and red blood cell count – during the first and early second trimesters, revealed their predictive potential for gestational diabetes mellitus (GDM) early in pregnancy. Notably, the mean value of haemoglobin, haematocrit, and fasting blood sugar was higher among women diagnosed with GDM compared to non-GDM [23]. Moreover, combining haematocrit with glycated haemoglobin A1c also increased the predictive accuracy for GDM, showing superior specificity and sensitivity than when using glycated haemoglobin A1c alone [24]. Biomarkers based on routine blood test parameters, such as blood counts, should be considered a cost-effective solution facilitating not only diagnosis but also the validation of predictive models in clinical practice.

In the context of limitations that make it difficult to compare different studies, it should be noted that in the studies conducted so far, a significant challenge in comparing various studies on gestational diabetes mellitus (GDM) biomarkers lies in fact that biological samples are collected at different stages of pregnancy. Further research should identify which biomarker is the most effective for a specific pregnancy stage (e.g., for the second trimester). Perhaps defining the trimester may also be too general, and it may be necessary to specify the time in terms of a range expressed in weeks. Since the concentration of some substances varies throughout the day, validation studies should determine the time of day at which samples should be taken to ensure reliable results.

Moreover, since GDM is associated with inflammatory processes and insulin resistance, further validation is needed, particularly among populations at higher risk, e.g., obese women. Establishing clear cut-off points for biomarkers remains a pivotal task. Furthermore, the cost of testing some of biomarkers may be prohibitive. Additionally, one of the biggest challenges might be the formulation of clear diagnostic criteria for GDM.

Last but not least, the emergence of new biomarkers requires continuous evaluation of their predictive and diagnostic values. For example, Ruszała et al. highlight irisin and under-carboxylated osteocalcin as emerging biomarkers in gestational diabetes mellitus (GDM) research, indicating that decreased irisin and elevated under-carboxylated osteocalcin levels could be markers of heightened GDM risk [25]. This underscores the dynamic nature of GDM research and the quest for improved diagnostic tools.

CONCLUSIONS

Analysis of the studies comparing TMAO levels in GDM and non-GDM patients revealed no significant difference between the groups; however, a notable elevation in TMA levels was observed within the GDM group. These findings suggest a potential involvement of TMA in the pathogenesis of GDM, highlighting the need for further research to explore its role and broader implications.

REFERENCES

1. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care 2021;44:S15–33. doi:10.2337/dc21-ad09
2. Wang H, Li N, Chivese T, Werfalli M, et al. IDF Diabetes Atlas: Estimation of Global and Regional Gestational Diabetes Mellitus Prevalence for 2021 by International Association of Diabetes in Pregnancy Study Group's Criteria. Diabetes Res Clin Pract. 2022;183. doi:j.diabres.2021.109050
3. Damm P, Houshmand-Oeregaard A, Kelstrup L, Lauenborg J, Mathiesen ER, Clausen TD. Gestational diabetes mellitus and long-term consequences for mother and offspring: a view from Denmark. Diabetologia. 2016;59:1396–1399. doi:10.1007/s00125-016-3985-5
4. Sparks JR, Ghildayal N, Hivert MF, Redman LM. Lifestyle interventions in pregnancy targeting GDM prevention: looking ahead to precision medicine. Diabetol. 2022;65:1814–1824. doi:10.1007/s00125-022-05658-w
5. ElSayed NA, Aleppo G, Aroda VR, et al. Management of Diabetes in Pregnancy: Standards of Care in Diabetes-2023. Diabetes Care. 2023;46(Suppl 1):S254-S266. doi:10.2337/dc23-S015
6. Janeiro MH, Ramírez MJ, Milagro FI, Martínez JA, Solas M. Implication of trimethylamine n-oxide (TMAO) in disease: Potential biomarker or new therapeutic target. Nutrients 2018;10. doi:10.3390/nu10101398
7. Tang WHW, Wang Z, Kennedy DJ, et al. Gut microbiota-dependent trimethylamine N-oxide (TMAO) pathway contributes to both development of renal insufficiency and mortality risk in chronic kidney disease. Circ Res2014;116:448–455. doi:10.1161/CIRCRESAHA.116.305360
8. Huo X, Li J, Cao YF, et al. Trimethylamine N-Oxide Metabolites in Early Pregnancy and Risk of Gestational Diabetes: A Nested Case-Control Study. J Clin Endocrinol Metab. 2019;104(11):5529–5539. doi:10.1210/jc.2019-00710
9. Li P, Zhong C, Li S, et al. Plasma concentration of trimethylamine-N-oxide and risk of gestational diabetes mellitus. Am J Clin Nutr. 2018;108(3):603–610. doi:10.1093/ajcn/nqy116
10. McArthur KL, Zhang M, Hong X, et al. Trimethylamine N-Oxide and Its Precursors Are Associated with Gestational Diabetes Mellitus and Pre-Eclampsia in the Boston Birth Cohort. Curr Dev Nutr. 2022;6. doi:10.1093/cdn/nzac108
11. Wang Z, Klipfell E, Bennett BJ, et al. Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. Nature. 2011;472:57–65. doi:10.1038/nature09922
12. Canyelles M, Tondo M, Cedó L, Farràs M, Escolà-Gil JC, Blanco-Vaca F. Trimethylamine N-oxide: A link among diet, gut microbiota, gene regulation of liver and intestine cholesterol homeostasis and HDL function. Int J Mol Sci. 2018;19. doi:10.3390/ijms19103228
13. Homayouni A, Bagheri N, Mohammad-Alizadeh-Charandabi S, et al. Prevention of Gestational Diabetes Mellitus (GDM) and Probiotics: Mechanism of Action: A Review. Curr Diabetes Rev. 2019;16:538–45. doi:10.2174/1573399815666190712193828
14. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi:10.1136/bmj.n71
15. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25:603–605. doi:10.1007/s10654-010-9491-z
16. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol. 2005;5:13. doi:10.1186/1471-2288-5-13
17. Gao Y, Chen H, Li J, Ren S, Yang Z, Zhou Y, Xuan R. Alterations of gut microbiota-derived metabolites in gestational diabetes mellitus and clinical significance. J Clin Lab Anal. 2022;36(4):e24333. doi:10.1002/jcla.24333
18. Gong X, Du Y, Li X, Yang J, Zhang X, Wei Y, Zhao Y. Maternal Plasma Betaine in Middle Pregnancy Was Associated with Decreased Risk of GDM in Twin Pregnancy: A Cohort Study. Diabetes Metab Syndr Obes. 2021 Jun 3;14:2495–2504. doi:10.2147/DMSO.S312334
19. Spanou L, Dimou A, Kostara CE, Bairaktari E, Anastasiou E, Tsimihodimos V. A Study of the Metabolic Pathways Affected by Gestational Diabetes Mellitus: Comparison with Type 2 Diabetes. Diagnostics. 2022;12:2881. doi:10.3390/diagnostics12112881
20. Lorenzo-Almorós A, Hang T, Peiró C, et al. Predictive and diagnostic biomarkers for gestational diabetes and its associated metabolic and cardiovascular diseases. Cardiovasc Diabetol. 2019;18(1):140. doi:10.1186/s12933-019-0935-9
21. Yuan XS, Shi H, Wang HY, Yu B, Jiang J. Ficolin-3/adiponectin ratio for the prediction of gestational diabetes mellitus in pregnant women. J Diabetes Investig. 2018;9(2):403–410. doi:10.1111/jdi.12688
22. Wander PL, Boyko EJ, Hevner K, et al. Circulating early- and mid-pregnancy microRNAs and risk of gestational diabetes. Diabetes Res Clin Pract. 2017;132:1–9. doi:10.1016/j.diabres.2017.07.024
23. Shaarbaf Eidgahi E, Nasiri M, Kariman N, et al. Diagnostic accuracy of first and early second trimester multiple biomarkers for prediction of gestational diabetes mellitus: a multivariate longitudinal approach. BMC Pregnancy Childbirth. 2022;22(1):13. doi:10.1186/s12884-021-04348-6
24. Wu K, Cheng Y, Li T, et al. The utility of HbA1c combined with haematocrit for early screening of gestational diabetes mellitus. Diabetol Metab Syndr. 2018;10:14. doi:10.1186/s13098-018-0314-9
25. Ruszała M, Niebrzydowska M, Pilszyk A, Kimber-Trojnar Ż, Trojnar M, Leszczyńska-Gorzelak B. Novel Biomolecules in the Pathogenesis of Gestational Diabetes Mellitus. Int J Mol Sci. 2021;22(21):11578. doi:10.3390/ijms222111578