

# The impact of diabetes mellitus on mortality and infection outcomes in burn patients: a meta-analysis

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**Abstract.** – **OBJECTIVE:** Burns are one of the most commonly occurring soft tissue injuries worldwide. It has been reported that burns are associated with a higher prevalence of complications, mortality, and hospitalization-related outcomes in patients with coexisting diabetes mellitus. Moreover, the morbidity and mortality related outcomes associated with diabetes in patients with burns. However, since then, several studies reporting the prognostic role of diabetes in patients with burns have been published. Therefore, in this present study, we attempt to develop a current state of evidence evaluating the prognostic influence of diabetes mellitus on infectious complications, duration of hospital stay and mortality-related outcomes in patients with burns. The aim of the study is to determine the overall effect of diabetes mellitus on infectious complications, duration of hospital stay and mortality-related outcomes in patients with burns.

**MATERIALS AND METHODS:** We performed a systematic search of the academic literature in four academic databases including EMBASE, CENTRAL, Scopus, and MEDLINE according to PRISMA guidelines. A random effect meta-analysis was carried out to evaluate the pooled effect size associated with diabetes mellitus on the outcome of infectious complications, duration of hospital stay and mortality in patients with burns.

**RESULTS:** From a total of 1,397 studies, 13 eligible studies with 16,538 patients (3415F, 8361M) with burns were included in the analysis. Among these patients, 1702 patients had diabetes, and 14,836 patients were reported to be non-diabetic. A random effect meta-analysis revealed small-to-large size positive effect of diabetes on the infectious outcome (Hedge's  $g$ : 0.2, 95% CI: -0.03 to 0.44), overall mortality (0.16, -0.06 to 0.39), and duration of hospital stay (0.98, 0.50 to 1.45) in patients with burns.

**CONCLUSIONS:** The present systematic review and meta-analysis provides evidence regarding the high morbidity and mortality related

outcomes for diabetic patients with burns. The present study confirms the findings of a previously published systematic review suggesting diabetes to be an important and independent risk factor delineating the prognostic outcome of burns.

*Key Words:*

Burn, Diabetes, Hyperglycemia, Complications, Infection.

## Introduction

Burns are one of the most common types of soft tissue injuries in the world<sup>1</sup>. Burns occur primarily on the skin as a result of excess heat, radiation, electricity, chemicals, or radioactivity<sup>2,3</sup>. According to the World Health Organization (WHO), burns are a global health concern that accounts for almost 300,000 deaths worldwide<sup>3</sup>, and have a significant impact on the Disability Adjusted Life Years especially in the middle- and low-income countries<sup>3,4</sup>. The pathophysiological mechanisms of burns can include the development of local responses which comprises zones of coagulation, stasis, or hyperemia<sup>5</sup>. In severe cases (with more than 30% body surface area impacted), a burn can result in systemic changes that eventually may lead to cardiovascular, metabolic, respiratory, and immunological changes<sup>5,6</sup>. Statistics from the recent 2016 Global Burden of Disease Studies suggest that although the incidence of burns has been decreasing with the development of medical infrastructure, the relative mortality, on the contrary, has remained constant during the last three decades<sup>7,8</sup>.

The prognostic outcome of burns has been reported to be dependent upon a range of variables, with co-existing medical conditions considered to

be the most important<sup>9-11</sup>. Diabetes mellitus, one of the most highly prevalent metabolic disorders in the world, affecting 8.5% of population<sup>12,13</sup>, has a profound impact on the prognostic outcome during recovery from burns<sup>7,14-17</sup>. Studies<sup>7,18</sup> have suggested several multifactorial underlying mechanisms for the observed negative effect of diabetes mellitus on the prognostic outcome of burns<sup>7,18</sup>. Greenhalgh et al<sup>19</sup> reported that diabetes mellitus can influence the healing outcome and eventually predispose a patient towards worsened morbidity and mortality related outcomes due to a range of hematological, neurological, metabolic, and cellular factors. For example, micro- and macro-vascular changes caused by atherosclerotic plaques in diabetes mellitus patients can impair healing by creating oxygen insufficiency due to partial or complete vascular occlusion<sup>19,20</sup>. Guthrie and Guthrie<sup>21</sup> suggested that vascular consequences of diabetes mellitus can also lead to neuropathic changes, primarily due to glycosylation of the vessels that supply the neural pathways. Similarly, a higher predisposition to renal insufficiency in diabetes mellitus patients was suggested as another important factor that can lead to impaired healing, primarily because of the changes in protein metabolism<sup>22,23</sup>. Furthermore, due to poor glycemic control in patients with diabetes, and impaired functioning of leukocytes, the diabetic patients are highly susceptible to a range of infectious diseases<sup>19,24</sup>.

Numerous reports<sup>25,26</sup> show acute stress-related changes in the glycemic levels in patients with burns. As was suggested by some studies, elevated blood glucose in patients with diabetes could potentially worsen the prognostic outcomes by promoting higher infection rates and mortality<sup>25,27</sup>. Despite having such a widespread influence on prognostic outcomes in patients with burns, a consensus regarding the influence of diabetes mellitus on morbidity- and mortality- related factors is still lacking.

To date, only one systematic review and meta-analysis has reported the prognostic impact of diabetes mellitus on morbidity- and mortality- related outcomes in burn patients<sup>7</sup>. This review showed a high relative risk ratio of infectious outcomes, mortality, and the duration of hospitalization for diabetic patients with burns. However, since this initial publication, several high-quality retrospective studies that evaluated the prognostic influence of diabetes on infectious outcomes, mortality, and duration of hospitalization in diabetic patients with burns have been

published<sup>14,16,17,28,29</sup>. The main goal of the present review and meta-analysis is to update the current state of evidence regarding the prognostic influence of diabetes mellitus in patients with burns, and to evaluate the influence of diabetes on infectious outcomes, overall mortality, and duration of hospitalization in patients with burns. These findings would further assist clinicians in developing best practice guidelines for burn management in patients with diabetes mellitus.

## Material and Methods

A systematic review and meta-analysis were performed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines<sup>30</sup>.

### Data Search Strategy

The literature search was performed in four scientific databases (EMBASE, MEDLINE, CENTRAL, and Scopus) from inception until October 2020. A combination of the following MeSH keywords “Burns”, “Diabetes”, “Mortality”, “Death rate”, “Case fatality rate”, “Mortality rate”, “Infections”, and “Hospital stay”, were used for the search across the academic databases. The bibliography section of the included studies was manually searched to identify further relevant studies. The inclusion criteria were as follows: a) Studies evaluated diabetic and non-diabetic patients with burns. b) Studies had to be performed in the human population. c) Studies evaluated mortality rates, infectious rates, and duration of hospital stays in diabetic and non-diabetic patients with burns. d) Studies reported the outcomes of mortality and hospitalization with the adjusted hazard ratio. e) Studies that were either randomized-controlled trials, quasi-randomized controlled trials, controlled-clinical trials, observational studies, prospective studies, or retrospective trials. f) Studies that were published in peer-reviewed scientific journals, or conferences. g) English language studies.

The screening of the studies was independently performed by two reviewers. Cases of disagreements were resolved by discussion with a third independent reviewer. Following data from the included studies were extracted: author information, descriptive data, sample distribution, infectious outcomes, mortality outcomes and duration of hospital stay. In cases of unavailable quantitative data, attempts were made to contact the re-

spective corresponding authors of the publication to gain access to the data.

### **Quality Assessment**

The appraisal of the risk of bias of the included studies was done by ROBINS-I, Cochrane risk of bias assessment tool for non-randomized controlled trials<sup>31</sup>. The ROBINS-I tool considers inadequate randomization, selective reporting, concealed allocation, classification, and missing data as major threats for instigating bias. The appraisal of methodological quality was done independently by two reviewers. Here as well, in case of disagreements between the two reviewers a third reviewer intervened to arbitrate.

### **Data Analysis**

We carried out a meta-analysis of the included studies by using Comprehensive Meta-analysis software version 2.0<sup>32</sup>. The within group meta-analysis was performed based on a random effects model<sup>33</sup>. We evaluated the pooled weighted effect size from the included studies. Weighted effect size of  $<0.2$  was considered as a small effect;  $0.2-0.8$  as a medium effect;  $>0.8$  was considered as a large effect.  $I^2$  statistics was used to assess the heterogeneity among the studies.  $I^2$  statistics of  $0-25\%$  was considered indicative of negligible heterogeneity,  $25\%-75\%$  -of moderate heterogeneity and  $\geq 75\%$  were considered to be of substantial heterogeneity<sup>33</sup>. We distributed the data and performed analysis for the overall mortality, infectious outcomes, and duration of hospital stay. Rate ratio, 95% confidence intervals, level of significance and heterogeneity have been reported. Publication bias was assessed using Duval and Tweedy's trim and fill procedure<sup>34</sup>. This method gives a nuanced perspective on the overall effect, and whether it would be affected by removal of the apparent bias. The analysis is characterized by imputation of studies from either side of the plotted graph to identify potential unbiased effects. The alpha level of significance was set at 95%.

## **Results**

A systematic search of five databases resulted in a total of 1,370 studies. Additional 27 studies were identified after screening of the bibliography section of the manuscripts (Figure 1). Finally, a total of 13 studies that met the inclusion criteria were included in this review. Only two of the included manuscripts were prospective cohort stud-

ies<sup>10,35</sup>. The rest 11 included studies were retrospective cohort studies<sup>14-17,28,29,36-40</sup>. We extracted and summarized the data of the included studies in details in Table II.

### **Participant Information**

A total of 16538 patients with heart failure were included in the 13 studies, among them 3415 females and 8361 males. The gender distribution was not reported by one study<sup>39</sup>, and one study did not report gender distribution for the non-diabetes group<sup>35</sup>. In the subgroup distribution for the patients with/without diabetes, a total of 1702 patients were reported to have diabetes, whereas 14836 patients did not have diabetes. From the studies that reported the gender distribution, a total of 532 diabetic females and 1040 diabetic males were reported, whereas 2883 females and 7321 males were reported to not be suffering from diabetes. The average age of the subsample with/without diabetes was  $57.6 \pm 2.6$ , and  $38.9 \pm 5.5$  years, respectively.

### **Publication Bias**

The Duval and Tweedy's trim and fill method were used to identify any missing studies according to the random effect model on both sides of the funnel plot. The overall random effect models determined the point estimates and the 95% confidence intervals for all the combined studies as 0.19 (0.03 to 0.35). While using the trim and fill method, we identified five studies that were missing on the left side of the funnel plot. The trim and fill method reported the imputed estimate to be 0.08 (-0.08 to 0.25) The publication bias is reported in Figure 2.

### **Quality Assessment for Non-Randomized Controlled Trials**

We analyzed the risk of bias in the methodology of the include non-randomized controlled trials using the ROBINS-I tool. The results are summarized in Table I. The overall risk was found to be low in the included studies. We observed that the methodological risk of bias was highest for the selection of reported results and measurement of the outcome. The overall risk of bias is also shown in Figure 3.

## **Meta-Analysis Report**

### **Infectious outcome**

The overall infection rates were reported by 11 studies<sup>10,14-17,29,35-39</sup>. A positive *small* effect size

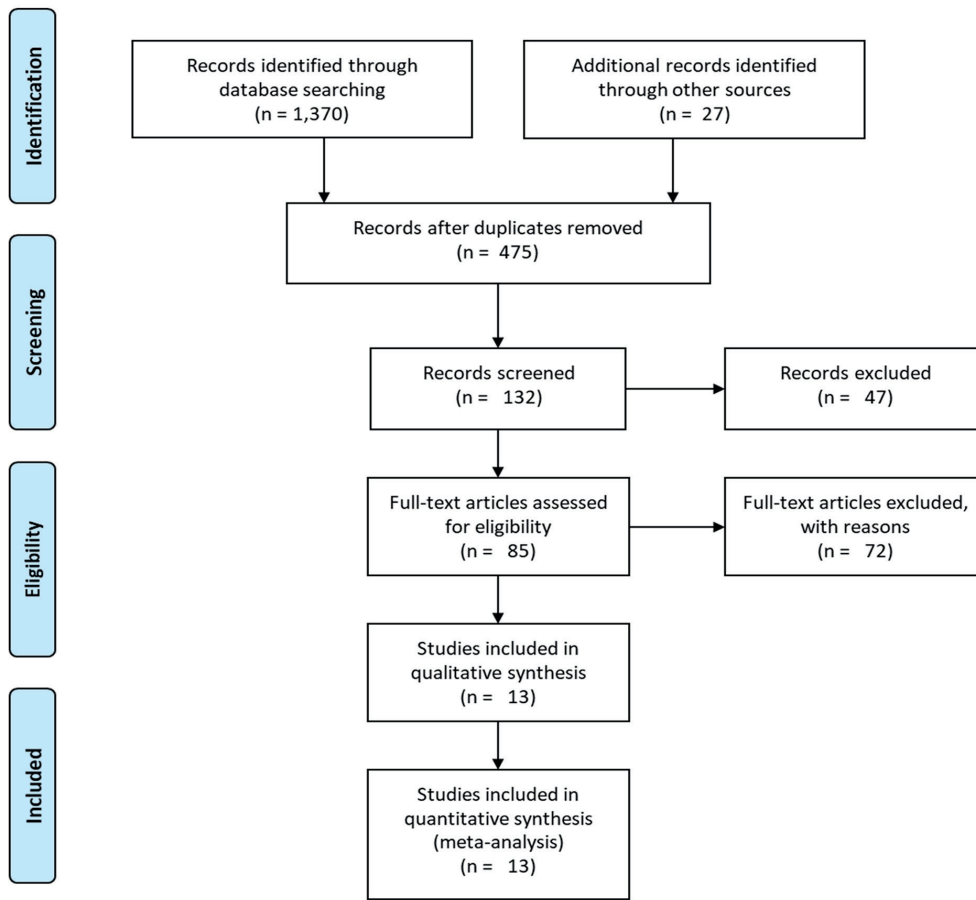


Figure 1. Illustrating the PRISMA flowchart.

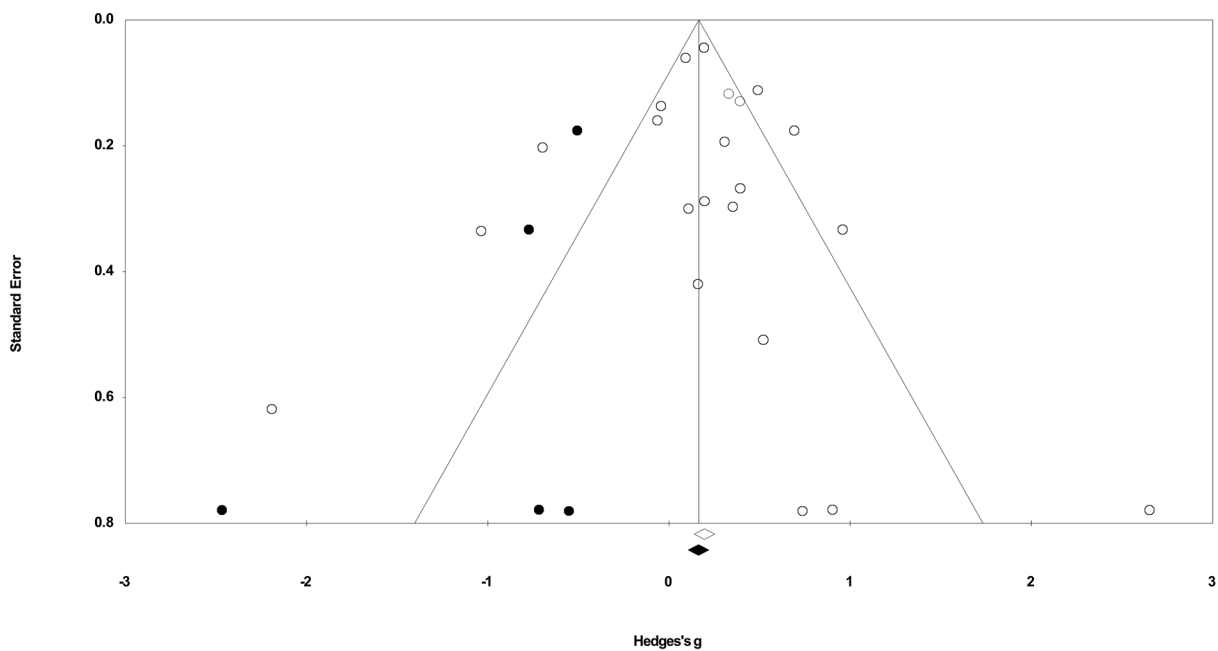


Figure 2. Illustrates the publication bias by Duval & Tweedy's trim and fill method.

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was reported to be 0.2 (95% CI: -0.03 to 0.44,  $p=0.09$ ) (Figure 4), with moderate heterogeneity ( $I^2: 67.8\%$ ).

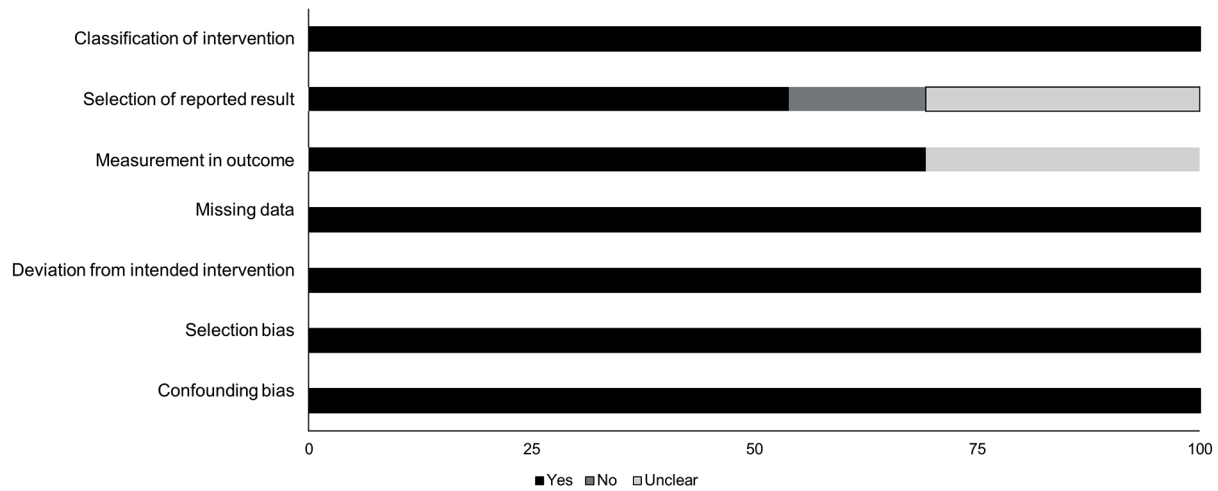
**Mortality outcome**

The overall mortality outcome was reported by 11 studies<sup>14,15,17,28,29,35-40</sup>. A *small* positive pooled

**Table I.** Details of the included studies.

Study	Country	Study design	Sample size (female, male)	Overall age: (M ± S.D) years	Infectious Complications (n)	Mortality (n)	Duration of hospital stay (n)
Vadala et al <sup>17</sup> (2020)	India	Retrospective cohort study	Diabetes: 18 (9F, 9M) Non-diabetes: 76 (24F, 52M)	Diabetes: 58.2 Non-diabetes: 36.3	Diabetes: 12 Non-diabetes: 47	Diabetes: 8 Non-diabetes: 27	Diabetes: 12.6 Non-diabetes: 16.2
Mai et al <sup>16</sup> (2020)	Australia	Retrospective cohort study	Diabetes: 169 (50F, 119M) Non-diabetes: 1932 (538F, 1394M)	Diabetes: 58.4 ± 15.5 Non-diabetes: 36.8 ± 16.4	Diabetes: 31 ± 18.3 Non-diabetes: 179 ± 9.1	Diabetes: - Non-diabetes: -	Diabetes: 10.3 ± 10 Non-diabetes: 6.1 ± 6.4
Diab et al <sup>29</sup> (2020)	Australia	Retrospective cohort study	Diabetes: 129 (20F, 109M) Non-diabetes: 668 (244F, 424M)	Diabetes: 60.5 ± 12.8 Non-diabetes: 39.7 ± 17.5	Diabetes: 123 Non-diabetes: 663	Diabetes: 1 Non-diabetes: 1	Diabetes: 7 ± 19.2 Non-diabetes: 0.8 ± 4.3
Dolp et al <sup>14</sup> (2019)	Canada	Retrospective cohort study	Diabetes: 76 (25F, 51M) Non-diabetes: 1186 (336F, 850M)	Diabetes: 59.8 ± 16.8 Non-diabetes: 44.8 ± 17.3	Diabetes: 35 Non-diabetes: 348	Diabetes: 5 Non-diabetes: 39	Diabetes: - Non-diabetes: -
Knowlin et al <sup>15</sup> (2018)	USA	Retrospective cohort study	Diabetes: 655 (223F, 432M) Non-diabetes: 4884 (1296F, 3588M)	Diabetes: 56.7 Non-diabetes: 39.9	Diabetes: 273 Non-diabetes: 1621	Diabetes: 106 Non-diabetes: 678	Diabetes: - Non-diabetes: -
Low et al <sup>36</sup> (2017)	Singapore	Retrospective cohort study	Diabetes: 53 (25F, 28M) Non-diabetes: 533 (202F, 331M)	Diabetes: 61 ± 12.7 Non-diabetes: 40 ± 16.2	Diabetes: 39 Non-diabetes: 234	Diabetes: 2 Non-diabetes: 15	Diabetes: 15 Non-diabetes: 9
Kimball et al <sup>35</sup> (2013)	USA	Retrospective cohort study	Diabetes: 43 (8F, 35M) Non-diabetes: 164 (45F, 119M)	Diabetes: 54.6 ± 13.7 Non-diabetes: 43.7 ± 18.9	Diabetes: 2 Non-diabetes: 3	Diabetes: 1 Non-diabetes: 1	Diabetes: 14.1 ± 10 Non-diabetes: 9.8 ± 9.3
Dahagam et al <sup>28</sup> (2011)	USA	Retrospective cohort study	Diabetes: 57 (16F, 41M) Non-diabetes: 405 (69F, 336M)	Diabetes: 57 Non-diabetes: 43	Diabetes: - Non-diabetes: -	Diabetes: 12 Non-diabetes: 53	Diabetes: 12 Non-diabetes: 9
Schwartz et al <sup>37</sup> (2011)	USA	Prospective cohort study	Diabetes: 24 (5F, 19M) Non-diabetes: 16 (6F, 10M)	Diabetes: -57 ± 26 Non-diabetes: 47 ± 22	Diabetes: 5 Non-diabetes: 15	Diabetes: - Non-diabetes: -	Diabetes: 22.9 Non-diabetes: 17.2
Maghsoudi et al <sup>34</sup> (2008)	Iran	Prospective cohort study	Diabetes: 94 (56F, 38M) Non-diabetes: 2968	Diabetes: 53.4 ± 16.3 Non-diabetes: 36 ± 13.4	Diabetes: 14 Non-diabetes: 482	Diabetes: 8 Non-diabetes: 729	Diabetes: 13 ± 8 Non-diabetes: 13.8 ± 13.5
Shalom et al <sup>39</sup> (2005)	USA	Retrospective cohort study	Diabetes: 73 (28F, 45M) Non-diabetes: 150 (54F, 96M)	Diabetes: 60.6 ± 1.8 Non-diabetes: 32.7 ± 1.8	Diabetes: - Non-diabetes: -	Diabetes: 10 Non-diabetes: 4	Diabetes: 17.1 ± 2 Non-diabetes: 8.8 ± 0.9
Memmel et al <sup>38</sup> (2004)	USA	Retrospective cohort study	Diabetes: 130 Non-diabetes: 1664	Diabetes: 54 ± 13 Non-diabetes: 27 ± 20	Diabetes: 130 Non-diabetes: 1126	Diabetes: 4 Non-diabetes: 27	Diabetes: 12.5 Non-diabetes: 9.5
McC Campbell et al <sup>37</sup> (2002)	USA	Retrospective cohort study	Diabetes: 181 (67F, 114M) Non-diabetes: 190 (69F, 121M)	Diabetes: - Non-diabetes: -	Diabetes: 81 Non-diabetes: 58	Diabetes: 38 Non-diabetes: 42	Diabetes: 23.2 ± 12.4 Non-diabetes: 12.2 ± 26.5

Legends: M: Male, F: Female, M: Mean, S.D: Standard deviation.



**Figure 3.** Illustrates the risk of bias according to the Cochrane risk of bias assessment for the non-randomized controlled trials.

effect size of Hedge’s *g*: 0.16 (95% CI: -0.06 to 0.39,  $p=0.15$ ) was reported (Figure 5), with negligible heterogeneity ( $I^2$ : 19.7%).

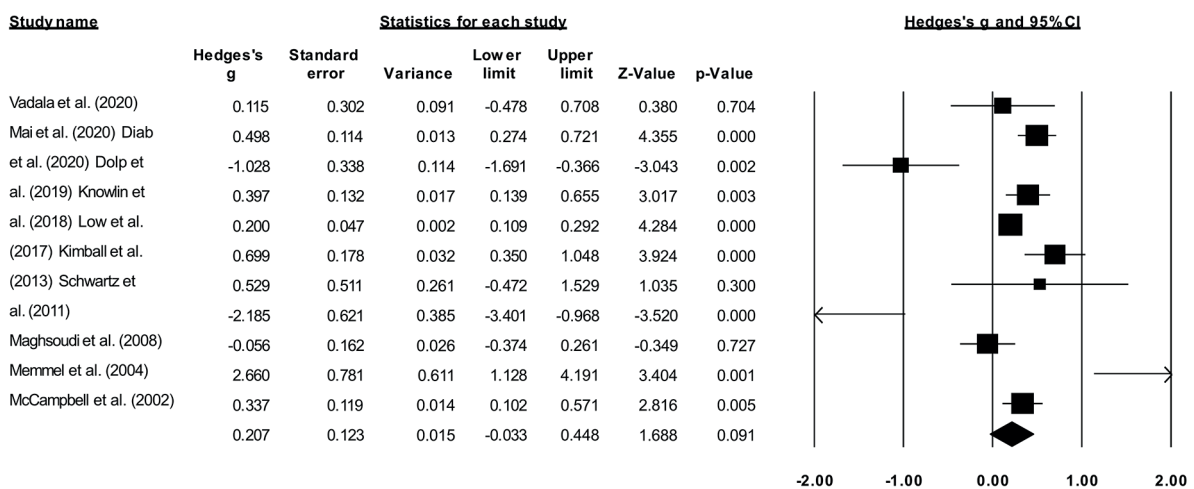
**Duration of hospital stay**

The duration of hospital stay was evaluated in 11 studies<sup>14,15</sup>. The pooled outcomes suggest an increased positive *large* effect of diabetes on the duration of hospital stay for burn patients 0.98 (95% CI: 0.50 to 1.45,  $p<0.01$ ) (Figure 6), with moderate heterogeneity ( $I^2$ : 77%).

**Discussion**

The present systematic review and meta-analysis provide a comprehensive state of evidence regarding the prognostic influence of diabetes mellitus in patients with burns. We observed a high overall detrimental effect of diabetes on infectious and mortality-related outcomes, and duration of hospitalization in burn patients.

The management of burns is one of the most challenging aspects for clinicians because of co-



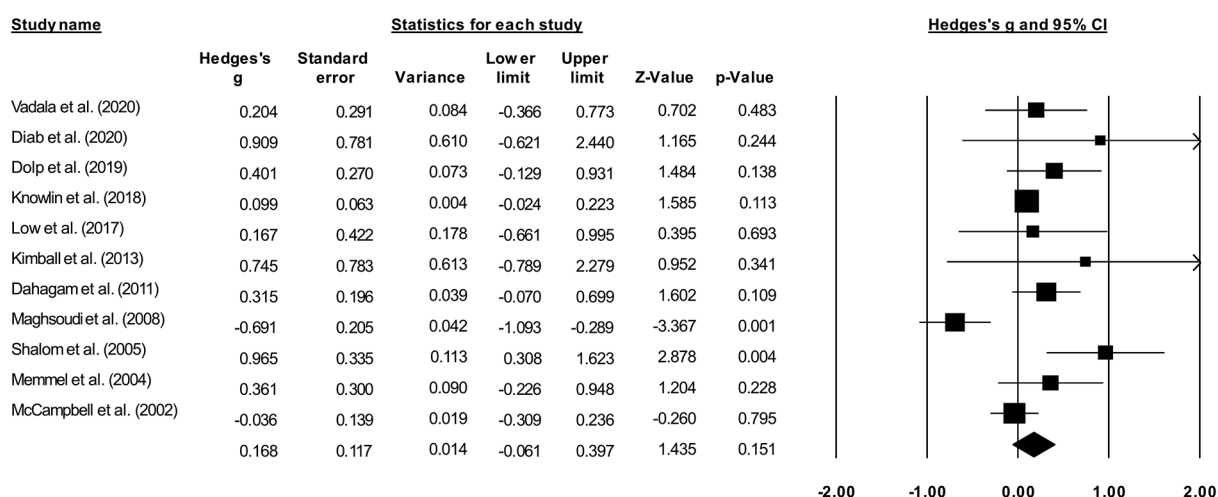
**Figure 4.** Illustrates the forest plot for studies evaluating the infection rate in diabetic and non-diabetic patients with burns. The weighted effect size is presented as black boxes whereas 95% confidence intervals are presented as whiskers. A negative effect size represents a higher infectious outcome in diabetic patients with burns, whereas the positive effect size represents a higher infectious outcome in non-diabetic patients with burns.

**Table II.** Illustrates risk of bias within studies according to ROBINS-I scale.

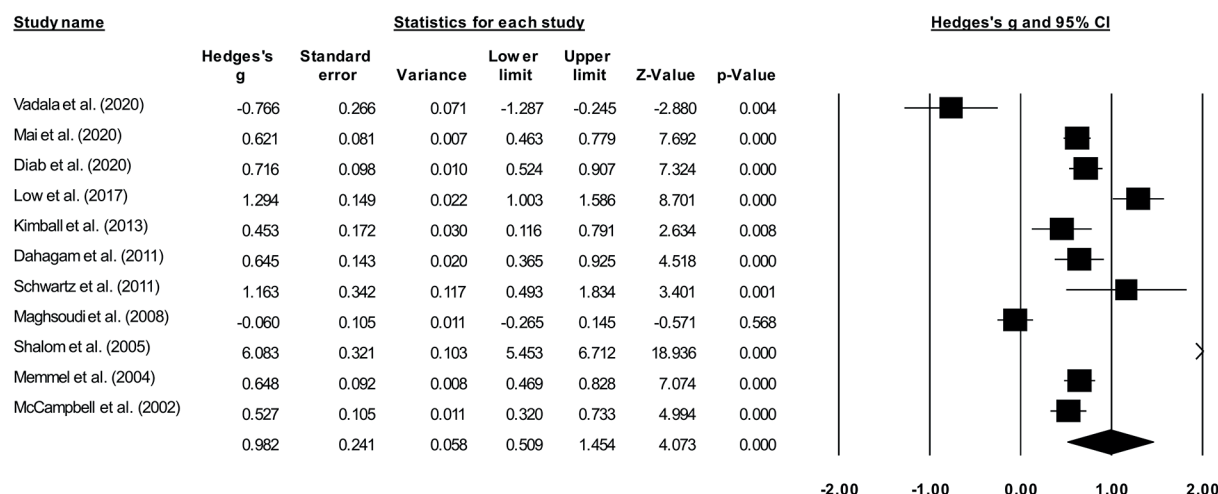
Study	Confounding bias	Selection bias	Deviation from intended intervention	Missing data	Measurement in outcome	Selection of reported result	Classification of intervention
Vadala et al <sup>17</sup> (2020)	+	+	+	+	+	+	+
Diab et al <sup>29</sup> (2020)	+	+	+	+	+	+	+
Mai et al <sup>16</sup> (2020)	+	+	+	+	+	?	+
Dolp et al <sup>14</sup> (2019)	+	+	+	+	+	?	+
Knowlin et al <sup>15</sup> (2018)	+	+	+	+	?	?	+
Low et al <sup>36</sup> (2017)	+	+	+	+	+	+	+
Kimball et al <sup>35</sup> (2013)	+	+	+	+	+	+	+
Dahagam et al <sup>28</sup> (2011)	+	+	+	+	+	+	+
Schwartz et al <sup>10</sup> (2011)	+	+	+	+	?	?	+
Maghsoudi et al <sup>34</sup> (2008)	+	+	+	+	+	+	+
Shalom et al <sup>39</sup> (2005)	+	+	+	+	+	+	+
Memmel et al <sup>38</sup> (2004)	+	+	+	+	?	-	+
McC Campbell et al <sup>37</sup> (2002)	+	+	+	+	?	-	+

existing morbidities, atypical pathophysiological mechanisms, and manifestations<sup>41,42</sup>. The presence of comorbidities, such as diabetes mellitus, adds to the difficulty for clinicians to delineate a prognostic course for a burn survivor, thereby largely increasing a chance of potential morbidity- and mortality- related outcomes<sup>43,44</sup>. The literature<sup>45-47</sup> has recognized the rising prevalence of diabetes mellitus in patients with burns. Moreover, studies have hypothesized that stress-related changes in glucose levels following a burn may aggravate the symptomatic manifestations of diabetes. Mecott et al<sup>48</sup> for instance, suggested that factors, such as facilitated gluconeogenesis, glycogenesis and insulin resistance play a criti-

cal role in worsening the prognostic outcomes in patients with diabetes. The authors noted that an increase in the levels of glucocorticoids and/or catecholamines due to prolonged activation of the hypothalamus-pituitary-adrenal axis during the acute phase of burn could be the main reason for hyperglycemia. Moreover, burn patients also exhibit resistance to insulin, primarily because of impaired insulin pathway signaling, catabolic response, up-regulation of the renin-angiotensin system and down-regulation of the Glucose transporter type 4<sup>49-51</sup>, respectively. These higher levels of glucose have eventually been associated with the suppression of interleukin factors 2, 6, 10<sup>52</sup>, and impaired activity of neutrophils<sup>53,54</sup>, ultimate-



**Figure 5.** Illustrates the forest plot for studies evaluating the mortality rate in diabetic and non-diabetic patients with burns. The effect size is presented as black boxes whereas 95% confidence intervals are presented as whiskers. A negative effect size represents a higher mortality outcome in diabetic patients with burns, whereas the positive effect size represents a higher mortality outcome in non-diabetic patients with burns.



**Figure 6.** Illustrates the forest plot for studies evaluating the duration of hospital stay rate in diabetic and non-diabetic patients with burns. The effect size is presented as black boxes whereas 95% confidence intervals are presented as whiskers. A negative effect size represents an increase in the duration of hospital stay in diabetic patients with burns, whereas the positive effect size represents an increase in the duration of hospital stay in non-diabetic patients with burns.

ly increasing the incidences of infection-led morbidity and mortality.

In our present review, we analyzed a range of studies that reported a predominant influence of diabetes on infectious outcomes in patients with burns. Dolp et al<sup>14</sup>, for instance, evaluated the overall burn wound infectious outcomes in a Canadian cohort of 1262 diabetic/non-diabetic patients, and reported a significant ( $p < 0.01$ ) increase in the wound-related infections for diabet-

ic patients (46.1%) as compared to non-diabetic patients (29.3%). The authors also reported that in addition to wound-related infections, higher blood glucose levels also led to increased incidences of urinary tract infection and septicemia. Similarly, Low et al<sup>36</sup> reported that in a cohort of 586 patients, the diabetic group (73.6%) had significantly higher infection-related outcomes as compared to the non-diabetic group (44.1%). By using a multivariate logistic regression model,



authors further reported that a higher incidence of infectious outcomes closely correlated with higher rates of hospital readmissions and a longer duration of hospital stays. While diabetic burn patients stayed in the hospital for an average of 9 to 29 days, an average hospital stay of non-diabetic patients was 4 to 14 days. Mai et al<sup>16</sup> reported similar increase in infectious outcomes and duration of hospitalization in diabetic patients with burns. Interestingly, the authors found a significant ( $p < 0.04$ ) correlation of higher levels of infection with an increased incidence of blood transfusion. This increased incidence was further associated with a longer duration of hospital stays for diabetic patients ( $10.3 \pm 10$  days) as compared to non-diabetic burn patients ( $6.1 \pm 6.4$  days). In agreement with these observations, the present meta-analysis, also reports an increased incidence of infections in diabetic patients with burns (Hedge's  $g$ : 0.2, 95% CI: -0.03 to 0.44). Moreover, we also report a *large* effect increase in the duration of hospitalization (0.98, 0.50 to 1.45) in diabetic patients with burns as compared to non-diabetic burn patients.

We also attempted to evaluate the overall mortality associated with diabetes mellitus in patients with burns. The majority of studies, included in our systematic review, did not report a significant influence of diabetes mellitus on the mortality-related outcomes in patients with burns<sup>14,37</sup>. Diab et al<sup>29</sup> reported no significant ( $p = 0.19$ ) difference in terms of mortality between the diabetic (0.8%) and non-diabetic (0.1%) patients with burns. Similarly, Knowlton et al<sup>15</sup> also did not report any difference between the diabetic and the non-diabetic burn patients during 30 days and 60 days follow-ups. However, the authors emphasized that while mortality in acute phases of burns is widely associated with infectious outcomes, early surgical intervention by the means of grafting could have reduced the incidence of early-onset septicemias and other infectious diseases, thereby preventing overall mortality. This hypothesis is supported by existing literature, as burn patients with diabetes usually undergo more surgeries as compared to non-diabetic patients<sup>16,17</sup>. Alternatively, as suggested by Dolp et al<sup>14</sup>, it is also possible that patients with severe diabetes usually do not survive burn-related injuries. Therefore, only patients with mild-to-moderate cases of diabetes are recruited in the studies. As a result, a significant difference in mortality is not observed<sup>55</sup>. From the studies included in

our review, only one study reported a significant influence of diabetes on mortality-related outcomes in burn patients<sup>40</sup>. Based on the existing evidence, the present meta-analysis reported positive but *small* overall influence of diabetes mellitus on mortality-related outcomes (0.16, -0.06 to 0.39) in patients with burns.

Our study has a few limitations. First and foremost, this systematic review and meta-analysis was not registered in a review repository such as PROSPERO. Although the lack of registration might raise concerns regarding the validity of this present review<sup>56</sup>, we would like to assure our readers that the attempts were made to register our review at these repositories, but because of the current pandemic crisis, the waiting time at the PROSPERO repository was  $>1$  year. Secondly, we were not able to evaluate the short- and long-term prognostic influence of diabetes mellitus on morbidity- and mortality- related outcomes in patients with burns. Moi et al<sup>57</sup> stressed upon the high risks of mortality-related outcomes especially during the long-term periods. Therefore, we would strongly recommend future studies to address these limitations by conducting more high-quality longitudinal studies and sharing their descriptive data in open access data repositories. The evaluation of these outcomes would be highly beneficial for medical practitioners, and will allow predicting the prognostic outcomes, such as infectious outcomes, mortality, and duration of hospitalization in diabetic patients with burns.

## Conclusions

In this systematic review and meta-analysis we provide confirmatory evidence of the detrimental prognostic influence of diabetes mellitus in patients with burns. We also provide statistical evidence regarding the high infectious outcomes, overall mortality, and especially the duration of hospitalization associated with diabetes in patients with burns. These findings can assist in further raising clinical awareness of the widespread prevalence of diabetes mellitus in patients with burns. These findings will help clinicians to develop best practice guidelines for determining the appropriate treatment approach for management of burns in patients with diabetes mellitus.

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### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Authors' contributions

BY conceived and designed the study. YC and XW collected the data and performed the literature search. BY was involved in the writing of the manuscript. All authors have read and approved the final manuscript.

### Ethical approval

Not applicable.

### Patients consent

Not applicable.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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