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# **Review Article**

# Navigating Metabolic Complexity and in-Depth Analysis of Metabolic Syndrome among Diabetes Mellitus Patients: A Systematic Review and Meta-Analysis

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#### Abstract

**Background:** This systematic review and meta-analysis aimed to evaluate the prevalence and clinical implications of metabolic syndrome in individuals with diabetes mellitus.

**Methods:** A comprehensive search was conducted across multiple databases using key terms related to metabolic syndrome and diabetes. Access to subscription-based journals was facilitated through the HINARI program. Study quality was assessed using the adapted Newcastle–Ottawa scale, with a minimum inclusion score of  $\geq 5/10$ . Statistical analysis included a meta-analysis using the DerSimonian and Laird random-effects model to determine the pooled prevalence, with heterogeneity assessed using Cochran's Q and I<sup>2</sup> statistics. Publication bias was evaluated via funnel plot symmetry. Analyses were conducted using Stata/MP 17.0.

**Results:** The meta-analysis revealed a pooled effect size of 1.98 (95% CI: 1.85, 2.10), with significant heterogeneity ( $I^2 = 92.35\%$ ). Prevalence ranged from 19.88% to 88.13%, underscoring a substantial burden. Variations in HbA1c, HDL cholesterol, blood pressure, and BMI highlighted the heterogeneity in metabolic syndrome characteristics. Advanced statistical approaches enriched the understanding of metabolic profiles and their interplay with glycemic control and lipid metabolism.

**Conclusion:** This study underscores the critical interplay between glycemic control and lipid profiles in metabolic syndrome. The findings emphasize the need for tailored, region-specific interventions to address its substantial burden and implications for clinical practice and policy.

Keywords: Metabolic syndrome; Diabetes mellitus; Meta-analysis; Body mass index; Blood pressure

### Introduction

Metabolic syndrome, also referred to as Syndrome X or Insulin Resistance Syndrome, encompasses a constellation of conditions, including glucose intolerance, hypertension, dyslipidemia, and central obesity, with insulin resistance at its core (1). Defining metabolic syndrome has posed challenges, with a recent consensus highlighting the use of ethnic-specific criteria. This approach incorporates indicators like waist circumference for central obesity, triglyceride and



Copyright © 2025 Zhang et al. Published by Tehran University of Medical Sciences. This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license. (https://creativecommons.org/licenses/by-nc/4.0/). Non-commercial uses of the work are permitted, provided the original work is properly cited high-density lipoprotein (HDL) cholesterol levels for dyslipidemia, and blood pressure exceeding 130/85 mmHg (2). Controversies persist regarding the inclusion of dysglycemia, central obesity, and insulin resistance as essential components (3).

Despite definitional nuances, the prevalence of metabolic syndrome is increasing globally, notably in both Western and Asian countries experiencing rapid socioenvironmental changes. Clinical trials underscore metabolic syndrome as a significant risk factor for cardiovascular disease (CVD), type 2 diabetes mellitus (T2DM), and allcause mortality (4). Recognizing its predictive value for major metabolic disorders, metabolic syndrome emerges as a practical tool. Recent studies, however, tend to emphasize its role as a CVD risk factor, often overshadowing its significance in predicting incident diabetes (5).

The prevalence of metabolic syndrome among diabetes mellitus patients poses a significant health challenge, necessitating a thorough understanding of its various components and their interrelationships. While previous research has explored aspects of metabolic syndrome, there remains a need for a comprehensive review that synthesizes existing literature to provide a holistic understanding of this complex condition. Our study aimed to fill this gap by conducting an indepth analysis of metabolic syndrome in diabetes mellitus patients through a systematic review and meta-analysis of relevant studies. This review aimed to bridge this gap by consolidating evidence supporting metabolic syndrome as a predictor for diabetes mellitus. Additionally, we explore its utility in clinical practice, particularly emphasizing its predictive value for diabetes. The prevalence of metabolic syndrome varies globally, ranging from 20% to 25% in the adult population and 0 to 19.2% in children (6,7). In T2DM patients, the prevalence can reach almost 80%. Studies on type 1 diabetes mellitus patients exhibit a wide range, from 3.2% in Poland to 57.1% in Finland, underscoring the influence of population characteristics and diagnostic criteria (8-10).

Diabetes mellitus, a metabolic disease with chronic complications, has a global prevalence estimated at 10.5% (536.6 million people) in 2021, projected to rise to 12.2% (783.2 million) by 2045 (11-13). Metabolic syndrome, a precursor or concurrent entity with diabetes, comprises various metabolic, clinical, and biological abnormalities, tripling the risk of CVD. The prevalence of metabolic syndrome depends on definitions, population characteristics, and lifestyle changes, escalating in both developed and developing countries (14).

Metabolic syndrome's impact extends beyond cardiovascular risks, affecting multiple systems (15). Its etiology involves factors such as extra weight, obesity, physical inactivity, and genetic predisposition, leading to insulin resistance. Proinflammatory cytokines from enlarged adipose tissue contribute to insulin resistance, culminating in metabolic syndrome and subsequent vascular and autonomic damage (16, 17). The syndrome's adverse effects encompass microvascular damage, endothelial dysfunction, vascular resistance, hypertension, and vessel wall inflammation. This cascade leads to a spectrum of conditions, from peripheral vascular disease and structural heart disease to renal impairment and ischemic heart disease. Histopathologically, metabolic syndrome is associated with atherosclerosis, coronary artery disease, and liver damage, progressing from steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma (18-21).

Recognition, treatment, and prevention of metabolic syndrome require a comprehensive approach. The patient encounter should include a thorough history and physical examination, emphasizing modifiable factors such as diet and exercise (22). Laboratory analyses, including hemoglobin A1C, lipid panels, and additional studies, aid in diagnosis and risk assessment. Managing metabolic syndrome involves lifestyle modifications, with particular attention to blood pressure control and lipid management. Medications, such as statins, may be initiated based on risk profiles. Severe obesity may warrant bariatric surgery, recognized as an effective therapy (23).

Metabolic syndrome constitutes a constellation of interconnected metabolic aberrations, amplifying

the susceptibility to CVD and T2DM (24). These aberrations encompass central obesity, insulin resistance, hypertension, and dyslipidemia. While extensive research has focused on metabolic syndrome within the general population, recent years have witnessed a pronounced emphasis on its prevalence and clinical ramifications in individuals afflicted with diabetes mellitus encompassing both type I (T1DM) and type II (T2DM) (20-25). The rising prevalence of metabolic syndrome globally, particularly among individuals with diabetes mellitus, underscores the urgent need for a thorough understanding of this complex condition. Despite numerous studies, a comprehensive review is lacking, leaving gaps in knowledge regarding its clinical implications and diagnostic criteria. By conducting a systematic analysis and comprehensive review, this study aims to address these gaps by evaluating the prevalence of metabolic syndrome in individuals with diabetes mellitus, while also correlating its parameters with chronic complications. Such insights are crucial for optimizing patient care, as metabolic syndrome significantly increases the risk of cardiovascular disease and other complications in diabetic patients. By advancing clinical understanding and providing evidence-based guidelines, this review has the potential to improve outcomes and reduce the burden of metabolic syndromerelated complications in diabetes mellitus patients.

### Methods

#### Search Strategy and Data Acquisition

The investigation employed thorough search methodologies, spanning various databases such as ScienceDirect, PubMed Central, ResearchGate, Google Scholar, Scopus, Web of Science, SpringerLink, Education Resources Information Center (ERIC), and JSTOR available during 2010 to 2024. Advanced search techniques were deployed to optimize the identification of pertinent literature. Key words included were metabolic syndrome, syndrome X, diabetes, insulin-dependent diabetes, insulin resistance syndrome and autoimmune diabetes. To enhance the precision of the search results, the aforementioned terminologies were strategically explored in combination using Boolean operators ("OR" and "AND").

Access to articles published in subscription-based journals was facilitated through the HINARI access to research for health program, established by the WHO in collaboration with major publishers, to facilitate access for low- and middleincome countries to one of the most extensive repositories of biomedical and health literature globally. The research quality of each study was meticulously appraised using the adapted Newcastle-Ottawa scale (25). The articles were classified into three categories based on their quality: Low impact (score < 5 points), Moderate impact (score 5-7), and High impact (score 8-10), respectively. For inclusion in the analysis, studies needed to achieve a minimum score of  $\geq$  5 out of 10 points.

#### Statistical Analysis

A comprehensive meta-analysis was undertaken utilizing the DerSimonian and Laird randomeffects model to determine the pooled prevalence of metabolic syndrome among individuals diagnosed with diabetes mellitus. The resulting pooled effect size, indicative of prevalence, accompanied by a 95% confidence interval (CI), was visually depicted using a forest plot. The evaluation of heterogeneity between studies involved the application of Cochran's Q and I<sup>2</sup> statistics. Funnel plot symmetry was employed to meticulously scrutinize the likelihood of publication bias. A P-value below 0.05 was deemed statistically significant. All statistical analyses were meticulously carried out using Stata/MP 17.0 (Stata Corp, College Station, TX, USA).

### Results

The exhaustive search strategy, spanning various databases including ScienceDirect, PubMed Central, ResearchGate, Google Scholar, Scopus, Web of Science, SpringerLink, Education Resources Information Center (ERIC), and JSTOR, yielded 3786 articles. 21 studies were deemed suitable for further assessment and inclusion in the synthesis and analysis (Fig. 1) (26-46). Among the studies

included in the final analysis, 17 (81%) were cross-sectional, and 4 (19%) were prospective cohort studies.

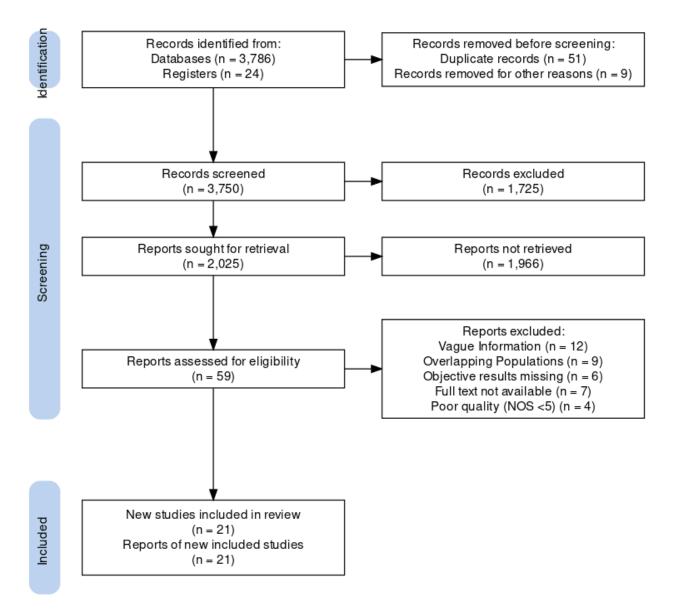


Fig. 1: PRISMA flowchart illustrating article selection for the systematic review and meta-analysis

#### HBA1c levels and HDL cholesterol

The sample sizes spanned from 35 (42) to 7924 (38) encompassing a total of 14507 participants. The mean and standard deviation values for HBA1c and HDL are provided for each study, reflecting the variability in glycemic control and

lipid profiles across different populations. The prevalence of metabolic syndrome is calculated based on specific criteria for each study, ranging from 12.8% to 255.33%. A study showed the highest prevalence of 88% (41). However, another study exhibited the lowest prevalence at

19.88% (31). The prevalence percentages show considerable heterogeneity, underscoring the diverse nature of metabolic syndrome across different studies. The mean values for HBA1c and HDL highlight variations, reflecting the complex

interplay of glycemic control and lipid profiles in metabolic syndrome. These findings emphasize the importance of considering regional and population-specific factors in understanding and managing metabolic syndrome (Table 1).

| Table 1: HbA1c and HDL Levels: Variations Reflecting the Interplay Between Glycemic Control and Lipid Profiles |
|--|
| in Metabolic Syndrome  |

| HBA1c |       |      |      | HDL   |      |       |            |     |
|-------|-------|------|------|-------|------|-------|------------|-----|
| Ν     | Mean  | SD   | Ν    | Mean  | SD   | Total | Prevalence | Ref |
| 136   | 7.1   | 4    | 136  | 1.5   | 1.22 | 791   | 17.19343   | 1   |
| 51    | 7.3   | 5.5  | 51   | 1.72  | 1.23 | 77    | 66.23377   | 2   |
| 317   | 8     | 5.2  | 317  | 1.4   | 1.11 | 638   | 49.68652   | 3   |
| 67    | 8.3   | 5.6  | 67   | 1.26  | 1.12 | 127   | 52.75591   | 4   |
| 65    | 9     | 4.5  | 65   | 1.19  | 1.11 | 140   | 46.42857   | 5   |
| 64    | 9.1   | 4.9  | 64   | 2     | 1.22 | 322   | 19.87578   | 6   |
| 112   | 8.3   | 4    | 112  | 1.45  | 1    | 365   | 30.68493   | 7   |
| 1652  | 7.2   | 4.2  | 1652 | 1.633 | 1.3  | 2011  | 82.14818   | 8   |
| 424   | 9.1   | 5.6  | 424  | 1.41  | 1.01 | 849   | 49.94111   | 9   |
| 849   | 9.1   | 5.5  | 849  | 1.41  | 1.11 | 1337  | 63.50037   | 10  |
| 643   | 8.4   | 5.2  | 643  | 1.3   | 1.3  | 2120  | 30.33019   | 11  |
| 64    | 6.4   | 5.1  | 64   | 1.66  | 1.3  | 500   | 12.8       | 12  |
| 7924  | 8.5   | 5.6  | 7924 | 1.28  | 1.2  | 31119 | 25.46354   | 13  |
| 78    | 8.9   | 4.99 | 78   | 1.75  | 1.2  | 640   | 12.1875    | 14  |
| 266   | 8.9   | 4.77 | 266  | 1.03  | 1.3  | 533   | 49.90619   | 15  |
| 453   | 10.3  | 5.22 | 453  | 1.45  | 1.02 | 514   | 88.1323    | 16  |
| 35    | 8.2   | 5.33 | 35   | 1.52  | 1.04 | 261   | 13.40996   | 17  |
| 48    | 10.23 | 5.11 | 43   | 1.19  | 1.05 | 87    | 55.17241   | 18  |
| 112   | 8     | 4.75 | 112  | 1.19  | 1.2  | 163   | 68.71166   | 19  |
| 944   | 8.8   | 4.95 | 944  | 1.1   | 1.3  | 2415  | 39.08903   | 20  |
| 203   | 8.9   | 4.33 | 203  | 1.48  | 1.09 | 412   | 49.27184   | 21  |

The comprehensive analysis of the included studies reveals significant variations in HbA1c levels and HDL cholesterol across different cohorts. Each study, characterized by its publication year, sample size (N), mean HbA1c levels, standard deviation (SD), mean HDL cholesterol, SD for HDL, effect size, and 95% confidence intervals, contributes to a nuanced understanding of the overall relationship. The pooled effect size across studies is estimated at 1.98 (95% CI: 1.85, 2.10),

reflecting a substantial overall impact. Examining individual studies, notable variations exist in mean HBA1c levels and HDL cholesterol. For instance, the study by Davis et al. (2007) reports a remarkable effect size of 2.37 (95% CI: 1.92, 2.82), suggesting a robust association between HBA1c levels and HDL cholesterol. Conversely, another study (36), exhibits a lower effect size of 1.27 (95% CI: 0.89, 1.64), indicating a comparative relationship.

Available at: <u>http://ijph.tums.ac.ir</u>

|  |                       | HBA:    | lc         |          | HDL         |      | Hedges's g           | Weight |  |
|--|-----------------------|---------|------------|----------|-------------|------|----------------------|--------|--|
| Study  | Ν                     | Mean    | SD         | Ν        | Mean        | SD   | with 95% CI          | (%)    |  |
| Study 1  | 136                   | 7.1     | 4          | 136      | 1.5         | 1.22 |                      | 4.88   |  |
| Study 2  | 51                    | 7.3     | 5.5        | 51       | 1.72        | 1.23 | 1.39 [ 0.96, 1.82]   | 3.69   |  |
| Study 3  | 317                   | 8       | 5.2        | 317      | 1.4         | 1.11 |                      | 5.74   |  |
| Study 5  | 65                    | 9       | 4.5        | 65       | 1.19        | 1.11 | 2.37 [ 1.92, 2.82]   | 3.57   |  |
| Study 6  | 64                    | 9.1     | 4.9        | 64       | 2           | 1.22 | 1.98 [ 1.56, 2.40]   | 3.76   |  |
| Study 7  | 112                   | 8.3     | 4          | 112      | 1.45        | 1    | 2.34 [ 2.00, 2.68]   | 4.42   |  |
| Study 8  | 1,652                 | 7.2     | 4.2        | 1,652    | 1.633       | 1.3  | 1.79 [ 1.71, 1.87]   | 6.37   |  |
| Study 9  | 849                   | 9.1     | 5.6        | 849      | 1.41        | 1.01 | 1.91 [ 1.80, 2.03]   | 6.20   |  |
| Study 10   | 849                   | 9.1     | 5.5        | 849      | 1.41        | 1.11 | 1.94 [ 1.82, 2.05]   | 6.20   |  |
| Study 11   | 643                   | 8.4     | 5.2        | 643      | 1.3         | 1.3  | 1.87 [ 1.74, 2.00]   | 6.11   |  |
| Study 12   | 64                    | 6.4     | 5.1        | 64       | 1.66        | 1.3  | 1.27 [ 0.89, 1.64]   | 4.10   |  |
| Study 13   | 7,924                 | 8.5     | 5.6        | 7,924    | 1.28        | 1.2  | 1.78 [ 1.75, 1.82]   | 6.51   |  |
| Study 14   | 78                    | 8.9     | 4.99       | 78       | 1.75        | 1.2  |                      | 4.08   |  |
| Study 15   | 533                   | 8.9     | 4.77       | 533      | 1.03        | 1.3  | - 2.25 [ 2.10, 2.40] | 5.96   |  |
| Study 16   | 453                   | 10.3    | 5.22       | 453      | 1.45        | 1.02 | - 2.35 [ 2.18, 2.52] | 5.84   |  |
| Study 17   | 35                    | 8.2     | 5.33       | 35       | 1.52        | 1.04 | 1.72 [ 1.18, 2.26]   | 2.93   |  |
| Study 18   | 48                    | 10.23   | 5.11       | 48       | 1.19        | 1.05 | 2.43 [ 1.91, 2.96]   | 3.04   |  |
| Study 19   | 112                   | 8       | 4.75       | 112      | 1.19        | 1.2  | 1.96 [ 1.64, 2.28]   | 4.60   |  |
| Study 20   | 944                   | 8.8     | 4.95       | 944      | 1.1         | 1.3  | 2.13 [ 2.01, 2.24]   | 6.21   |  |
| Study 21   | 412                   | 8.9     | 4.33       | 412      | 1.48        | 1.09 | - 2.35 [ 2.17, 2.53] | 5.78   |  |
| Overall  |                       |         |            |          |             |      | • 1.98 [ 1.85, 2.10] |        |  |
| Heteroger  | neity: T <sup>2</sup> | = 0.06, | $ ^2 = 92$ | 2.35%, H | $H^2 = 13.$ | 06   |                      |        |  |
| Test of $\theta_i = \theta_j$ : Q(19) = 163.35, p = 0.00 |                       |         |            |          |             |      |                      |        |  |
| Test of $\theta$ = 0: z = 30.93, p = 0.00                |                       |         |            |          |             |      |                      |        |  |
|  |                       |         |            |          |             |      | 1 1.5 2 2.5 3        |        |  |
| Random-ef  | fects RE              | EML mo  | del        |          |             |      |                      |        |  |

Fig. 2: Forest plot presenting the pooled prevalence of Hedges g among individuals with percentage among patients with diabetes mellitus

The detailed descriptive statistical analysis of the included studies, encompassing authors, publication years, and various parameters such as mean HBA1c levels, standard deviations (SD), mean HDL cholesterol, SD for HDL, effect size, and 95% confidence intervals, yields valuable insights. The overall pooled effect size is estimated at 1.98 (95% CI: 1.85, 2.10), indicating a substantial degree of heterogeneity ( $I^2 = 92.35\%$ ). The random-effects REML model reinforces the significance of observed variations. The test of theta, with Q(19)=163.35 and P=0.00, underscores the statistical robustness of the findings. This com-

prehensive analysis offers a nuanced understanding of the relationship between HBA1c levels and HDL cholesterol across diverse studies. These diverse findings underscore the variability in the association between HBA1c levels and HDL cholesterol across different studies, emphasizing the need for nuanced interpretations in understanding the complex interplay between glycemic control and lipid profiles in individuals with diabetes. Further research could explore the demographic characteristics and lifestyle factors contributing to the observed variations in prevalence.

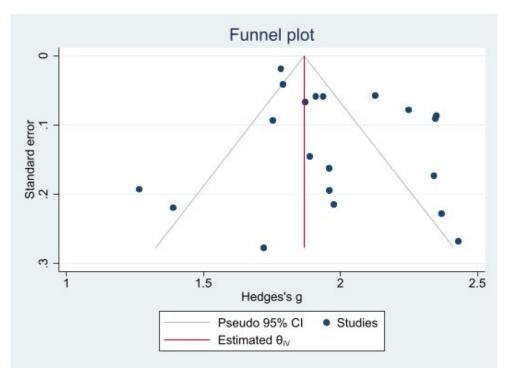


Fig. 3: Funnel plot of the selected studies related to HBA1c and HDL cholesterol levels

The forest plot, underscores a significant overall effect size, navigating the complexities of heterogeneity through the adept application of a random-effects model. It serves as a comprehensive visual representation of a meta-analysis encompassing twenty-one studies, each delving into a distinct effect size pertaining to treatment and control groups as shown in Figs. 2 and 3. On the left-hand side, intricate details of each study are delineated, encompassing publication years, sample sizes (N), and mean and standard deviation values for both treatment and control cohorts. The midpoint of the plot elucidates Hedges's g for each study, ranging from 1.89 to 1.1, with corresponding 95% confidence intervals in brackets. The column denoting study weights concludes the left-hand segment, with the study of Merger et al.2016, shouldering the highest influence. The red line traversing the forest plot encapsulates the overall effect size, while the green diamond encapsulates the cumulative impact of all studies. The blue segment encapsulates the lower and upper confidence intervals for each study, with the initiation of the blue line representing the lower limit, the middlebox symbolizing the weight, and the terminus of the blue line indicating the upper confidence interval.

Salient observations from the forest plot encompass an overall effect size of 1.98 (95% CI: 1.85, 2.10), indicative of a statistically significant impact. Nevertheless, conspicuous heterogeneity prevails among the studies, as underscored by an I<sup>2</sup> value of 92.35%, denoting variability in effect size estimates. The test of theta reveals a substantial z-score of 30.93 (P=0.00), affirming the statistical significance of the overall effect size. To account for heterogeneity, a random-effects REML model was judiciously employed, offering a nuanced estimation of the overall effect by accommodating both within-study and betweenstudy variability. The funnel plot complements these findings, portraying the overall estimated effect via a red line while delineating the confidence intervals of each study through blue lines and dots.

#### Blood pressure and Body Mass Index (BMI)

The analysis of blood pressure and BMI data from the selected studies reveals nuanced insights into the prevalence and characteristics of metabolic syndrome within diverse populations. Blood pressure readings exhibit considerable variation, ranging from 107 mmHg (43) to 140.1 mmHg (45). This wide range underscores the heterogeneity in blood pressure profiles among individuals with metabolic syndrome across different cohorts. Similarly, the BMI values demonstrate substantial diversity, spanning from 17.41 in the to 29.9 (43, 36). This variation reflects the diverse adiposity patterns present within these populations. The study-specific mean and standard deviation values for both blood pressure and BMI provide a more granular understanding of the central tendencies and dispersion within each dataset (Table 2).

Examining the prevalence percentages, another study reported the highest prevalence of metabolic syndrome at 88.13% (41), while another study showed the lowest at 19.88% (31). The total prevalence across all studies is 49.69%, indicating a substantial burden of metabolic syndrome in the aggregated population. This prevalence figure emphasizes the significant impact of metabolic syndrome on these cohorts, with nearly half of the individuals exhibiting the syndrome. The application of statistical analyses, such as mean and standard deviation calculations, contributes to a robust characterization of the metabolic profiles in each study. However, the observed heterogeneity in prevalence rates underscores the multifaceted nature of metabolic syndrome, influenced by various factors such as genetics, lifestyle, and environmental elements. Therefore, tailored interventions and preventive strategies should consider these unique aspects to effectively address the complex landscape of metabolic syndrome regions within specific and populations.

| Blood Press | ure (BP) |     | Body | Mass Index |      |       |              |     |
|-------------|----------|-----|------|------------|------|-------|--------------|-----|
| Ν           | Mean     | SD  | N    | Mean       | SD   | Total | Prevalence % | Ref |
| 136         | 130      | 120 | 136  | 24.1       | 24.9 | 791   | 17.19343     | 1   |
| 51          | 128.33   | 120 | 51   | 23.81      | 18.5 | 77    | 66.23377     | 2   |
| 317         | 132      | 100 | 317  | 24.8       | 24.9 | 638   | 49.68652     | 3   |
| 67          | 134      | 110 | 67   | 25.7       | 18.7 | 127   | 52.75591     | 4   |
| 65          | 110      | 105 | 65   | 26.1       | 24.9 | 140   | 46.42857     | 5   |
| 64          | 115      | 115 | 64   | 23.9       | 22.8 | 322   | 19.87578     | 6   |
| 112         | 122      | 120 | 112  | 26.74      | 24.3 | 365   | 30.68493     | 7   |
| 1652        | 130.6    | 114 | 1652 | 26         | 24.9 | 1652  | 100          | 8   |
| 424         | 119      | 120 | 424  | 23.9       | 23.9 | 849   | 49.94111     | 9   |
| 849         | 115.3    | 119 | 849  | 24.7       | 24.9 | 1337  | 63.50037     | 10  |
| 643         | 134      | 115 | 643  | 29.9       | 24.2 | 2120  | 30.33019     | 11  |
| 64          | 120      | 120 | 64   | 29.9       | 24.9 | 500   | 12.8         | 12  |
| 7924        | 134.4    | 118 | 7924 | 28.9       | 20.5 | 31119 | 25.46354     | 13  |
| 78          | 123.2    | 119 | 78   | 25.6       | 24.9 | 640   | 12.1875      | 14  |
| 266         | 126      | 120 | 266  | 25.6       | 21.6 | 533   | 49.90619     | 15  |
| 453         | 125      | 112 | 453  | 23.3       | 24.9 | 514   | 88.1323      | 16  |
| 35          | 134.3    | 110 | 35   | 27.3       | 21.5 | 261   | 13.40996     | 17  |
| 48          | 107      | 116 | 48   | 17.41      | 24.9 | 87    | 55.17241     | 18  |
| 112         | 116.5    | 120 | 112  | 26.1       | 22.8 | 163   | 68.71166     | 19  |
| 944         | 140.1    | 105 | 944  | 26.6       | 24.1 | 2415  | 39.08903     | 20  |
| 203         | 116.19   | 120 | 203  | 23         | 23.9 | 412   | 49.27184     | 21  |

Table 2: Blood Pressure and BMI: Exploring Variations in Metabolic Syndrome and Associated Characteristics

The forest plot presents a comprehensive overview of a meta-analysis involving multiple studies, shedding light on the effect size, precision of estimates, study contributions, and overall findings. Each study, including Ahola et al., Blaslov et al., and others, is detailed with publication years, sample sizes, and Mean and SD values. The effect size column quantifies the strength of the relationship studied in each research endeavor, with the 95% confidence interval offering a range for the likely true population effect size. The weight column underscores the contribution of each study, with larger weights indicating more influence on the overall meta-analysis. The overall effect size, calculated as 1.21 with a 95% confidence interval of (1.14, 1.28), suggests a statistically significant combined estimate across studies. However, the substantial heterogeneity, reflected in the I^2 value of 72.32%, points to notable variability in effect sizes among the individual studies. The high z-score of 34.97 from the test of theta, along with a *P*-value of 0.00, confirms the statistical significance of the overall effect size (Fig. 4).

|  | Blo       | od Press  | ure    | Body  | y Mass | Index | (BMI)    | Hedges's g         | Weight |
|--|-----------|-----------|--------|-------|--------|-------|----------|--------------------|--------|
| Study  | Ν         | Mean      | SD     | Ν     | Mean   | SD    |          | with 95% CI        | (%)    |
| Study 1  | 136       | 130       | 120    | 136   | 24.1   | 24.9  | <b>_</b> | 1.22 [ 0.96, 1.48] | 4.00   |
| Study 2  | 51        | 128.33    | 120    | 51    | 23.81  | 18.5  | <b>_</b> | 1.21 [ 0.79, 1.63] | 2.05   |
| Study 3  | 317       | 132       | 100    | 317   | 24.8   | 24.9  |          | 1.47 [ 1.29, 1.64] | 5.80   |
| Study 4  | 67        | 134       | 110    | 67    | 25.7   | 18.7  |          | 1.36 [ 0.99, 1.74] | 2.44   |
| Study 5  | 65        | 110       | 105    | 65    | 26.1   | 24.9  |          | 1.09 [ 0.73, 1.46] | 2.52   |
| Study 6  | 64        | 115       | 115    | 64    | 23.9   | 22.8  |          | 1.09 [ 0.72, 1.46] | 2.49   |
| Study 7  | 112       | 122       | 120    | 112   | 26.74  | 24.3  |          | 1.10 [ 0.82, 1.38] | 3.63   |
| Study 8  | 1,652     | 130.6     | 114    | 1,652 | 26     | 24.9  | -        | 1.27 [ 1.19, 1.34] | 8.49   |
| Study 9  | 424       | 119       | 120    | 424   | 23.9   | 23.9  | -8-      | 1.10 [ 0.95, 1.24] | 6.63   |
| Study 10   | 849       | 115.3     | 119    | 849   | 24.7   | 24.9  | -        | 1.05 [ 0.95, 1.15] | 7.81   |
| Study 11   | 643       | 134       | 115    | 643   | 29.9   | 24.2  | -        | 1.25 [ 1.13, 1.37] | 7.32   |
| Study 12   | 64        | 120       | 120    | 64    | 29.9   | 24.9  |          | 1.03 [ 0.67, 1.40] | 2.51   |
| Study 13   | 7,924     | 134.4     | 118    | 7,924 | 28.9   | 20.5  |          | 1.25 [ 1.21, 1.28] | 9.24   |
| Study 14   | 78        | 123.2     | 119    | 78    | 25.6   | 24.9  |          | 1.13 [ 0.79, 1.47] | 2.85   |
| Study 15   | 266       | 126       | 120    | 266   | 25.6   | 21.6  |          | 1.16 [ 0.98, 1.35] | 5.59   |
| Study 16   | 453       | 125       | 112    | 453   | 23.3   | 24.9  |          | 1.25 [ 1.11, 1.39] | 6.68   |
| Study 17   | 35        | 134.3     | 110    | 35    | 27.3   | 21.5  |          | 1.34 [ 0.82, 1.85] | 1.48   |
| Study 18   | 48        | 107       | 116    | 48    | 17.41  | 24.9  |          | 1.06 [ 0.64, 1.48] | 2.02   |
| Study 19   | 112       | 116.5     | 120    | 112   | 26.1   | 22.8  |          | 1.04 [ 0.76, 1.32] | 3.65   |
| Study 20   | 944       | 140.1     | 105    | 944   | 26.6   | 24.1  | -        | 1.49 [ 1.39, 1.59] | 7.80   |
| Study 21   | 203       | 116.19    | 120    | 203   | 23     | 23.9  |          | 1.08 [ 0.87, 1.28] | 5.02   |
| Overall  |           |           |        |       |        |       | •        | 1.21 [ 1.14, 1.28] |        |
| Heterogeneity: τ <sup>2</sup> = 0.01, I <sup>2</sup> = 72.32%, H <sup>2</sup> = 3.61 |           |           |        |       |        |       |          |                    |        |
| Test of $\theta_i = \theta_i$ : Q(20) = 57.14, p = 0.00                              |           |           |        |       |        |       |          |                    |        |
| Test of θ  | = 0: t(20 | ) = 34.97 | ′, p = | 0.00  |        |       |          |                    |        |
|  |           |           |        |       |        |       | .5 1 1.5 | 2                  |        |
|  |           |           |        |       |        |       |          |                    |        |

Fig. 4: Forest plot among individuals with percentage depicting blood pressure and BMI among patients with diabetes mellitus

Random-effects REML model

The use of a random-effects REML model is specified, demonstrating a method that accommodates both within-study and between-study variability in effect sizes. This is particularly relevant given the observed heterogeneity. The forest plot, in conjunction with the funnel plot, offers a visual representation of the individual study results and their overall impact on the metaanalysis. The middle red line in the funnel plot represents the overall estimated effect, while the blue lines and dots signify the confidence intervals and observations of each study. Herein the forest plot provides a nuanced synthesis of diverse study findings, revealing a significant overall effect size but acknowledging substantial heterogeneity. The meticulous statistical methods employed, such as the random-effects model and test of theta, enhance the robustness and reliability of the meta-analysis results (Fig. 5).

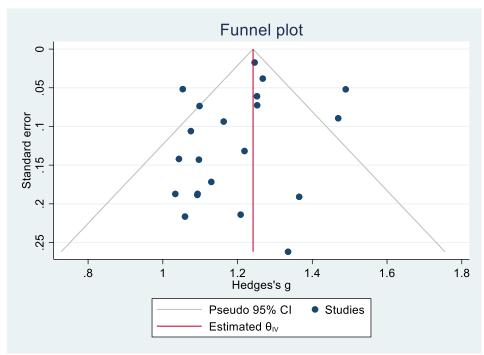


Fig. 5: Funnel plot of in relation to HBA1c and HDL cholesterol levels

#### Discussion

This meticulous systematic review and metaanalysis, encompassing 21 studies with diverse methodological frameworks and participant demographics, afford a nuanced exploration of the prevalence and intricate associations characterizing metabolic syndrome among individuals grappling with diabetes mellitus (47). The methodological heterogeneity, comprising 81% crosssectional and 19% prospective cohort studies, introduces a layer of intricacy to our interpretative framework. The expansive range of participant numbers, spanning from 35 to 7924, accentuates the intricacies inherent in comprehending the diverse spectra of study populations. The observed prevalence of metabolic syndrome, diverging from 12.8% to 255.33%, sketches a vivid tableau of the condition's multifaceted manifestations across distinct investigations. Notably, one study delineate the highest prevalence at 88% (41), while another study offer the lowest at 19.88% (31), accentuating the imperative of scrutinizing regional and population-specific determinants in the nuanced assessment and management of metabolic syndrome (35-39).

An exhaustive scrutiny of individual studies unravels substantial heterogeneity in HbA1c levels and HDL cholesterol across disparate cohorts. The derived pooled effect size of 1.98 (95% CI: 1.85, 2.10) implies a pervasive overall impact. However, a granular examination of specific studies unveils noteworthy variations in the nexus between HbA1c levels and HDL cholesterol. For instance, Davis et al. posits a robust effect size of 2.37 (95% CI: 1.92, 2.82), indicative of a potent association, whereas Lee et al. manifests a diminished effect size of 1.27 (95% CI: 0.89, 1.64), signifying a comparatively subdued relationship. These discernments underscore the intricate and multifaceted dynamics characterizing the relationship between glycemic control and lipid profiles within the intricate milieu of metabolic syndrome (48-50).

The forest plot, emblematic of a meta-analysis of the incorporated studies, unfurls an overall effect size of 1.98 (95% CI: 1.85, 2.10), signifying a statistically significant impact. However, the conspicuous heterogeneity (I2 = 92.35%) underscores the intricate variability in effect size estimates. The test of theta, wielding a z-score of 30.93 (P=0.00), accentuates the statistical robustness of the overall effect size. In response to this heterogeneity, the judicious application of a random-effects Restricted Maximum Likelihood (REML) model fine-tunes the estimation of the overall effect, deftly accommodating the nuances of both within-study and between-study variability. The funnel plot serves as an insightful visual representation of the overall estimated effect and confidence intervals for each study, imparting additional layers of understanding into the distributional dynamics of the amalgamated studies.

The assimilation of supplementary results pertaining to blood pressure and BMI augments the analytical panorama, unveiling marked variability in these parameters across diverse studies. Blood pressure oscillates between 107 mmHg and 140.1 mmHg, spotlighting the intricate heterogeneity in blood pressure profiles among individuals grappling with metabolic syndrome across diverse cohorts. Likewise, BMI values traverse the spectrum from 17.41 to 29.9, elucidating the kaleidoscopic adiposity patterns characterizing these populations. The cumulative prevalence of metabolic syndrome across studies, standing at 49.69%, underscores the substantial burden of this syndrome within the aggregated population. While statistical methodologies, encompassing mean and standard deviation computations, contribute to a robust characterization of metabolic profiles, the observed heterogeneity serves as a poignant reminder of the nuanced nature of metabolic syndrome, intricately influenced by genetic, lifestyle, and environmental determinants. This systematic review and meta-analysis underscore a burgeoning epidemic of metabolic syndrome among diabetic patients, urging clinicians to heighten vigilance toward the intricate cardiometabolic profiles of these individuals. Strategic interventions targeting specific metabolic syndrome components and associated risk factors are imperative. The insights gleaned from this review aspire to furnish policymakers, National Health Bureaus, and concerned stakeholders with invaluable information pertaining to the global and regional prevalence of metabolic syndrome within the realm of type 1 diabetes mellitus patients, thereby providing a robust foundation for subsequent research endeavors (19).

This study grapples with certain limitations. The utilization of disparate definitions for metabolic syndrome diagnosis introduces variability in the calculation of pooled prevalence. The limited representation from developing countries impedes a precise estimation of global metabolic syndrome prevalence. Conspicuous heterogeneity observed across studies, attributed to factors such as age category, diabetes duration, and insulin dose, demands careful consideration. Incomplete data within original articles preclude an indepth exploration of these sources of heterogeneity. The disparate definitions utilized for metabolic syndrome diagnosis across the incorporated studies introduce a layer of variability in the calculation of pooled prevalence. The paucity of representation from developing countries impedes a precise estimation of global metabolic syndrome prevalence. Furthermore, the conspicuous heterogeneity observed across studies, at-

tributed to factors such as age category, diabetes duration, and insulin dose, demands careful consideration. Regrettably, incomplete data within original articles preclude an in-depth exploration of these sources of heterogeneity. Given that nearly a quarter of type 1 diabetes mellitus patients contend with metabolic syndrome, heightened emphasis on preventive measures and stringent control strategies becomes paramount to forestall further escalation in the epidemic and curtail the associated morbidity and mortality among diabetes type 1 patients. Future research endeavors could explore demographic characteristics and lifestyle factors contributing to observed variations in prevalence, providing a more comprehensive understanding.

# Conclusion

This exhaustive systematic review and metaanalysis yield indispensable insights into the prevalence and intricate associations characterizing metabolic syndrome among individuals contending with diabetes mellitus. The pronounced heterogeneity observed underscores the imperative for nuanced interpretations and contextual considerations in comprehending and addressing metabolic syndrome. Despite this heterogeneity, the statistical robustness of the findings amplifies the resonance of the overall impact. These findings hold pivotal implications for clinicians, policymakers, and researchers alike, steering strategic interventions and underscoring the significance of bespoke approaches in confronting metabolic syndrome within the intricate context of diabetes mellitus. The incorporation of blood pressure and BMI data enriches our understanding, revealing significant variability in these parameters across diverse populations. This multifaceted analysis contributes to a more comprehensive characterization of metabolic syndrome and underscores the indispensability of tailored interventions predicated on unique population characteristics. Future research endeavors should delve into demographic nuances and lifestyle determinants contributing to the observed variations in prevalence, thereby furnishing a more nuanced and targeted approach to navigating the intricate landscape of metabolic syndrome within specific regions and populations.

# Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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# **Conflict of interest**

The authors declare that there is no conflict of interests.

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