Hidden hunger in patients with type 2 diabetes (T2D) and its effect on glycaemic control: a protocol for systematic review and meta-analysis

Daya Krishan Mangal, Diksha Gautam, Anuj Kumar Pandey, Nida Shaikh, Sidharth Sekhar Mishra, Himanshu Tolani, Yeshwanth Sonnathi, Shiv Dutt Gupta, Kamlesh Chand Sharma, Jagdish Prasad, Rajeev Tewari, Fahmina Anwar

ABSTRACT

Introduction Hidden hunger or micronutrient deficiencies are quite common in many parts of the world, particularly in the countries of sub-Saharan Africa and South Asia. Micronutrient deficiencies may impact insulin signalling pathways and glucose metabolism, potentially accelerating the onset and development of type 2 diabetes (T2D). This review aims to estimate the prevalence of multiple micronutrient deficiencies among patients with T2D and assess the effect of their deficiency on glycaemic control.

Methodology The review follows the Cochrane Handbook and PRISMA 2020 guidelines. It includes all eligible studies reporting the prevalence of micronutrient deficiencies and their effect on glycaemic control in T2D patients. We would undertake a comprehensive literature search across databases: PubMed, Scopus, EMBASE, LILACS, ProQuest, Google Scholar and grey literature, and identify the studies meeting the inclusion criteria. We would perform data extraction using a pre piloted data extraction sheet and record relevant study characteristics and outcomes.

Analysis Data will be analysed using JBI Sumari software and R software. Pooled prevalence/incidence of micronutrient deficiency will be estimated, and variance will be stabilised using logit transformation and a double arcsine transformation of the data. The OR and risk ratio of glycaemic control among T2D cases with and without micronutrient deficiency will be estimated using the ‘rma’ function under the ‘meta’ and ‘metafor’ packages.

The study findings will have implications for diabetes management strategies and may inform interventions targeting improved glycaemic control through addressing micronutrient deficiencies.

Ethics and dissemination This systematic review will be based on the scientific information available in the public domain; therefore, ethics approval is not required. We will share the study findings at national and international conferences and submit them for publication in relevant scientific journals.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Using a pre designed protocol with a comprehensive search strategy will reduce associated bias.
⇒ A unique feature of this study would be stratified analyses to assess the effect of micronutrient deficiencies on glycaemic control.
⇒ A robust statistical approach—double arcsine transformation would be another essential strength for estimating summary prevalence.
⇒ Seven electronic databases will be searched without any language or geographical restrictions. Despite being comprehensive, it may be possible to miss some research evidence on the topic.
⇒ If the research articles finally included in the study are not population-based studies or have a high risk of bias, it may influence the generalisability of our review results.

INTRODUCTION

Diabetes, one of the four major non-communicable diseases, is a ‘silent epidemic’ across populations in the world. Policymakers and researchers around the world have identified it as a high-priority health problem and are working to combat the disease. Over the past few decades, diabetes has been progressively rising in both incidence and prevalence. Since 2000, the global prevalence of diabetes among people (20–79 years) has increased nearly three times, from 4.6% to 10.5%, and is estimated to rise to 11.3% and 12.2% by 2030 and 2045, respectively. Diabetes accounts for around 1.5 million fatalities annually. Type 2 diabetes (T2D) accounts for the vast majority (over 90%) of diabetes worldwide. T2D is also becoming more prevalent among children and younger populations, with a concomitant rise in obesity, lack of physical activity and poor dietary habits.
encouraging healthy lifestyles and dietary habits, which include a balanced diet, regular exercise and maintaining a healthy body weight. Additionally, it is important to maintain good glycaemic control to prevent long-term complications.6 7

The role of micronutrient deficiency and the hidden hunger in T2D has not received the attention of researchers. It is a form of undernutrition that occurs with the inadequacy of micronutrients in diet or inadequate absorption of vitamins and minerals, which may not clinically manifest in early deficiencies.7 8 WHO (2006) reported that more than two billion people, or one-third of the population globally, suffer from various micronutrient deficiencies.9 This hidden hunger is alarmingly high in several sub-Saharan African and South Asian countries. Several other countries in these regions exhibit moderate-to-severe vitamin deficiencies. Most countries across North Africa, Central Europe, Latin America and East Asia are considered to have ‘mild’ hidden hunger issues.10 It is reported that 7 out of 10 non-pregnant women of reproductive age and 6 out of 10 children less than 5 years old suffer from at least one micronutrient deficiency.11 Evidence supports that obese people with diabetes are predisposed to micronutrient deficiency that impairs glycaemic control.12

The relevance of several micronutrients as cofactors in the insulin signalling cascade, pancreatic beta-cell activity and glucose metabolic pathways raises the possibility that a lack of the micronutrients contributes to the onset of T2D. There is mounting clinical evidence that supports the theory of metabolic effects of deficiency of micronutrients such as vitamin C, vitamin D, biotin, thiamine and chromium. Among obese and diabetic individuals, the deficiency of these vitamins is quite high.12

Obese individuals are at four times higher risk of developing T2D.12 The development of diabetes among obese people is influenced by factors such as pancreatic beta-cell dysfunction, behavioural characteristics, genetics, increased incretin hormone resistance and oxidative stress. Specific micronutrient deficiencies among obese people may potentially have an impact on the development of T2D.12

Oxidative stress significantly contributes to the pathophysiology of diabetes and its consequences.13 14 Micro-nutrients regulate the expression of genes, metabolism and the onset or progression of chronic diseases like diabetes. Micronutrient deficiencies of zinc, chromium, magnesium, copper, manganese and vitamin B are linked to glucose intolerance. Zinc is a powerful antioxidant required for numerous enzyme functions and insulin metabolism. Additionally, chromium affects how well insulin works. It enhances tolerance to glucose. Chromium insufficiency is related to elevated serum triglyceride, serum cholesterol levels and impaired glucose tolerance.15

Evidence suggests that micronutrients significantly influence the pathophysiology and development of insulin resistance, a root cause of diabetes and maladies of cardiometabolic disorders. Certain micronutrient deficiencies linked to insulin action play a potential catalyst role in the reaction pathways of several MetS cluster diseases, namely T2DM, hypertension, dyslipidaemia, obesity, hyper-uricaemia, prothrombotic and pro-inflammatory state. Therefore, a deficit in insulin action because of oxidative stress or a deficit in the activity of insulin-associated enzymes is the link between the MetS clusters and micronutrient deficiency.16–20

The authors’ preliminary review revealed different prevalences of micronutrient deficiencies and contradictory findings on the effect of micronutrient deficiencies on glycaemic control in T2D. For example, Bashir et al reported an 80.4% prevalence of vitamin D deficiency among T2D patients.21 Jung et al reported a lower prevalence of 32.7%.22 Similarly, Raqib et al reported a 48% prevalence of vitamin B12 deficiency,23 while Abubakr et al found a prevalence of 24.6%.24

Iqbal et al reported a positive association between vitamin D deficiency and poor glycaemic control.25 In contrast, another study by Olt et al found no significant correlation between vitamin D and glycaemic control in T2D despite an elevated vitamin D deficiency.26 Similarly, Abubakr et al found no statistically significant correlation between B12 deficiency and HbA1c in Iraq’s Sulaimani governorate/Kurdistan region,24 while Lee et al reported a significant negative correlation between vitamin B-12 status and blood glucose levels.27

Perez et al reported no significant relationships between zinc status and glycaemic control parameters in patients with well-controlled T2D. In contrast, a significant inverse correlation was found between zinc and fasting blood glucose, HbA1c% in another study by Sudan et al.28 29

The proposed systematic review and meta-analysis study will be perhaps the first comprehensive study to assess the burden of multiple micronutrient deficiencies and evaluate evidence of cause-and-effect relationship between various micronutrients and glycaemic control in T2D. The study would attempt to synthesise pieces of conflicting and inconclusive evidence generated in studies, mostly focused on a particular singular micronutrient. The article based on systematic review and meta-analysis may be helpful to clinicians, professional diabetes associations and policy makers in need for micronutrient supplementation in T2D disease management and associated comorbidities.

**REVIEW QUESTION**

1. What is the burden of micronutrient deficiency among patients with T2D?
2. What is the effect of micronutrient deficiency on glycaemic control among patients with T2D?
METHODOLOGY

Reporting guidelines

This paper follows the protocol version of the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines (ie, PRISMA-P).30 In this systematic review, we propose including studies published globally based on sound methodology per specified inclusion and exclusion criteria. In addition, grey literature studies and reports will be included in the review.

Time frame of the study: 1 July 2023 to 31 March 2024.

Patient and public involvement

None

Eligibility criteria

The systematic review follows the PI/ECO (ECO, exposure, comparator and outcome) protocol for systematic review research.31 Table 1 represents PICO description.

Types of studies for inclusion in the review

The review will include observational studies, that is, cross-sectional and cohort studies, to assess the prevalence/incidence/burden of micronutrient deficiency of iron, zinc, copper, chromium, fluoride, iodine, selenium, manganese, molybdenum, calcium, phosphorus, potassium, magnesium, sodium, vitamin A, vitamin B1, vitamin B2, vitamin B3, vitamin B5, vitamin B6, vitamin B7, vitamin B9, vitamin B12, folic acid, vitamin C, vitamin D, vitamin E, and vitamin K among T2D patients. Analytical epidemiological studies will include case-control, cohort and randomised control trials (RCT) reporting the association and effect of micronutrient deficiency on T2D and glycaemic control.

All studies from 1998 to 2023, irrespective of country, economy, demography, language, etc, will be included in the review. Expert opinions, narrative reviews, case reports, editorials, newspaper reports, posters, and conference abstracts will be excluded.

Search strategy for the identification of relevant studies

We propose to develop a search strategy to conduct an extensive literature search in PubMed, EMBASE, ProQuest, Cochrane Library, Google Scholar, LILACS and Scopus. Keywords for the study are described in box 1. A careful examination of references of relevant studies and review papers will also be carried out. Whenever required, specific study investigators will be contacted to get further details. We will assess all articles published in any language on the prevalence/incidence/burden of micronutrient deficiencies and their association/effect on glycaemic control in T2D patients. We will develop a separate search strategy to conduct a Grey Literature search using the ProQuest database, Scopus, Embase and Google Scholar hand searches, and institutional repositories such as the international diabetes federation and

Table 1: Population, exposure, comparator and outcome description

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention(s), exposure</th>
<th>Comparator</th>
<th>Outcomes</th>
<th>Study types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>► T2D patients with or without complications.</td>
<td>► T2D patients with micronutrient deficiency</td>
<td>► T2D patients without micronutrient deficiency.</td>
<td>► Burden (prevalence/incidence) of multiple micronutrient deficiencies among patients with T2D.</td>
<td>► Cross-sectional study for prevalence and longitudinal or cohort study for incidence.</td>
</tr>
<tr>
<td>► 18 years of age or older.</td>
<td></td>
<td></td>
<td>► Glycaemic control measured by HbA1c, fasting blood sugar, postprandial blood sugar.</td>
<td></td>
</tr>
<tr>
<td>► Patients of all sexes and ethnic.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Exclusion criteria:

| | | | |
|► Patients with type 1 diabetes mellitus. | ► Supplementation of micronutrients. | | ► Case reports, case series, reviews, ecological studies. |
|► Gestational diabetes. | | | |
|► T2D among persons less than 18 years. | | | |

T2D, type 2 diabetes.

Box 1: Tentative key search words

other international organisations/associations related to diabetes and micronutrients.

We propose to develop a search string for Embase initially. Later, we will adapt the search terms/keywords and create search strings for other electronic databases mentioned earlier. A repeat of the search on electronic databases is proposed on 1 January 2024 to include newer articles published on the subject before submission of the manuscript for publication in a journal (online supplemental file 1).

We propose a peer review of the search strategy using a checklist—PRESS Evidence-Based Checklist to assess the search strategy’s adequacy (online supplemental file 2).

**Selection of studies**

It is proposed to retrieve the titles/abstracts of all relevant research articles and unpublished reports using the search strategy and other additional sources separately for prevalence/incidence/burden and effect studies. We will import all selected research studies to Mendeley/Rayyan software for reference management to check for duplicates and screening. We will also undertake a manual search to check for any duplicate articles. Four reviewers (NS, DG, AKP and YS) will independently screen the search results to identify the studies that comply with the inclusion and exclusion criteria outlined above using Rayyan software.

Articles other than English will be translated into English using Google Translate and reviewed for title/abstract screening.

We will record all decisions related to the inclusion or exclusion of the studies on a Rayyan software/Microsoft Excel spreadsheet. After screening titles and abstracts, eligible citations will be retrieved, and the full texts will be sought and imported. The selected articles will then undergo a full-text screening by NS, DG and AKP. Any difference in study selection will be discussed among the reviewers to prepare a final list of articles for the review. Any discrepancies in the article selection process, screening of title/abstract and full-text review will be resolved by fifth and sixth reviewers (SSM and DKM).

The PRISMA flow chart will be prepared to report the process and facilitate replication (figure 1).

**Data extraction and management**

Prepiloted data extraction sheet in MS Excel will be used for data extraction. The extraction sheet would cover the following fields: study characteristics (author name, year of publication, country, language and study type), the number of study participants, number of micronutrient deficient patients among T2D patients/events, effect on glycaemic control measured by HbA1c, fasting blood sugar and postprandial blood sugar. We will contact the authors to share the data if the information is insufficient to support data extraction. The same will be noted and reported appropriately.

Two reviewers will independently extract data for burden (NS and YS) and effect study (DG and AKP) on a predesigned format to capture information related to the study design and key outcome variables. Any differences in data extraction will be discussed among the reviewers to prepare a final extracted spreadsheet. Discrepancies will be resolved by fifth and sixth reviewers for burden

---

**Figure 1** PRISMA flow chart. PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.
studies (SSM and RT) and effect studies (DKM and DG). Table 2 discusses the data extraction plan.

### Types of outcome measures

We propose to include the following outcomes:

1. Burden (prevalence/incidence) of multiple and individual micronutrient deficiencies among patients with T2D.
2. Effect of micronutrient deficiency on glycaemic control among patients with T2D compared with patients without micronutrient deficiency.

### Measures of effect

1. To assess the burden, the measure of effect will be the proportion of the population with micronutrient deficiency measured as prevalence or incidence among T2D patients.
2. To assess the effect of micronutrient deficiency on glycaemic control among patients with T2D, the risk ratio (cohort and RCT) or OR (analytical cross-sectional and case–control study) of glycaemic control levels among T2D with micronutrient deficiency compared with those without micronutrient deficiency.

### Risk of bias (quality) assessment

The reviewers (DKM, DG and SSM) will independently evaluate the risk of bias in each selected research article. All the articles selected for the review will be assessed for methodological quality using the various Joanna Briggs Institute (JBI) checklists for the analytical and observational studies.36 The third reviewer will settle any disagreements over the assessment of the risk of bias and research quality between the two reviewers. We will report the risk of bias for each of the articles and summarise the results of the risk of bias assessment in a tabular form which will be presented in the final paper. We will generate a risk of bias plot under R’s ‘robvis’ package.

### Data analysis

#### Data synthesis, statistical analysis and investigation of heterogeneity

Data will be analysed using JBI Sumari software and R software. We will use R software mainly because of the better visualisation of Forest and Funnel Plots and its adaptability for advanced statistical modelling. HT, DG, NS and AKP will do the analysis. The authors will present the data from the selected studies in the form of an evidence table followed by a descriptive table. Descriptive analysis of prevalence among different studies will be visualised through Heatmaps for relative comparison among various studies categorised by age groups and geographies. Pooled prevalence/incidence of micronutrient deficiency will be estimated, and variance will be stabilised using logit transformation and a double arcsine transformation of the data.37 In cases where prevalence is close to zero or 100%, GLMM (generalised linear mixed model) and Bayesian methods will be incorporated.38 39 We will report the pooled prevalence/incidence of micronutrient deficiencies in the form of a Forest plot separately for each subgroup. The OR and risk ratio of glycaemic control among T2D cases with and without micronutrient deficiency will be estimated using the ‘rma’ function under the ‘meta’ and ‘metafor’ packages.

The variation in the estimates from different studies or the between-study heterogeneity will be assessed through a random-effect model and subgroup analysis. The between-study heterogeneity will be quantified by Cochrane’s Q Statistic and Higgins and Thompson’s $I^2$ Statistic. We will categorise heterogeneity as low (= 25%), medium (=50%) and high (=75%). Results for

### Table 2 Data extraction plan

<table>
<thead>
<tr>
<th>Category</th>
<th>Variables for extraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic information</td>
<td>Author name, year of publication, country, language, study type.</td>
</tr>
<tr>
<td>Research question(s)</td>
<td>Objectives, research questions.</td>
</tr>
<tr>
<td>Participant characteristics</td>
<td>Number of patients in the study, the number of patients with micronutrient deficiency among T2D patients/events and other important details like gender, age group.</td>
</tr>
<tr>
<td>Intervention/exposure characteristics</td>
<td>Intervention/exposure name, intervention description.</td>
</tr>
<tr>
<td>Study design</td>
<td>Cross-sectional, observational studies and RCTs.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Primary outcome variables are the burden (prevalence/incidence) of multiple micronutrient deficiencies in T2D patients. Effect of multiple micronutrient deficiencies on glycaemic control/glycaemic variability/postprandial glucose/fasting blood glucose/insulin insensitivity in T2D patients.</td>
</tr>
<tr>
<td>Measures</td>
<td>Prevalence or incidence of micronutrient deficiency among T2D patients. Risk ratio/Odds Ratio for glycaemic control among T2D patients with micronutrient deficiency measured by HbA1c, fasting blood sugar, postprandial blood sugar.</td>
</tr>
</tbody>
</table>

RTs, randomised control trials; T2D, type 2 diabetes.
meta-analysis of prevalence will be generated using the ‘metaprop’ function in R. These statistics will be generated as a part of Forest plot, which will be produced using the ‘forest.meta’ function under ‘meta’ and ‘metafor’ package in R.

Publication bias
Egger’s regression test and funnel plot will be used to assess for publication bias. Sensitivity analyses will be performed to determine whether a single study was dominant in the overall estimates and to gauge the impact of individual studies on the pooled results. A ‘p-value’ of 0.05 will be considered significant.

Subgroup analysis
Depending on the availability of data, we will do subgroup analysis for both the burden and effect of micronutrient deficiency on glycaemic control studies by the following:
- Age groups: 18–29, 30–39, 40–49, 50–59, 60–70 and 70+.
- Gender—male/female.
- Geographical regions—WHO regions.

The effect of each subgroup will be assessed through the ‘rma’ function in R.

OVERALL QUALITY OF THE EVIDENCE
Grading of Recommendations Assessment, Development and Evaluation Working Group (GRADE Working Group) checklist will be employed to evaluate the confidence in the estimates for study results.40 This approach will help assess the evidence based on study limitations, consistency, directness, reporting bias and precision. The evidence will be categorised as very low, low, moderate, or high quality.

DISCUSSION
In this section, we will discuss the study results, relate these with other studies and explore possible reasons for any discordance in results. We will discuss the summary prevalence of each micronutrient among patients with T2D and the variance between genders, different geographic areas and time frames. We will also discuss the relevance of the association or no association between micronutrient deficiency and glycaemic control, variability and insulin insensitivity.

The systematic review and meta-analysis will settle the conflicting research findings related to the association between micronutrient deficiency and glycaemic control, fasting blood sugar, postprandial blood sugar and insulin insensitivity. This will enable practitioners and programme managers to revise or fine-tune their clinical management of type two diabetes.

We will also discuss certainty in the body of evidence using GRADE criteria. We will discuss the study results and comment on future research needs.

We will describe the limitations of the systematic review and meta-analysis study related to the process and the quality of research studies included in the review. The systematic review and meta-analysis study will be performed using a comprehensive search strategy developed based on the key concepts of the research questions. We propose to search seven electronic databases without any language or geographical restrictions. Despite being comprehensive, it may be possible to miss some research evidence on the topic. If the research articles finally included in the study are not population-based studies or have a high risk of bias, it may influence the generalisability of our review results.

ETHICS AND DISSEMINATION
The study will use data and information available in the public domain in scientific databases; thus, ethics approval is not required.

The review results will then be submitted for publication in an international journal and presented at international and national conferences. We will follow the PRISMA 2020 guidelines for reporting on the systematic review and writing the scientific paper based on the research.35

Acknowledgements We would like to thank Dr PR Sodani, President, IHHMR University, Jaipur, and Dr Swatapa Neogi, Director, International Institute of Health Management Research, Delhi, for supporting the research.

Contributors DKM, SG, SSM and FA conceptualised the research question and objectives. DKM, NS, DG, AKP, SSM and HT have contributed substantially to the article’s concept and design. RT provided project management support to the research study. DKM, NS, DG and AKP drafted the protocol. HT conceptualised the statistical analysis of the data for meta-analysis. It was critically reviewed for the proper intellectual content after inputs by DKM, SG, RT, NS, DG, SSM, HT, FA, AKP and YS. They have accessed and verified the underlying data reported in the manuscript. DKM, NS, DG, AKP, KCS and JP prepared the search strategy for the study. DKM, SG, RT, NS, DG, SSM, FA, AKP and YS critically reviewed and approved the version for submission.

Funding Abbott Nutrition Research and Development. Grant Number: RA40.

Competing interests FA declares potential conflicts of interest as employees of Abbott, the study sponsor.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.
REFERENCES
### Impact AND micronutrient deficiency AND glycemic control AND diabetes

<table>
<thead>
<tr>
<th>Date</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,118</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,118</td>
<td></td>
</tr>
</tbody>
</table>

### Impact/association/role AND micronutrient deficiency AND glycemic control AND diabetes

<table>
<thead>
<tr>
<th>Date</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,220</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,220</td>
<td></td>
</tr>
</tbody>
</table>

**BMJ Open** 2024; 14:e078688. doi: 10.1136/bmjopen-2023-078688
Hidden hunger in type 2 diabetics (T2D) and its effect on glycaemic control

REVIEW QUESTION:
1. What is the burden of micronutrient deficiency among people with T2D?
2. What is the effect of micronutrient deficiency on glycaemic control among people with T2D?

Search strategy:
Electronic databases:
PubMed, Embase, Scopus, Cochrane Library, Google Scholar, LILACS

Key concepts based on PI/ECO
1. Diabetes Mellitus Type 2, its synonyms, abbreviations, different spellings, Mesh terms, Emtree terms NOT diabetes Type 1 OR Gestational diabetes.
2. Hidden Hunger OR Micronutrient Deficiency OR Micronutrient malnutrition OR Micro-mineral deficiency OR Trace elements deficiency (14 micro-minerals) OR Vitamin Deficiency (13 vitamins)
3. Prevalence OR Burden OR Status
4. Incidence OR Cumulative Incidence OR Incidence Density OR Incidence rate, and its synonyms.
5. Glycemic control OR Glycemic variability OR Post Prandial blood sugar OR fasting Blood sugar OR Insulin Resistance
6. Impact OR Effect OR Association OR Role

MESH terms, Emtree terms, and synonyms:
Refer to the attached Excel sheet*

PRESS Checklist

<table>
<thead>
<tr>
<th>Translation of the research question</th>
<th>RQ 1. For the Prevalence study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• P –T2D people/patients</td>
</tr>
<tr>
<td></td>
<td>• I/E- Micronutrient deficiency</td>
</tr>
<tr>
<td></td>
<td>• Comparator - NA</td>
</tr>
<tr>
<td></td>
<td>• O- Prevalence/ Incidence/ burden of micronutrient deficiency</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>RQ 2. For the Effect study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• P –T2D people/patients</td>
</tr>
<tr>
<td></td>
<td>• Intervention/Exposure-</td>
</tr>
<tr>
<td></td>
<td>Micronutrient deficiency</td>
</tr>
<tr>
<td></td>
<td>• C-T2D people without micronutrient deficiency</td>
</tr>
<tr>
<td></td>
<td>• O- Effect on Glycaemic control</td>
</tr>
<tr>
<td>Boolean and proximity operators (these vary based on search service)</td>
<td>Refer to the search string below* it includes Boolean operators.</td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Subject headings (database-specific)</td>
<td>Refer to the search string below* it includes subject headings.</td>
</tr>
<tr>
<td>Text word searching (free text)</td>
<td>Keywords, synonyms, MESH terms, and Emtree Terms were identified. (For details refer to the attached Excel sheet *)</td>
</tr>
<tr>
<td>Spelling, syntax, and line numbers</td>
<td>Refer to the search string below *for details.</td>
</tr>
<tr>
<td>Limits and filters</td>
<td>Title/abstract and results by year 1998-2023, filters are applied. No other filters are used.</td>
</tr>
</tbody>
</table>

**Embase search string**

**QUERY**

**STEP 1 -**

**Population -**

((("non insulin dependent diabetes mellitus'/exp OR 'NIDDM (non insulin dependent diabetes mellitus')":ti,ab OR 'T2DM':ti,ab OR 'adult onset diabetes':ti,ab OR 'adult onset diabetes mellitus':ti,ab OR 'diabetes mellitus type 2':ti,ab OR 'diabetes mellitus type ii':ti,ab OR 'diabetes mellitus, maturity onset':ti,ab OR 'diabetes mellitus, non insulin dependent':ti,ab OR 'diabetes mellitus, non-insulin-dependent':ti,ab OR 'diabetes mellitus, type 2':ti,ab OR 'diabetes mellitus, type II':ti,ab OR 'diabetes type 2':ti,ab OR 'diabetes type II':ti,ab OR 'diabetes, adult onset':ti,ab OR 'dm 2':ti,ab OR 'insulin independent diabetes':ti,ab OR 'insulin independent diabetes mellitus':ti,ab OR 'ketosis resistant diabetes mellitus':ti,ab OR 'maturity onset diabetes':ti,ab OR 'maturity onset diabetes mellitus':ti,ab OR 'maturity onset diabetes of the young':ti,ab OR 'niddm':ti,ab OR 'non insulin dependent diabetes':ti,ab OR 'non-insulin dependent diabetes mellitus':ti,ab OR 'noninsulin dependent diabetes':ti,ab OR 'noninsulin dependent diabetes mellitus':ti,ab OR 'type 2 diabetes':ti,ab OR 'type 2 diabetes mellitus':ti,ab OR 'type II diabetes':ti,ab OR 'type II diabetes mellitus':ti,ab OR 'brittle diabetes':ti,ab OR 'brittle diabetes mellitus':ti,ab OR 'brittle diabetes mellitus type 1':ti,ab OR 'brittle diabetes mellitus type i':ti,ab OR 'diabetes mellitus, brittle':ti,ab OR 'diabetes mellitus, insulin dependent':ti,ab OR 'diabetes mellitus, insulin-dependent':ti,ab OR 'diabetes mellitus, juvenile onset':ti,ab OR 'diabetes mellitus, type 1':ti,ab OR 'diabetes mellitus, type i':ti,ab OR 'diabetes type 1':ti,ab OR 'diabetes type i':ti,ab OR 'diabetes, juvenile':ti,ab OR 'dm 1':ti,ab OR 'early onset diabetes mellitus':ti,ab OR 'iddm':ti,ab OR 'insulin dependent diabetes':ti,ab OR 'insulin dependent diabetes mellitus':ti,ab OR 'insulin-dependent diabetes mellitus':ti,ab OR 'juvenile diabetes':ti,ab OR 'juvenile diabetes mellitus':ti,ab OR 'juvenile onset diabetes':ti,ab OR 'juvenile onset diabetes mellitus':ti,ab OR 'ketoacidotic diabetes':ti,ab OR 'labile diabetes mellitus':ti,ab OR 'mckusick 22210':ti,ab OR 'type 1 diabetes':ti,ab OR 'type 1 diabetes mellitus':ti,ab OR 'type I diabetes':ti,ab OR 'type I diabetes mellitus':ti,ab OR 'gestational diabetes':/exp OR 'diabetes mellitus gravidarum' OR 'diabetes mellitus of pregnancy' OR 'diabetes of pregnancy' OR 'diabetes, gestational' OR 'diabetes, pregnancy' OR 'gestational diabetes' OR 'gestational
diabetes mellitus' OR 'maternal gestational diabetes mellitus' OR 'pregnancy diabetes' OR 'pregnancy diabetes mellitus' OR 'pregnancy-induced diabetes')

STEP 2 -
Intervention/Exposure
AND
('hidden hunger':ti,ab OR 'micronutrient deficiency':ti,ab OR 'micronutrient malnutrition':ti,ab OR 'Micro-mineral deficiency'.ti,ab OR 'Trace elements deficiency':ti,ab OR 'Vitamin Deficiency':ti,ab OR 'Iron':ti,ab OR Zinc:ti,ab OR Copper:ti,ab OR Chromium:ti,ab OR Fluoride:ti,ab OR Iodine:ti,ab OR Selenium:ti,ab OR Manganese:ti,ab OR Molybdenum:ti,ab OR Calcium:ti,ab OR Phosphorus:ti,ab OR Potassium:ti,ab OR Vanadium:ti,ab OR Magnesium:ti,ab OR Salt:ti,ab OR 'sodium chloride':ti,ab OR 'Vitamin A':ti,ab OR 'Vitamin B':ti,ab OR 'Vitamin B1':ti,ab OR 'Vitamin B2':ti,ab OR 'Vitamin B3':ti,ab OR 'Vitamin B5':ti,ab OR 'Vitamin B6':ti,ab OR 'Vitamin B7':ti,ab OR 'Vitamin B9':ti,ab OR 'Vitamin B12':ti,ab OR Thiamine:ti,ab OR Riboflavin:ti,ab OR Niacin:ti,ab OR Cobalamin:ti,ab OR 'Vitamin C':ti,ab OR 'Ascorbic acid':ti,ab OR 'Vitamin D':ti,ab OR 'Calciferol, 1,25-dihydroxy, vitamin D':ti,ab OR 'Vitamin E':ti,ab OR Tocopherol:ti,ab OR 'Vitamin K':ti,ab OR ('mineral deficiency'/exp OR 'micro-element deficiency'.ti,ab OR 'micro-elements deficiency'.ti,ab OR 'microelement deficiency'.ti,ab OR 'mineral deficiency'.ti,ab OR 'minerals deficiency'.ti,ab OR 'trace element deficiency'.ti,ab OR 'trace element deficit'.ti,ab OR 'trace elements deficiency'.ti,ab) OR ('vitamin deficiency'/exp OR 'avitaminosis'.ti,ab OR 'corrinoid deficiency'.ti,ab OR 'deficiency, vitamin'.ti,ab OR 'hypo-vitaminosis'.ti,ab OR 'hypovitaminosis'.ti,ab OR 'multivitamin deficiency'.ti,ab OR 'vit. deficiency'.ti,ab OR 'vitamin deficiency'.ti,ab OR 'vitamins deficiency'.ti,ab) NOT macronutrients:ti,ab)

STEP 3 -
Outcome
AND
((prevalence/exp OR 'prevalence'.ti,ab OR 'prevalence study'.ti,ab) OR burden:ti,ab OR status:ti,ab))
AND [1998-2023]/py

STEP 4 -
LIMIT TO –
Publication Years - 1998-2023

Final search strategy–
STEP 1 + STEP 2 + STEP 3 + STEP 4

((('non insulin dependent diabetes mellitus'/exp OR 'NIDDM (non insulin dependent diabetes mellitus'):ti,ab OR 'T2DM':ti,ab OR 'adult onset diabetes':ti,ab OR 'adult onset diabetes mellitus':ti,ab OR 'diabetes mellitus type 2':ti,ab OR 'diabetes mellitus type ii':ti,ab OR 'diabetes mellitus, maturity onset':ti,ab OR 'diabetes mellitus, non insulin dependent':ti,ab OR 'diabetes mellitus, non-insulin-dependent':ti,ab OR 'diabetes mellitus type 2':ti,ab OR 'diabetes mellitus, type II':ti,ab OR 'diabetes type 2':ti,ab OR 'diabetes type II':ti,ab OR 'diabetes, adult onset':ti,ab OR 'dm 2':ti,ab OR 'insulin independent diabetes mellitus' OR 'maternal gestational diabetes mellitus' OR 'pregnancy diabetes' OR 'pregnancy diabetes mellitus' OR 'pregnancy-induced diabetes'))
RESULTS

ANNEXURE:

1. Excel sheet attached for Embase search strategy and Keywords used.