International Journal of Scientific Research in Dental and Medical Sciences

www.ijsrdms.com

The Effect of Treatment with Mesenchymal Stem Cells on HbA1c and Insulin Requirement in Diabetic Patients: A Systematic Review and Meta-analysis

Parsa Eshragh Abad Shapori [a], Maryam Fathi [b, *]

[a] *Faculty of Medicine, Sharekod University of Medical Sciences, Shahrekord, Iran*
[b] *Faculty of Health Sciences of Sorbonne, Antoine Béclère Hospital, Paris, France*

ARTICLE INFO

Article history:
Received 18 March 2025
Received in revised form 09 May 2025
Accepted 10 June 2025
Available online 12 June 2025

Keywords:
Diabetes Mellitus
Insulin
Mesenchymal Stem Cells

ABSTRACT

Background and aim: This study explores the use of mesenchymal stem cells (MSCs) as a potential therapeutic option for diabetes treatment, addressing the increasing global prevalence of the condition, the lack of glucose control, the need for insulin injections, patient quality of life, and associated side effects. It investigates the impact of MSC treatment on HbA1c levels and insulin requirements in patients with diabetes.

Material and methods: The present study included 13 RCT studies from international databases (PubMed, EMBASE, Web of Science, and Cochrane Library) up to April 30, 2025, identified using relevant keywords and based on study inclusion and exclusion criteria. The statistical analysis was performed using Stata/MP v17 as a fixed-effects model.

Results: HbA1c levels in the group receiving MSC therapy were significantly lower than in the placebo group, with the mean changes of HbA1c being -0.72 (MD: -0.72; 95% CI, -0.95,-0.50). The mean changes of FPG in T1DM were -29.65 (MD: -29.65; 95% CI, -47.2, -12.28), and in T2DM were -0.68 (MD: -0.68; 95% CI, -1.56, -0.20). The test of group differences showed that the effectiveness of MSC therapy on both types of diabetes (T1DM and T2DM) in terms of C-peptide levels is similar (p = 0.08).

Conclusions: A decrease in HbA1c levels, a decrease in fasting blood sugar, and an increase in C-peptide levels were observed after treatment with mesenchymal stem cells compared to the placebo group, indicating that mesenchymal stem cells can effectively affect the treatment process of diabetes.

1. Introduction

One of the significant concerns regarding non-communicable diseases in the world is the increase in the prevalence of diabetes; statistics show that the overall prevalence of diabetes mellitus will reach 783.2 million people by 2045.[1] Several factors contribute to the development of diabetes mellitus, including environmental, genetic, and lifestyle factors.[2] Two types of diabetes are classified: in children and adults, type 1 diabetes mellitus (T1DM),[3] which is related to the body's autoimmune response, is more common, and in adults and older, lifestyle, obesity, physical inactivity, genetics, etc. lead to type 2 diabetes mellitus or T2DM.[4] The prevalence of T2DM is significantly higher than that of T1DM, accounting for approximately 90 to 95% of cases.[5] According to statistics reported by the World Health Organization (WHO), diabetes mellitus has caused a three percent increase in mortality in recent years; this has increased the need for healthcare.[6] Complications from it have also led to an increase in mortality rates, including stroke, cardiovascular disease, vision loss, and ulceration of the toes. Since diabetes mellitus disrupts a person's life and reduces the quality of life, lifestyle modifications can help the recovery process, and drug therapy and insulin therapy should be carried out according to the doctor's recommendations.[7] One of the most important factors in the treatment process is controlling high blood glucose levels; therefore, developing new and effective methods to manage diabetes mellitus and its complications is of paramount importance.[8] One of the new methods mentioned in studies is the use of stem cells; two types of stem cells have been reported: embryonic stem cells (ESCs) and non-embryonic stem cells;[9] mesenchymal stem cells (MSCs) derived from non-embryonic stem cells have become very popular; MSCs are isolated from adipose tissue, skin, fetal umbilical cord, dental pulp, liver tissues, and amniotic fluid;[10] MSCs can differentiate into muscle, cartilage, fat, bone marrow stroma, and bone. Studies have shown that MSCs have many applications due to their multiple activities, including multipotent, immunomodulatory, and regenerative properties. One of the most prominent MSCs is human umbilical cord MSCs (UC-MSCs), which are easily isolated, non-invasive, and economically viable.[11] UC-MSCs have a high proliferation capacity and, according to the findings of the studies, also have anti-apoptotic and angiogenic properties. The findings indicate that UCMSCs

* *Corresponding author. Maryam Fathi*
E-mail address: *Maryam.fathi@aphp.fr*
Faculty of Health Sciences of Sorbonne, Antoine Béclère hospital, Paris, France
https://doi.org/10.30485/IJSRDMS.2025.532144.1664

can differentiate into islet insulin-secreting clusters, playing a crucial role in blood glucose control and insulin release. Animal studies have shown that in animals with T1DM and T2DM, UCMSCs have demonstrated positive efficacy in blood glucose control and beta cell activity.[12-14] Given the high prevalence of diabetes, the lack of definitive treatment options, and the importance of utilizing modern methods, this study aimed to examine the safety and clinical efficacy of mesenchymal stem cells in diabetes treatment based on a consensus of study findings and provide strong evidence. The present study aimed to evaluate the effect of treatment with MSCs on HbA1c and insulin requirements in diabetic patients.

2. Material and methods

Search strategy and selection criteria

A targeted search was conducted to identify articles related to the study objective in the international databases PubMed, EMBASE, and Web of Science up to April 30, 2025. Additionally, the reference lists of all review articles closely related to the study objective were searched to find relevant articles. The Google Scholar search engine was also used for the search. Two authors, working independently and blind to each other's results, began searching, and the obtained articles were entered into the Database.Note.X8 software (to make it easier to identify duplicate articles and identical titles); step-by-step writing and conducting of the present study were carried out based on the PRISMA 2020 checklist.[15]

Inclusion criteria were determined by answering the research question with the PICO strategy:

Does mesenchymal stem cells (Intervention (I)) have high safety and clinical efficacy (Outcome (O)) in treating various types of diabetes mellitus (Population (P)) compared to the control group (without treatment) (Comparison (C))?

The English language restriction was applied to the search, and randomized controlled trials (RCTs) and cohort studies were included in the study. Review studies, case reports, letters to the editor, conference abstracts, case studies, and studies for which only abstracts were provided were excluded from the study.

The terms used to retrieve literature were the following:

("mesenchymal stem cells"[Mesh]) AND ("diabetes mellitus"[Mesh] OR " Type 1 diabetes "[Mesh] OR " Type 2 diabetes "[Mesh])) OR " HbA1c"[Mesh]) OR " insulin requirement"[Mesh]).

Data extraction

After an initial review of the articles, the authors designed a preliminary form for data extraction. Then, two authors, independently and blinded to the study's purpose, extracted the primary and demographic data by reviewing the full texts of the articles. The third author selected the required data by reviewing the relevant form and resolving disagreements between the two authors. In this form, all articles were identified by the name of the first author and the year of publication, and demographic information and main results were entered. The methods, findings, and conclusions were then extracted.

Bias assessment

Two authors independently assessed the quality of the studies. The Newcastle-Ottawa Scale (NOS) was used to assess the quality of the included studies for cohort studies,[16] and Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) was used for RCT studies.[17] Three criteria (selection, comparability, and outcomes) were considered in the NOS tool, while three criteria (trial design, conduct, and reporting) were considered in the ROB 2 tool. The NOS tool is scored from zero to nine (0-3, 4-6, and 7-9) and the Rob2 tool is scored from zero to six (0-2, 3-4, 5-6). Scores of 7-9 for NOS and 5-6 for Rob2 indicate a low risk of bias.

Statistical analysis

Statistical heterogeneity among studies was evaluated with the use of I2 statistic and Q test p-value < 0.05: No heterogeneity: $0.0\% < I^2 < 24.9\%$; low heterogeneity: $25.0\% < I^2 < 49.9\%$; Moderate heterogeneity: $50.0\% < I2 < 74.9\%$; High heterogeneity: $75.0\% < I^2 < 100\%$. The mean differences were analyzed using the fixed effects model and the inverse-variance method. STATA/MP.v17 (College Station, Texas, USA) was used to perform the analyses.

3. Results

Literature search and study characteristics

Fig. 1 illustrates the flowchart of searching articles based on PRISMA 2020. After extensive keyword searches in international databases, a total of 416 articles were found. After removing duplicates and inconsistencies in the title of the articles with the aim of the present study, 207 of these citations were removed. In the next step, 175 articles were excluded after matching the abstracts with the study selection criteria. As a result, the full text of 34 articles was evaluated, and after being read by two independent and blinded authors, thirteen articles that met the inclusion criteria and aligned with the study objectives were selected.

Study characteristics

All included studies were RCTs with 283 patients in the experimental group and 263 patients in the control group. Six studies investigated the effect of MSCs on type 2 diabetes, and seven studies examined the effect on type 1 diabetes. Other demographic and clinical characteristics are summarized in Table 1.

Bias assessment results

The risk of bias in the included studies was considered low based on the risk of bias assessment tool (seven RCTs: 5/6; six RCTs: 6/6) (Table 2).

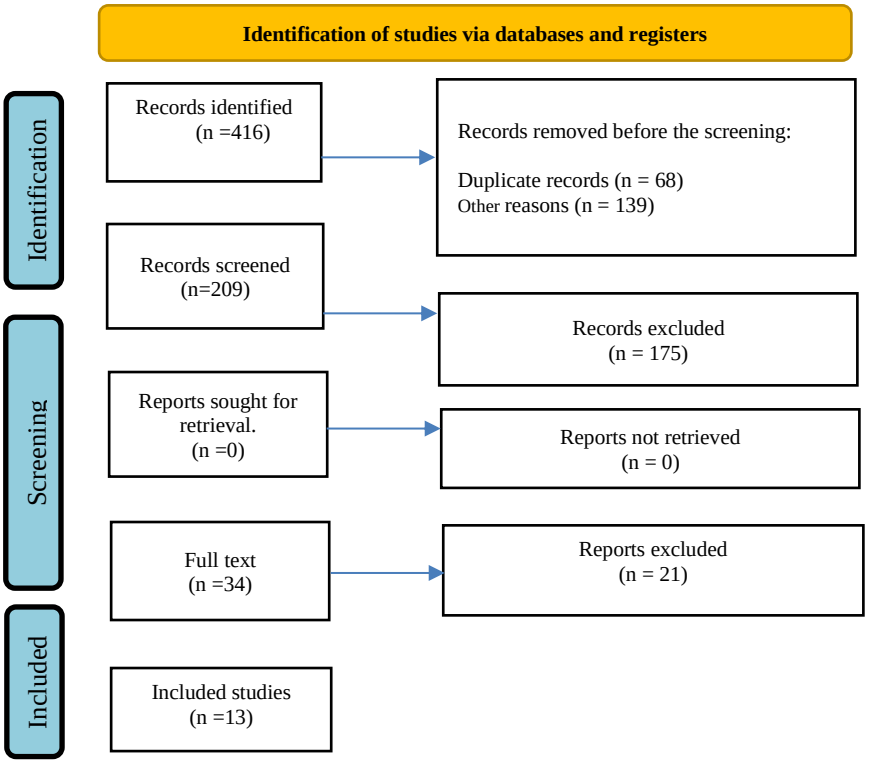

Fig. 1. PRISMA 2020 Checklist.

Table 1. Summary of demographic and methodological characteristics of included studies

Study. Years	Study Design	Number of Participants				Mean Age	Mean BMI		Type of Diabetes	Type of MSCs	Duration of Diabetes (Month)
		Experimental		Control			Experimental	Control			
		Female	Male	Female	Male						
Carlsson et al., 2025[18]	RCT	7	10	2	5	31	24.2	23.5	T1DM	WJ-MSCs	12
Wang et al., 2024[19]	RCT	12	25	12	25	40	23.3	24.5	T2DM	UC-MSC	12
Zhu et al., 2024[20]	RCT	10	5	8	7	67.2	24.03	24.9	T2DM	hUC-MSC	NR
Carlsson et al., 2023[21]	RCT	7	10	2	5	31	24.2	23.5	T1DM	WJ-MSCs	12
Fen Lian et al., 2022[22]	RCT	4	12	4	12	52.5	24.4	24.4	T2DM	hUC-MSC	NR
Zang et al., 2022[23]	RCT	17	28	16	30	50	28.6	30	T2DM	hUC-MSC	<240
Izadi et al., 2022[24]	RCT	5	6	5	5	10.2	16.7	18.9	T1DM	aBM-MNCs	NR
Wu et al., 2022[25]	RCT	15	6	15	9	35.8	28.7	26.1	T1DM	hUC-MSC	16
Lu et al., 2021[26]	RCT	15	12	13	13	22.4	18.7	19.1	T1DM	WJ-MSCs	2
Bhansali et al., 2017[27]	RCT	5	5	5	5	39.1	30.8	31.1	T2DM	ABMSCs	12
Hu et al., 2016[28]	RCT	14	17	14	16	52.4	26.7	27	T2DM	WJ-MSCs	NR
Cai et al., 2016[29]	RCT	12	9	10	11	18.29	21.4	26.19	T1DM	hUC-MSC	9
Hu et al., 2013[30]	RCT	6	9	6	8	17.6	20.9	21.3	T1DM	WJ-MSCs	24

WJ-MSCs: allogeneic Wharton's jelly-derived MSCs; aBM-MNCs: autologous bone marrow-derived MSCs; ABMSCs: autologous marrow-derived MSCs.

Table 2. Risk of bias assessment (Cochrane Collaboration's tool).

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Total Score
Carlsson et al., 2025[18]	+	+	?	+	+	+	5
Wang et al., 2024[19]	+	+	+	+	+	+	6
Zhu et al., 2024[20]	+	+	+	+	+	+	6
Carlsson et al., 2023[21]	+	+	?	+	+	+	5
Fen Lian et al., 2022[22]	+	+	+	+	+	+	6
Zang et al., 2022[23]	+	+	?	+	+	+	5
Izadi et al., 2022[24]	+	+	+	+	+	+	6
Wu et al., 2022[25]	-	+	+	+	+	+	5
Lu et al., 2021[26]	+	+	?	+	+	+	5
Bhansali et al., 2017[27]	+	+	+	+	+	+	6
Hu et al., 2016[28]	+	+	+	+	+	+	6
Cai et al., 2016[29]	-	+	+	+	+	+	5
Hu et al., 2013[30]	+	+	?	+	+	+	5

HbA1c

HbA1c levels in the group receiving MSC therapy were significantly lower than in the placebo group, with a mean change in HbA1c of -0.72 (MD: -0.72; 95% CI, -0.95 to -0.50). The I2 coefficient of 64.72% indicates moderate heterogeneity between studies ($p < 0.001$) (Figure 2). The mean changes of HbA1c in T1DM was -0.74 (MD: -0.74; 95% CI, -1.12, -0.35), and in T2DM was -0.72 (MD: -0.72; 95% CI, -0.99, -0.44). The test of group differences revealed that the effectiveness of MSC therapy in achieving target HbA1c levels for both types of diabetes (T1DM and T2DM) is similar ($p = 0.93$) (Fig. 2).

FBG

The FPG mean was significantly reduced in the MSC group compared to the placebo group at -0.76 (MD: -0.76; 95% CI, -1.64, 0.12). The I2 coefficient of 90.09% indicates high heterogeneity between studies ($p < 0.001$) (Fig. 3). The mean changes of FPG in T1DM was -29.65 (MD: -29.65; 95% CI, -47.2, -12.28), and in T2DM was -0.68 (MD: -0.68; 95% CI, -1.56, -0.20). The test of group differences showed that treatment with MSC in T1DM was more effective in reducing FBS. ($p<0.001$) (Fig. 3).

C-peptide levels

The mean difference in C-peptide level was 0.11 (MD: 0.11; 95% CI, 0.09,0.13). C-peptide level was significantly lower in the control group than in the MSC group ($p<0.001$). The I^2 coefficient of 32.20% indicates low heterogeneity between studies ($p = 0.13$) (Fig. 4). The mean difference of C-peptide level in T1DM was 0.12 (MD: 0.12; 95% CI, 0.10,0.15), and in T2DM was 0.07 (MD: 0.07; 95% CI, 0.02, 0.12) (Fig. 4). The test of group differences revealed that the effectiveness of MSC therapy on both types of diabetes (T1DM and T2DM) in terms of C-peptide levels is similar ($p = 0.08$) (Fig. 4).

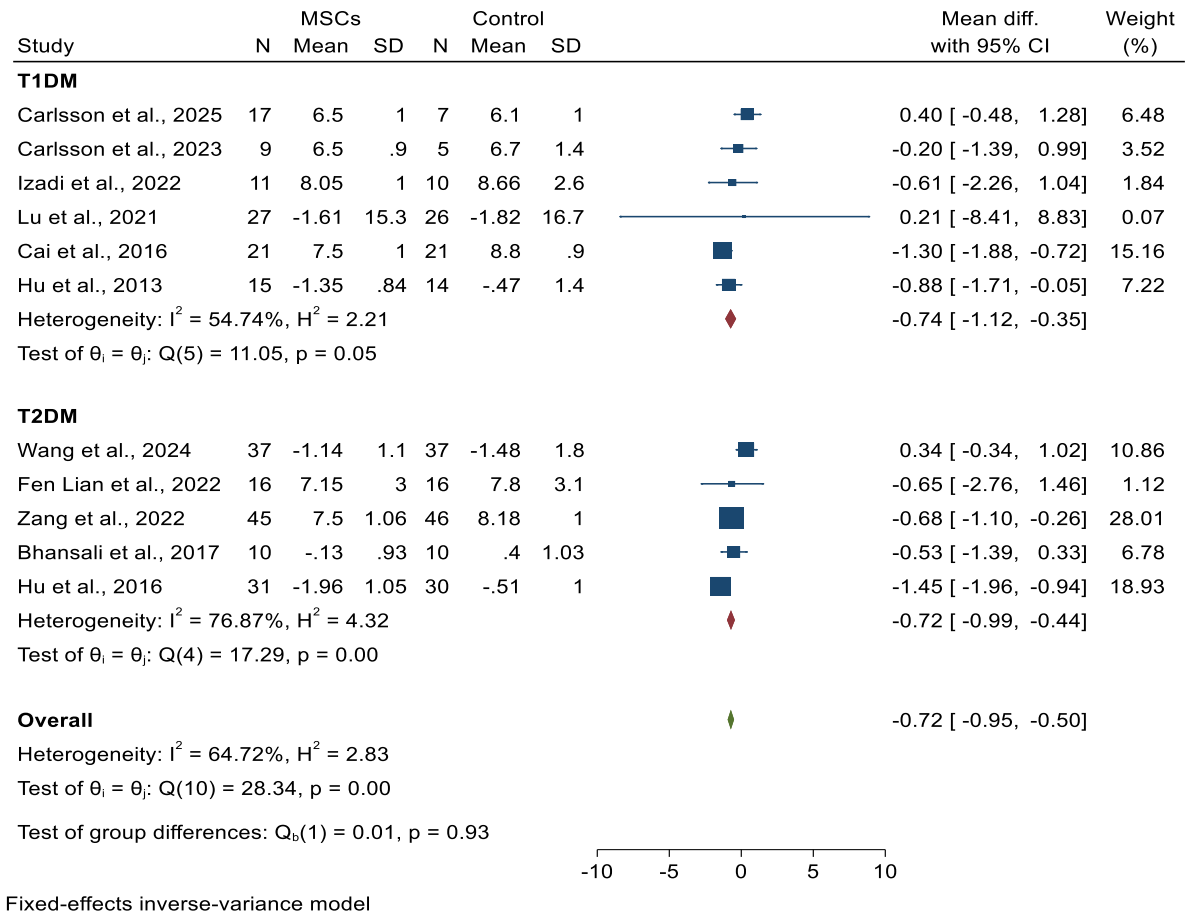

Fig. 2. Forest plot of subgroup meta-analysis for changes in HbA1c.

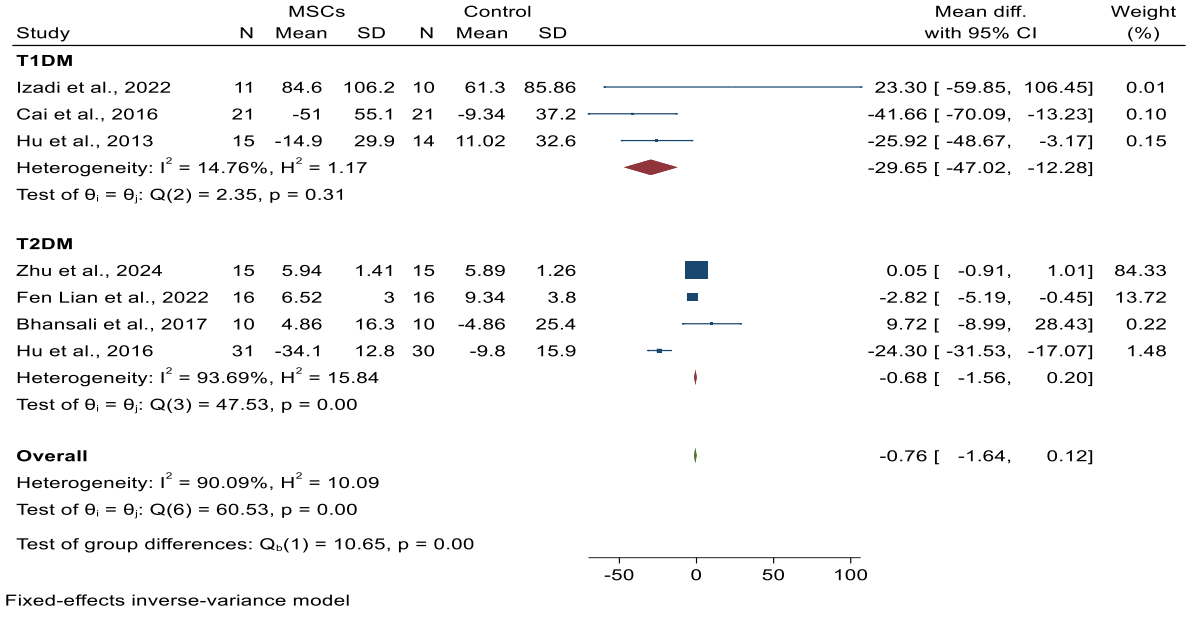

Fig. 3. Forest plot of subgroup meta-analysis for changes in FBG.

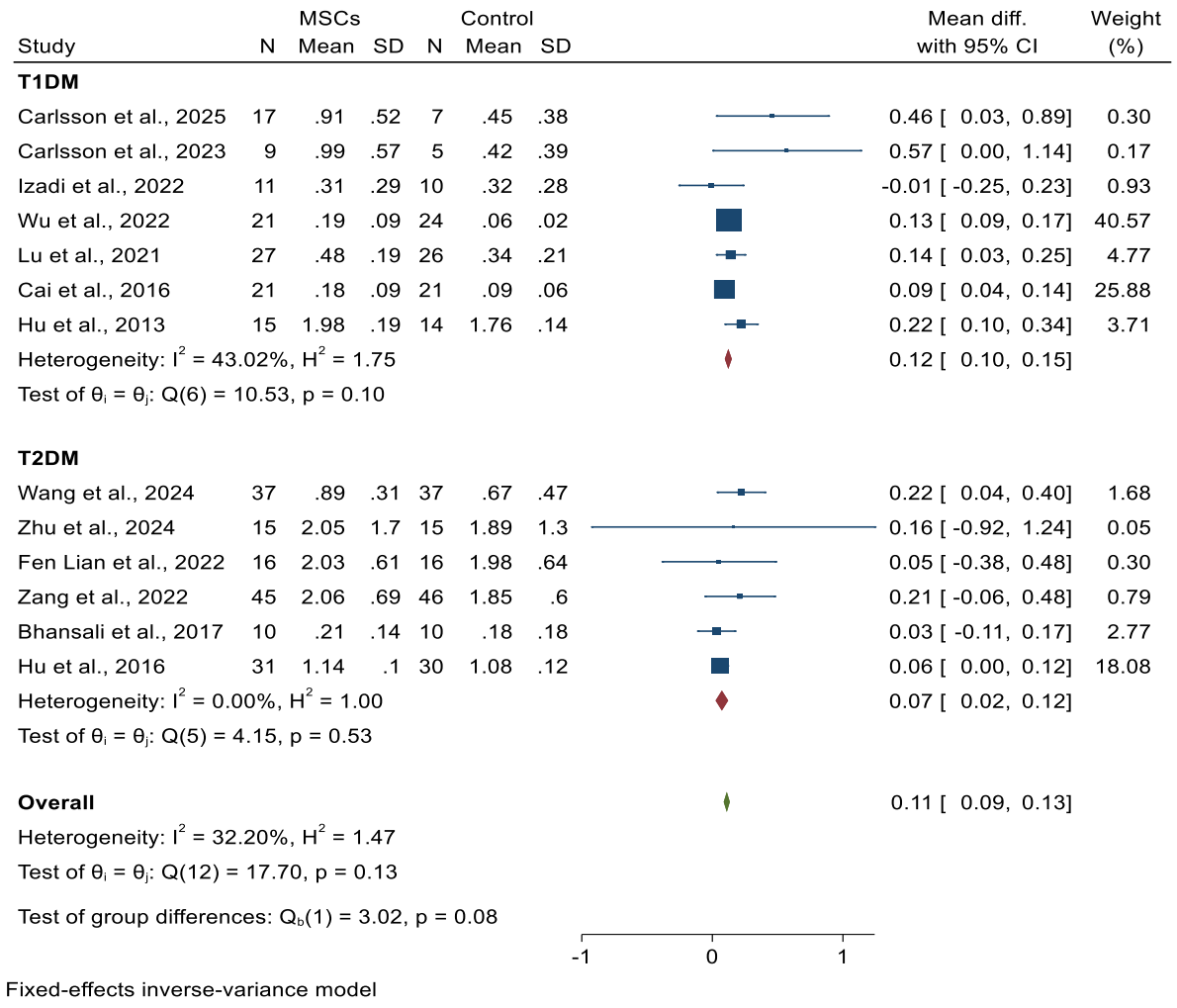

Fig. 4. Forest plot of subgroup meta-analysis for C-peptide levels.

4. Discussion

The high global prevalence of diabetes mellitus has led to the evaluation of new therapies with higher efficacy. Stem cells are effective therapeutic methods for treating many diseases. The present study was conducted to investigate the effectiveness of MSC in the treatment of diabetes mellitus; thirteen RCT studies were included in the research. The findings showed that compared to the placebo group, the MSC group has good and promising results in the treatment of diabetes mellitus. With significant reductions in HbA1c and FBS, the need for insulin in diabetic patients is also reduced. C-peptide levels were significantly higher in the MSCs receiving group, indicating improved beta cell function in basal insulin secretion. Research shows that stem cell therapy can have promising results. A previous study reported that insulin production increased after treatment with MSCs and significantly reduced HbA1c.[31] Other similar studies have confirmed the present findings. However, the results of MSC treatment have only been investigated in T2DM.[32, 33] Studies also show that MSC treatment can be effective in treating diabetes mellitus by examining various parameters.[34, 35] It is essential to note that multiple parameters must be evaluated to determine the effectiveness of antidiabetic treatment, and relying solely on HbA1c results cannot provide strong evidence; however, this parameter does indicate disease status and treatment progress.[36] Assessing tissue sensitivity to insulin by FBG evaluation is a good parameter to determine effectiveness.[37] On the other hand, determining C-peptide levels indicates the pancreas's ability to produce insulin. Therefore, in the present study, these three parameters were chosen to determine effectiveness; future studies should examine other parameters involved in diabetes mellitus to establish effectiveness with stronger evidence.[38] Another reason for choosing these three parameters was that they had been reported in more studies. Studies have shown that patients treated with MSCs have a reduced need for insulin. Changes in C-peptide indicate increased B-cell function, which is considered important and explains the effectiveness of MSCs.[39] Heterogeneity in some parameters was considered high; the reason for this could be related to the size and methodological approach of the studies; the sample size of the studies was small, which requires studies with similar methodology and a higher sample size to interpret the findings and provide stronger evidence; it was also observed that MSCs are effective in the treatment of both types 1 and 2 diabetes. Studies show that multiple factors are effective in reducing blood sugar, and fasting blood sugar can depend on the duration of fasting of the patient before the test, diet, physical activity level, insulin resistance, and comorbidities; therefore, the high heterogeneity between studies in the evaluation of this parameter can depend on all of these factors. Treating diabetics with MSCs aims to reduce the total daily insulin dose, thereby

improving the quality of life for patients and, in addition, reducing the economic burden on their families. Furthermore, side effects associated with insulin injection or use may also be reduced. The small sample size was one of the important limitations of the present study, as it raised concerns about statistical power. In almost all selected studies, the sample sizes were insufficient, with ranges of 10 to 45 for the experimental group and 7 to 46 for the control group. The complexity of MSC treatment and the various types of MSC used in the treatment may also impact the study results. In the selected studies, WJ-MSCs, hUC-MSCs, and ABMSCs were used most frequently, respectively. Additionally, the therapeutic dose can be effective in the clinical efficacy process; it is essential to determine the different routes of administration of mesenchymal cells, which vary across studies (the main confounder). To provide strong evidence and reliability of findings, all biases need to be examined, and then trial designs need to be conducted with higher precision and larger sample sizes.

5. Conclusion

According to the present meta-analysis, MSCs have good efficacy in the treatment of diabetes mellitus and provide favorable clinical results; a decrease in HbA1c levels, a decrease in fasting blood sugar, and an increase in C-peptide levels were observed following treatment with MSCs compared to the placebo group, indicating that MSCs can effectively affect the treatment process of diabetes; also, the need for insulin is significantly reduced after treatment with MSCs. Comparing the two types of diabetes, the improvement in HbA1c after treatment with MSCs and the increase in C-peptide levels were similar in type 1 and type 2 diabetes. In contrast, the decrease in fasting blood sugar after treatment with MSCs was more pronounced in patients with type 1 diabetes.

Conflict of Interest

The authors declared that there is no conflict of interest.

Acknowledgments

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

[1] Yang X, Sun J, Zhang W. Global trends in burden of type 2 diabetes attributable to physical inactivity across 204 countries and territories, 1990-2019. Frontiers in Endocrinology. 2024;15:1343002. https://doi.org/10.3389/fendo.2024.1343002.

[2] Tremblay J, Hamet P. Environmental and genetic contributions to diabetes. Metabolism. 2019;100:153952. https://doi.org/10.1016/j.metabol.2019.153952.

[3] Katsarou A, Gudbjörnsdottir S, Rawshani A, Dabelea D, Bonifacio E, Anderson BJ, et al. Type 1 diabetes mellitus. Nature reviews Disease primers. 2017;3(1):1-7. https://doi.org/10.1038/nrdp.2017.16.

[4] Ruze R, Liu T, Zou X, Song J, Chen Y, Xu R, et al. Obesity and type 2 diabetes mellitus: connections in epidemiology, pathogenesis, and treatments. Frontiers in endocrinology. 2023;14:1161521. https://doi.org/10.3389/fendo.2023.1161521.

[5] Gregory GA, Robinson TI, Linklater SE, Wang F, Colagiuri S, de Beaufort C, et al. Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: a modelling study. The lancet Diabetes & endocrinology. 2022;10(10):741-60. https://doi.org/10.1016/S2213-8587(22)00218-2.

[6] Gregg EW, Buckley J, Ali MK, Davies J, Flood D, Mehta R, et al. Improving health outcomes of people with diabetes: target setting for the WHO Global Diabetes Compact. the lancet. 2023;401(10384):1302-12. https://doi.org/10.1016/S0140-6736(23)00001-6.

[7] Kropp M, Golubnitschaja O, Mazurakova A, Koklesova L, Sargheini N, Vo TT, et al. Diabetic retinopathy as the leading cause of blindness and early predictor of cascading complications—risks and mitigation. Epma Journal. 2023;14(1):21-42. https://doi.org/10.1007/s13167-023-00314-8.

[8] Tomic D, Shaw JE, Magliano DJ. The burden and risks of emerging complications of diabetes mellitus. Nature Reviews Endocrinology. 2022;18(9):525-39. https://doi.org/10.1038/s41574-022-00690-7.

[9] Capuzzo MA, Ossanna R, Quintero Sierra LA, Virla F, Negri A, Conti A, et al. From the classification of stem cells to the release of potential in cell therapies: limits, considerations and future aspects in regenerative medicine. InPossibilities and limitations in current translational stem cell research 2023;44:1-17.

[10] Squillaro T, Peluso G, Galderisi U. Clinical trials with mesenchymal stem cells: an update. Cell transplantation. 2016;25(5):829-48. https://doi.org/10.3727/096368915X689622.

[11] Friedenstein AJ, Chailakhjan RK, Lalykina K. The development of fibroblast colonies in monolayer cultures of guinea‐pig bone marrow and spleen cells. Cell Proliferation. 1970;3(4):393-403. https://doi.org/10.1111/j.1365-2184.1970.tb00347.x.

[12] Li L, Li J, Guan H, Oishi H, Takahashi S, Zhang C. Human umbilical cord mesenchymal stem cells in diabetes mellitus and its complications: applications and research advances. International journal of medical sciences. 2023;20(11):1492-1507. https://doi.org/10.7150/ijms.87472.

[13] Al Naem M, Bourebaba L, Kucharczyk K, Röcken M, Marycz K. Therapeutic mesenchymal stromal stem cells: Isolation, characterization and role in equine regenerative medicine and metabolic disorders. Stem cell reviews and reports. 2020;16:301-22. https://doi.org/10.1007/s12015-019-09932-0.

[14] Ghassemifard L, Hasanlu M, Parsamanesh N, Atkin SL, Almahmeed W, Sahebkar A. Cell therapies and gene therapy for diabetes: current progress. Current Diabetes Reviews. 2025;21(8):e130524229899. https://doi.org/10.2174/0115733998292392240425122326.

[15] Tugwell P, Tovey D. PRISMA 2020. Journal of Clinical Epidemiology. 2021;134:A5-6. https://doi.org/10.1016/j.jclinepi.2021.04.008.

[16] Luchini C, Stubbs B, Solmi M, Veronese N. Assessing the quality of studies in meta-analyses: Advantages and limitations of the Newcastle Ottawa Scale. World Journal of Meta-Analysis. 2017;5(4):80-4. http://dx.doi.org/10.13105/wjma.v5.i4.80.

[17] Higgins JP, Savović J, Page MJ, Elbers RG, Sterne JA. Assessing risk of bias in a randomized trial. Cochrane handbook for systematic reviews of interventions. 2019:205-28. https://doi.org/10.1002/9781119536604.ch8.

[18] Carlsson PO, Espes D, Sisay S, Davies LC, Smith CE, Svahn MG. Correction: Umbilical cord-derived mesenchymal stromal cells preserve endogenous insulin production in type 1 diabetes: a Phase I/II randomised double-blind placebo-controlled trial. Diabetologia. 2025:1-2. https://doi.org/10.1007/s00125-023-05934-3.

[19] Wang Y, Chen H, Li Y, Hao H, Liu J, Chen Y, et al. Predictive factors that influence the clinical efficacy of umbilical cord–derived mesenchymal stromal cells in the treatment of type 2 diabetes mellitus. Cytotherapy. 2024;26(3):311-6. https://doi.org/10.1016/j.jcyt.2023.12.006.

[20] Zhu Y, Huang C, Zheng L, Li Q, Ge J, Geng S, et al. Safety and efficacy of umbilical cord tissue-derived mesenchymal stem cells in the treatment

of patients with aging frailty: a phase I/II randomized, double-blind, placebo-controlled study. Stem Cell Research & Therapy. 2024;15(1):122. https://doi.org/10.1186/s13287-024-03707-2.

[21] Carlsson PO, Espes D, Sisay S, Davies LC, Smith CE, Svahn MG. Umbilical cord-derived mesenchymal stromal cells preserve endogenous insulin production in type 1 diabetes: a Phase I/II randomised double-blind placebo-controlled trial. Diabetologia. 2023;66(8):1431-41. https://doi.org/10.1007/s00125-023-05934-3.

[22] Lian XF, Lu DH, Liu HL, Liu YJ, Han XQ, Yang Y, et al. Effectiveness and safety of human umbilical cord-mesenchymal stem cells for treating type 2 diabetes mellitus. World Journal of Diabetes. 2022;13(10):877-87. https://doi.org/10.4239/wjd.v13.i10.877.

[23] Zang L, Li Y, Hao H, Liu J, Cheng Y, Li B, et al. Efficacy and safety of umbilical cord-derived mesenchymal stem cells in Chinese adults with type 2 diabetes: a single-center, double-blinded, randomized, placebo-controlled phase II trial. Stem Cell Research & Therapy. 2022;13(1):180. https://doi.org/10.1186/s13287-022-02848-6.

[24] Izadi M, Sadr Hashemi Nejad A, Moazenchi M, Masoumi S, Rabbani A, Kompani F, et al. Mesenchymal stem cell transplantation in newly diagnosed type-1 diabetes patients: A phase I/II randomized placebo-controlled clinical trial. Stem Cell Research & Therapy. 2022;13(1):264. https://doi.org/10.1186/s13287-022-02941-w.

[25] Wu Z, Xu X, Cai J, Chen J, Huang L, Wu W, et al. Prevention of chronic diabetic complications in type 1 diabetes by co-transplantation of umbilical cord mesenchymal stromal cells and autologous bone marrow: a pilot randomized controlled open-label clinical study with 8-year follow-up. Cytotherapy. 2022;24(4):421-7. https://doi.org/10.1016/j.jcyt.2021.09.015.

[26] Lu J, Shen SM, Ling Q, Wang B, Li LR, Zhang W, et al. One repeated transplantation of allogeneic umbilical cord mesenchymal stromal cells in type 1 diabetes: an open parallel controlled clinical study. Stem cell research & therapy. 2021;12(1):340. https://doi.org/10.1186/s13287-021-02417-3.

[27] Bhansali S, Dutta P, Kumar V, Yadav MK, Jain A, Mudaliar S, et al. Efficacy of autologous bone marrow-derived mesenchymal stem cell and mononuclear cell transplantation in type 2 diabetes mellitus: a randomized, placebo-controlled comparative study. Stem cells and development. 2017;26(7):471-81. https://doi.org/10.1089/scd.2016.0275.

[28] Hu J, Wang Y, Gong H, Yu C, Guo C, Wang F, et al. Long term effect and safety of Wharton's jelly-derived mesenchymal stem cells on type 2 diabetes. Experimental and therapeutic medicine. 2016;12(3):1857-66. https://doi.org/10.3892/etm.2016.3544.

[29] Cai J, Wu Z, Xu X, Liao L, Chen J, Huang L, et al. Umbilical cord mesenchymal stromal cell with autologous bone marrow cell transplantation in established type 1 diabetes: a pilot randomized controlled open-label clinical study to assess safety and impact on insulin secretion. Diabetes care. 2016;39(1):149-57. https://doi.org/10.2337/dc15-0171.

[30] Hu J, Yu X, Wang Z, Wang F, Wang L, Gao H, et al. Long term effects of the implantation of Wharton's jelly-derived mesenchymal stem cells from the umbilical cord for newly-onset type 1 diabetes mellitus. Endocrine journal. 2013;60(3):347-57.

[31] Hamad FR, Rahat N, Shankar K, Tsouklidis N. Efficacy of stem cell application in diabetes mellitus: promising future therapy for diabetes and its complications. Cureus. 2021;13(2):e13563. https://doi.org/10.7759/cureus.13563.

[32] Mathur A, Taurin S, Alshammary S. The safety and efficacy of mesenchymal stem cells in the treatment of type 2 diabetes-A literature review. Diabetes, Metabolic Syndrome and Obesity. 2023;16:769-77.

[33] Pawitan JA, Yang Z, Wu YN, Lee EH. Towards standardized stem cell therapy in type 2 diabetes mellitus: a systematic review. Current Stem Cell Research & Therapy. 2018;13(6):476-88. https://doi.org/10.2174/1574888X13666180502143657.

[34] Ranjbaran H, Mohammadi Jobani B, Amirfakhrian E, Alizadeh‐Navaei R. Efficacy of mesenchymal stem cell therapy on glucose levels in type 2 diabetes mellitus: A systematic review and meta‐analysis. Journal of Diabetes Investigation. 2021;12(5):803-10. https://doi.org/10.1111/jdi.13404.

[35] Nada AH, Ibrahim IA, Oteri V, Shalabi L, Asar NK, Aqeilan SR, et al. Safety and efficacy of umbilical cord mesenchymal stem cells in the treatment of type 1 and type 2 diabetes mellitus: a systematic review and meta-analysis. Expert Review of Endocrinology & Metabolism. 2025;20(2). https://doi.org/10.1080/17446651.2025.2457474.

[36] Association AD. Improving Care and Promoting Health in Populations: Standards of Medical Care in Diabetes—2021. Diabetes Care. 2021;44:S7-14. https://doi.org/10.2337/dc21-S001.

[37] Hill NR, Levy JC, Matthews DR. Expansion of the homeostasis model assessment of β-cell function and insulin resistance to enable clinical trial outcome modeling through the interactive adjustment of physiology and treatment effects: iHOMA2. Diabetes care. 2013;36(8):2324-30. https://doi.org/10.2337/dc12-0607.

[38] Madan R, Varghese RT. Assessing insulin sensitivity and resistance in humans. Endotext. 2024.

[39] Päth G, Perakakis N, Mantzoros CS, Seufert J. Stem cells in the treatment of diabetes mellitus—Focus on mesenchymal stem cells. Metabolism. 2019;90:1-5. https://doi.org/10.1016/j.metabol.2018.10.005.

How to Cite this Article: Shahpori PE, Fathi M. The Effect of Treatment with Mesenchymal Stem Cells on HbA1c and Insulin Requirement in Diabetic Patients: A Systematic Review and Meta-analysis. International Journal of Scientific Research in Dental and Medical Sciences. 2025;7(2):88-95. https://doi.org/10.30485/IJSRDMS.2025.532144.1664.