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ORIGINAL ARTICLE

Ultrasound assessment of foetal pancreatic circumference and gestational diabetes: a state-of-the-art of current evidence

Foetal pancreas and GDM: state-of-the-art

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ABSTRACT

Objective. This state-of-the-art review aims to evaluate the current evidence on the association between foetal pancreatic circumference (PC) and Gestational Diabetes Mellitus (GDM), analysing the feasibility, diagnostic performance, and methodological consistency of this novel sonographic parameter.

Materials and Methods. A comprehensive literature search was conducted to March 2025. Studies were included if they evaluated foetal PC via ultrasound in the second trimester and assessed its

association with GDM. Quality was assessed using the MINORS tool. Due to the limited number and heterogeneity of studies, data were synthesized narratively.

Results. Twenty studies were screened. Three observational studies met the inclusion criteria. Two studies reported a significant association between increased foetal PC and GDM, suggesting PC ≥ 80th percentile as a potential predictive threshold. Conversely, one study found no significant correlation. All studies confirmed the technical feasibility and reproducibility of PC measurement during mid-gestation. Quality assessment revealed moderate-to-high methodological rigour.

Conclusions. Despite preliminary results suggesting foetal PC as a promising and accessible marker for early GDM risk stratification, current evidence remains inconclusive. The novelty of this approach highlights the urgent need for standardised protocols and large-scale multicentre studies. If validated, foetal PC could offer a reliable alternative to the oral glucose tolerance test (OGTT), especially in settings where OGTT adherence is low or infeasible.

Key words

Foetal Pancreas; ultrasonography; glucose tolerance test; prenatal screening; gestational diabetes.

Introduction

Gestational Diabetes Mellitus (GDM) is the leading health disease in pregnant women [1], affecting approximately 16.5% of pregnant women worldwide [2]. GDM is associated with multiple risk factors [3], including low pre-pregnancy physical activity, advanced maternal age, and a family history of diabetes, with pre-pregnancy overweight and obesity representing a particularly significant determinant [4].

GDM pose significant foetal complications, such as adverse perinatal outcomes and a longer-term risk of obesity and glucose intolerance in offspring [5]. Moreover, mothers with GDM have a high risk of developing hypertensive disorders during pregnancy and a high risk of diabetes mellitus thereafter [5].

Early identification of women at risk for GDM is crucial for implementing timely interventions and improving perinatal outcomes [6].

According to the 2021 Recommendation Statement by the US Preventive Services Task Force (USPSTF) [7], there is moderate certainty of benefit in screening for GDM at 24 weeks of gestation or later, as it may improve maternal and foetal outcomes [8].

Actually, an Oral Glucose Tolerance Test (OGGT) remains the gold standard for the screening and diagnosis of GDM [9]; [10].

The OGTT is the only test recommended by the World Health Organization (WHO) [11] , the National Institute for Health and Care Excellence (NICE) [12], the American Diabetes Association (ADA) [13] and the International Federation of Obstetrics and Gynaecology (FIGO) [14].

From a clinical point of view, ultrasound remains central in follow-up: it allows not only monitoring growth (preventing macrosomia and guiding possible therapies such as insulin) [15], but also identifying signs of foetal distress (via Doppler such as Umbilical Artery Pulsatility Index or Cerebro-placental ratio) [16] to optimise the timing of delivery [17].

Beyond growth surveillance, ultrasound Doppler provides a haemodynamic context in GDM, with diabetic pregnancies exhibiting higher umbilical artery resistance and thicker placentae; such evidence supports the novel parallel exploration of foetal ultrasound markers, such as pancreatic circumference (PC), for risk stratification [18].

In recent years, there has been growing interest in utilizing ultrasound measurements of PC as a potential predictive marker for GDM [19]. This approach is relatively novel, with initial studies emerging only in the past few years, suggesting a possible link between foetal pancreatic growth and maternal glycaemic status.

However, the clinical application of foetal pancreatic measurements remains under investigation, indicating the need for further research to validate these findings and establish standardized measurement protocols.

Given the novelty of this topic in the literature and the importance of early detection of GDM, this state-of-the-art review aims to critically evaluate the current evidence on the association between foetal pancreatic size and the risk of GDM, assessing the validity and reliability of this measurement as a predictive tool.

Materials and Methods

Study Design

This state-of-the-art review was conducted in accordance with the principles of systematic exploration and synthesis, adapted to reflect the early and limited body of literature on this emerging topic. Given the small number of eligible studies, no meta-analysis was performed at this stage, and the emphasis was placed on a comprehensive qualitative appraisal of the available evidence.

Eligibility Criteria

Studies were included if they met the following criteria: (1) pregnant women with singleton gestations undergoing second-trimester foetal ultrasound; (2) measurement of foetal PC; (3) diagnosis of GDM as an outcome; (4) observational study design; (5) English language; (6) full-text availability. Case reports, reviews, editorials, and studies without data on GDM were excluded.

Information Sources and Search Strategy

A comprehensive literature search was conducted in March 2025 using PubMed, Scopus, Web of Science, and Embase, spanning from inception to March 2025 (with the last research update on 28 March 2025).

The search strategy included the terms: ("foetal pancreas" OR "foetal pancreatic circumference" OR "foetal pancreas size") AND ("gestational diabetes" OR "GDM").

Study Selection

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) [20] guidelines were used to improve the reporting of the reviewers. All retrieved records were imported into a reference manager, and duplicates were removed. Two reviewers (MCS, FP) independently screened titles and abstracts. Full texts were then assessed for eligibility. Discrepancies were resolved by consensus.

No ethical approval or patient consent is required, as all analyses were based on previously published studies. The analysis is not a registered study. Reviewers used the search protocol previously described to identify the literature. The reviewers initially screened titles, then abstracts, and later full papers. When a paper was considered potentially relevant, its full text was reviewed. If a study could not be unequivocally excluded due to its title and abstract, a discussion ensued between the two independent reviewers. The full text of all papers not excluded was evaluated. The number of articles excluded or included was registered and reported in a PRISMA flowchart [21] (Figure 1) [22].

Data Collection Process and Data Items

Data were extracted using a standardized Excel sheet. Variables included: author, year, study design, population characteristics, gestational age at measurement, ultrasound method, PC values, diagnostic criteria for GDM, effect estimates, confounding factors, and conclusions.

Quality assessment of studies and risk of bias

The reviewers (M.C.S. and FP) performed a qualitative analysis of the studies. The Methodological Index for Non-Randomized Studies (MINORS) [23] was used for quality assessment of non-randomized studies. The reliability of this score has already been demonstrated. The simplicity of MINORS, comprising only 12 items, makes this item readily usable by both readers and researchers. Given that all included studies employed non-randomised observational designs, and none were structured as classical cohort or case-control comparisons, the MINORS tool was deemed the most suitable instrument for quality assessment.

Statistical Analysis

Given the limited number of included studies and the heterogeneity of their designs and outcomes, no formal meta-analysis was conducted. Instead, the findings were synthesized narratively, highlighting key similarities, differences, and methodological considerations.

Study Flow and Justification for Inclusion Numbers

The initial search identified 20 studies. After abstract screening, 13 studies were excluded. Three studies were excluded due to a lack of full-text access. One study was excluded as a duplication. Thus, only three studies met the eligibility criteria and were included in the present state-of-the-art review, as shown in Figure 1. Due to the novelty of the topic, the number of eligible studies is limited. This reflects the emerging interest in using foetal pancreas measurements to predict GDM.

Results

Three observational studies investigating the relationship between PC and the risk of GDM were included in this article.

The first study, conducted by Gilboa et al. [24], was a prospective cross-sectional observational study involving 91 pregnancies complicated by GDM and 34 with pregestational diabetes mellitus (PGDM). The authors measured foetal PC using high-resolution ultrasound machines (Voluson 730, E8, and E10; GE Medical Systems) between the 19th and 38th weeks of gestation. Their findings showed that foetal PC was significantly larger in pregnancies complicated by GDM compared to normoglycemic pregnancies. Additionally, the foetal PC significantly correlated with estimated foetal weight (EFW), abdominal circumference (AC), and gestational age (Pearson correlation coefficient = 0.802, 0.762, 0.764, $p < 0.001$) [24].

In the study conducted by Gilboa et al.[24], Thirty-four women with pregestational diabetes Mellitus (PGDM) were also included; all were treated with insulin, and 82.3% received therapy via an insulin pump. In this subgroup, foetal PC correlated significantly with abdominal circumference

(AC), estimated foetal weight (EFW), and gestational age (Pearson's r = 0.817, 0.681, and 0.710, respectively; all p < 0.001). When plotted against the normal 5th–95th centile reference range, PGDM PC values clustered around the median with wide dispersion (r^2 = 0.508, p < 0.001); the weekly mean Z-score decreased across gestation, positive until ~25 weeks and negative toward term. Notably, PC did not correlate with the EFW centile (r = 0.156, p = 0.446; cubic r^2 = 0.026, p = 0.741).

Findings reported in the article[24] suggest that all included patients (GMD and PGDM) achieved effective glycaemic control under multidisciplinary follow-up in the endocrinology/maternal-foetal medicine clinic. In fact, authors discuss that the observed findings may reflect optimal pre-conception glycaemic control in the population. Study reports that within the GDM cohort, glycaemic control was achieved with lifestyle measures in 14/91 (15.4%) women, while the remaining required insulin or oral hypoglycaemic agents; all PGDM patients were on insulin therapy (most on pumps). Overall, the authors concluded that foetal PC could serve as a potential early ultrasound marker for the detection of GDM. By contrast, in women with PGDM, foetal PC was comparable to non-diabetic controls, and the EFW centile remained around the median, possibly reflecting effective pre-conception glycemic control [24].

The second study, a retrospective cohort by Gilboa et al. [25], examined 195 pregnancies (24 with GDM and 171 normoglycemic) assessed between the 20th and 25th weeks of gestation using the same ultrasound equipment. This study introduced percentile-based cut-offs and identified that a foetal pancreatic circumference ≥80th percentile was significantly associated with the later diagnosis of GDM (82.4 ± 14.6 in the GDM group vs 62.8 ± 7.6 in the non-GDM group; P < 0.001 [22]).

The article reported that the foetal pancreatic circumference centile was correlated positively with the EFW centile (Pearson's coefficient, 0.243; P=0.001) [25]. Specifically, the odds ratio for developing GDM in foetuses with a PC ≥80th percentile was approximately 5.0, and the area under the receiver operating characteristic curve (AUC) for GDM prediction was 0.71, indicating moderate diagnostic accuracy. The authors suggested that foetal PC could be integrated into second-trimester screening as an early, non-invasive tool to identify pregnancies at high risk of GDM [25].

The third study, by Guleroglu et al. [26], was a prospective observational study involving 109 pregnant women (19 with GDM and 90 normoglycemic), in which foetal PC was measured at two time points: between the 20th and 22nd weeks, and between the 24th and 28th weeks of gestation. Unlike the previous two studies, this study did not find a statistically significant difference ($p > 0.05$) in the median values of foetal PC between women who developed GDM and those who did not, reporting that the increase in pancreatic size observed between 20–22 and 24–28 weeks in both groups was interpreted as a physiological consequence of overall foetal growth, remaining comparable between GDM and normoglycemic pregnancies at each time point, and concluding that foetal pancreatic size does not provide potential for early prediction of GDM at 20–22 weeks of gestation.

The authors [26] also investigated other maternal serum biomarkers, such as glycated albumin, suggesting that while biochemical markers might offer predictive value, foetal PC alone did not demonstrate a clear correlation with GDM in their cohort.

A qualitative assessment of the methodological quality of the included studies was conducted using the Methodological Index for Non-Randomized Studies (MINORS) [23]. Total scores ranged from 11 to 13 out of 16, indicating moderate to high quality, as shown in Table 1

Gilboa et al. [24] obtained the highest score (13/16), reflecting a clearly stated aim, prospective design, appropriate endpoints, and adequate follow-up. Both Gilboa et al. [25] and Guleroglu et al. [26] received a total score of 11/16, with limitations primarily due to retrospective data collection in one case, and the lack of prospective sample size calculation and fully unbiased endpoint assessment in both. Overall, the quality of the evidence was acceptable but underlined the need for larger, standardised prospective studies in this field. Due to the limited number and heterogeneity of studies, no meta-analysis was performed.

Discussion

The measurement of PC has emerged as a novel ultrasonographic marker with potential application in the early identification of pregnancies at risk for GDM.

Regarding the diagnostic criteria for GDM, studies adopted different thresholds, thereby reducing comparability among studies.

Gilboa et al.[24] adopted the Israeli Society of Obstetrics and Gynecology two-step approach[27]: GDM was diagnosed by 1-h 50 g GCT ≥ 200 mg/Dl followed by) 100 g OGTT (3 h) using Carpenter–Coustan cut-offs[28] (95/180/155/140 mg/dL at 0/60/120/180 min); PGDM was defined by a pre-pregnancy diabetes diagnosis.

Likewise, in the study by Gilboa et al.[25], a two-step strategy was used at 25–28 weeks (screening 50 g GCT with a 140 mg/dL threshold, followed, if positive, by 100 g OGTT (3 h) with Carpenter–Coustan cut-offs). In contrast, Guleroglu et al.[26] applied a one-step 75 g OGTT (2 h) at 24–28 weeks (International Association of Diabetes and Pregnancy Study Group -IADPSG- criteria[29]). This heterogeneity in testing strategy (one- vs two-step), timing (24–28 vs 25–28 weeks), and diagnostic cut-offs is a potential source of clinical and methodological variability when comparing associations between foetal PC and GDM across studies.

In all three studies included in the present article [24–26], detailed protocols were provided regarding the ultrasound technique used to assess PC, ensuring the comparability of data across cohorts. The foetal pancreas is visualized as a hyperechoic structure bordered by the stomach and spine, enabling consistent identification.

All three studies employed 2D ultrasound to assess foetal pancreatic circumference using a transverse abdominal view, with the pancreas identified between the stomach and the aorta. In both 2021 and 2024 studies by Gilboa et al.[24],[25] The foetal spine was positioned to optimise visualisation, and a consistent sonographic technique was applied. The 2021 study focused on biometric correlations, while the 2024 study evaluated diagnostic cut-offs, particularly the 75th and 80th percentiles, for predicting GDM.

Guleroglu et al. [26] used a similar imaging approach but with slight caudal angulation and specific spine positioning (between 3–5 or 7–9 o'clock) to enhance visibility. Unlike the others, this study

performed measurements at two time points (20–22 and 24–28 weeks) and reported high intra-observer agreement (Kappa 0.83–0.89), underscoring the method's reproducibility.

Despite slight variations in technique and timing, all studies confirmed that foetal pancreatic circumference can be reliably measured in the second trimester using standard ultrasound.

The feasibility of foetal pancreatic measurement via ultrasound was previously demonstrated by Hata et al., who reported that the pancreas can be consistently visualised (up to 80% of cases) from 20 weeks of gestation onward as an echogenic, S-shaped structure [30]. Building on this, more recent work by Yang Li et al. [25] confirmed that the optimal visualisation of the PC is reached between 22 and 27 weeks, highlighting the need for standardised protocols for measurement.

A valuable technical reference on foetal pancreatic imaging has been recently provided by Singh [31], who described a reproducible sonographic approach using splenic vessels as anatomical landmarks. According to the author, by positioning the foetal spine between 3–5 or 7–9 o'clock and applying a slight caudal angulation, the pancreas can be clearly visualized from as early as 18 weeks [31]. The use of high-definition power Doppler further enhances identification, highlighting the importance of standardized imaging protocols to improve reproducibility and diagnostic consistency [31].

From a clinical perspective, the measurement of foetal PC may serve as an indirect marker of foetal exposure to maternal glycemia. In line with Pedersen's hypothesis in 1920, maternal hyperglycaemia induces foetal hyperinsulinemia, which may lead to β-cell hyperplasia and pancreatic enlargement as an adaptive foetal response [32].

A key advantage of incorporating foetal PC as a potential screening tool for GDM lies in its non-invasive nature and its compatibility with routine mid-trimester ultrasound evaluations. Currently, the OGTT remains the gold standard for GDM screening, despite being considered imperfect. However, it is increasingly being challenged for its clinical practicality, reliability, and patient acceptability [33].

A recent study by Lachmann et al. [34], conducted in a large UK tertiary obstetric centre, found that 12.7% of women invited for OGTT did not complete testing, with 32.2% never completing the protocol

at all. The most frequently cited barriers were the inability to tolerate the test protocol (e.g., nausea, vomiting, prolonged fasting), social or mental health issues, and difficulty managing multiple antenatal appointments. Notably, younger age, lower socio-economic status, higher parity, and minority ethnic background were all significantly associated with non-completion. The authors [34] emphasise the need for alternative methods of GDM testing that are easier to schedule and tolerate, especially for vulnerable populations.

In this context, foetal PC measurement offers several practical advantages. It is non-invasive, quick, and requires no additional maternal preparation, unlike the OGTT, which necessitates fasting and multiple venous blood draws over two hours. Additionally, it can be integrated seamlessly into the standard second-trimester anomaly scan, minimizing the need for separate clinical visits and improving adherence to screening protocols, particularly in under-resourced settings.

A detailed critical analysis of the included studies highlights both the potential and limitations of foetal PC as a marker related to GDM.

Gilboa et al.[24] conducted a prospective cross-sectional study that provided clear sonographic imaging protocols and distinct analyses for GDM and PGDM subgroups. The study's prospective nature and detailed foetal pancreatic measurements represent its principal strengths. However, its cross-sectional design precludes temporal inference, thereby limiting the ability to draw causal conclusions. Moreover, the absence of a prespecified sample size calculation and the lack of multivariable adjustment for confounding variables, such as AC, EFW, maternal body mass index (BMI), and gestational age at scanning, reduce the robustness. The single-centre setting and lack of external validation limit the generalizability of the findings.

Gilboa et al.[25] conducted a retrospective cohort design involving a low-risk population assessed during routine second-trimester anatomy scans. A key innovation of this retrospective cohort was the introduction of centile-based thresholds for foetal PC. In their analyses, the 80th centile cut-off yielded the highest sensitivity and positive predictive value (PPV) for subsequent maternal GDM, with corresponding increases in odds ratios for higher PC centiles. This approach is clinically relevant due to alignment with standard prenatal screening. However, limitations include the retrospective

design, a relatively small GDM subgroup (n = 24), and a lack of external validation. Notably, despite observing correlations between PC and EFW centiles, the study did not conduct analyses to isolate the independent predictive value of PC beyond standard foetal biometric parameters.

The prospective study by Guleroglu et al.[26] focused on assessing the reproducibility of PC measurement at two clinically pertinent gestational periods (20–22 and 24–28 weeks). This study demonstrated high intra-observer reliability for PC measurement, thereby reinforcing the feasibility of the measurement. However, no significant differences in PC were found between the GDM and control groups (normal glucose tolerance group, NGT) at either time point. The study's limited sample size (90 women with NGT and 19 women with GDM), single-centre design, and minimal adjustment for maternal and foetal covariates restrict statistical power and external validity.

A central clinical question is whether an increased foetal PC reflects a pancreas-specific enlargement related to GDM, or instead mirrors overall foetal macrosomia, a well-known consequence of GDM[35].

Across all three studies, PC showed strong positive correlations with standard growth measures. In the study by Gilboa et al.[24], Even if PC was higher in GDM, the strong correlations with AC, EFW and gestational age (Pearson's $r > 0.7$) indicate that larger PC may partly capture overall foetal size. Notably, in the PGDM subgroup with glycaemic control, PC and EFW centiles hovered around the median, suggesting that pancreatic enlargement is not evident when overgrowth is mitigated. Gilboa et al.[25] Likewise, higher PC centiles were linked to subsequent GDM; however, correlations with EFW centiles and the absence of adjustment analyses leave it uncertain whether PC has predictive value independent of overall size. Consistently, Guleroglu et al.[26] found no between-group differences in PC at mid-gestation, aligning with the lack of an overgrowth signal.

Taken together, these findings support a biologically plausible pathway whereby maternal hyperglycaemia in GDM induces foetal hyperinsulinemia, which can drive both pancreatic enlargement and macrosomia. Thus, the observed association between foetal PC and GDM may be partly confounded or mediated by foetal size. Disentangling these mechanisms requires analyses that (i) adjust for AC/EFW and key maternal covariates, (ii) test the incremental predictive value of

PC beyond standard biometry, and (iii) explore mediation to quantify the indirect effect through macrosomia.

Future studies should therefore aim to determine whether foetal PC offers incremental predictive value beyond conventional biometric parameters, through multivariable and mediation analyses that could clarify its role as an independent sonographic marker of GDM.

This article presents several strengths, including its systematic methodology, the inclusion of detailed ultrasound protocols, and its focus on a novel, non-invasive parameter for early assessment of GDM risk. The most significant limitation of this study is the small number of studies included, which reflects the overall scarcity of literature on this emerging topic. In fact, three potentially relevant studies were excluded due to the unavailability of full-text access, which may have limited the completeness of the evidence synthesis. Moreover, two out of the three studies were authored by the same research group. They employed similar methodologies, further limiting the heterogeneity of the available evidence and potentially affecting the generalizability of the findings, as results from a single research team may reflect centre-specific practices or population characteristics.

Methodologically, the three studies included in the present article share a broadly similar sonographic approach, confirming the technical feasibility and reproducibility of PC measurement. However, differences in study design, cohorts, sample sizes, OGTT criteria and analytical framework may affect interpretability and generalizability.

If future prospective studies confirm the diagnostic validity and reproducibility of foetal PC as a predictive biomarker for GDM, it could represent a paradigm shift in prenatal care, allowing earlier and more acceptable risk stratification. This could be especially relevant in populations where compliance with OGTT is low or in settings lacking resources for universal biochemical screening. Nevertheless, further research is needed to determine optimal cut-off values, standardize measurement protocols, and assess the added value of foetal PC compared to traditional risk factors or combined predictive models.

Conclusions

Building upon the findings of a limited number of studies, considering the novelty of the topic, we explored the technical methodology and clinical implications of foetal pancreatic circumference measurement. The ultrasound assessment of foetal pancreatic circumference represents a promising, non-invasive indicator for early risk stratification of GDM.

While two studies supported the predictive value of foetal PC for GDM, one failed to demonstrate a significant association, reflecting variability in current findings.

Overall, the results of currently available evidence, although suggesting a possible association between this ultrasound parameter and GDM, are still preliminary and do not allow definitive conclusions due to the limited number of included studies, methodological heterogeneity, and the lack of large-scale studies.

The study suggests the technical feasibility and reproducibility of the measurement in the second trimester, but highlights the need for further investigations to validate this marker and to establish standardized measurement protocols.

It is also necessary to clarify whether pancreatic circumference serves as an independent predictor with respect to standard foetal biometric measurements, such as estimated foetal weight and abdominal circumference.

If validated, foetal PC could serve as a practical and patient-friendly alternative to the OGTT, particularly in settings with low screening adherence. Its integration into routine second-trimester ultrasound could improve early risk stratification and enhance prenatal care.

Compliance with Ethical Standards

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Authors' Contributions

M.C.S.: Conceptualisation, Methodology, Writing – original draft, Supervision

C.D.C.N.: Formal Analysis, Data curation, Writing – review & editing

R.M.: Investigation, Visualization, Writing – review & editing

D.L.: Resources, Validation

F.G.: Project administration, Writing – review & editing

R.A.: Supervision, Validation

C.T.: Data curation, Writing – review & editing

F.P.: Supervision, Final approval

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Study Registration

Not applicable. This is a state-of-the-art review, not a clinical trial or prospective observational study.

Disclosure of interests

All authors declare that they have no competing financial or non-financial interests relevant to the content of this article. There are no conflicts of interest related to employment, consultancies, stock ownership, honoraria, patents, or any political, personal, religious, or academic biases.

Ethical approval

This article is a systematic review and does not involve new studies with human participants or animals performed by any of the authors. Therefore, approval by an ethics committee was not required.

Informed consent

Not applicable.

Data sharing

The data used in this review are publicly available and derived from previously published articles.

No new datasets were generated or analyzed in this study.

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Table 1: Methodological quality assessment of the studies included in the review according to the Methodological Index for Non-Randomized Studies (MINORS).

Study	1. Clearly stated aim	2. Inclusion of consecutive patients	3. Prospective data collection	4. Endpoints appropriate to the aim of the	5. Unbiased assessment of the study	6. Follow-up period appropriate to	7. Loss to follow-up less than 5%	8. Prospective calculation of the	Total Score
Gilboa et al. (2022)	2	2	2	2	1	2	1	1	**13**
Gilboa et al. (2024)	2	2	0	2	1	2	2	0	**11**
Guleroglu et al. (2022)	2	1	2	2	1	2	1	0	**11**

Figure 1: Prisma 2020 flow diagram illustrating the selection process of studies included in the state-of-the-art review.