Impact of diabetes and hypertension for the development of cardiovascular diseases: a systematic review

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ABSTRACT
This study aimed to systematically evaluate the evidence respecting the association of risk factors for the development of cardiovascular disease (CVD) among patients with diabetes and hypertension (HTN). Articles were searched from 2015 to 2022 through PubMed, MEDLINE, and Embase. The inclusion criteria included risk factors such as hemoglobin A1c (HbA1c), blood pressure measurement, body mass index, determining the glomerular filtration rate (GER), and blood lipid profile in patients with HTN and diabetes. The quality of the study was assessed by assessment Newcastle-Ottawa scale (NOS). After thorough research, only seven out of 170 articles were selected. The systolic blood pressure (SBP) and GER were calculated. All studies' quality was good under the NOS criteria. Generally, high HbA1c: 138 mmHg, high or low GFR: >60 ml/minute/1.75 m²), and increasing SBP (SBP from 120 to 139 to ≥140 mmHg) are great risk factors for CVD among diabetes and HTN patients. No data on blood lipid profile and body mass index was available among the selected studies. It was concluded that relatively well-controlled HTN and diabetes might reduce the risk factors for the development of CVD.

Keywords: Cardiovascular diseases, diabetes, hypertension, impact, systemic review.

Introduction
Cardiovascular diseases (CVDs) are a considerably extensive cause of death in developed and developing countries. Gradually raising CVD is due to some risk factors such as diabetes and hypertension (HTN). HTN and diabetes are important risk factors for CVD. Diabetes mellitus (DM) and HTN are approximately 425 million and 1.13 billion affected globally, respectively [1,2]. DM is a chronic disease that impacts people around the world and leads to a gradually higher level and it is considered as an epidemic disease [1]. The rise of diabetes, especially type 2 diabetes (T2D), exists in developed and developing countries. However, increased mortality and morbidity cause CVD among patients with T2D [3,4]. The National Cholesterol Education Program determined that diabetes is the risk for the development of coronary heart disease.

Several studies estimated the correlation of the risk of CVD due to risk factors of higher hemoglobin A1c (HbA1c) and fasting glucose levels, high blood pressure, and glomerular filtration rate (GER) [5,6]. The previous study conducted on the Hong Kong population detected a correlation between DM and coronary artery disease (CAD), with increased levels of HbA1c [7]. Besides, it has been established that there is a positive association between HTN with risk for CVD in hypertensive patients [8]. Currently, no study was available on detailed causes, risk factors even outcomes of DM and HTN patients, especially...
those developing CVD in a systematic review. Therefore, the present study aimed to find out the association between DM and HTN with CVD in a systematic review.

**Subjects and Methods**

**Search of literature**

A systematic review was performed under the preferred reporting items of the systematic review [9]. Literature was searched from MEDLINE, PubMed, and Embase from 2015 to 2021. The following terms were used for searching the literature such as “complication of diabetes,” “CAD,” “HTN,” “complication of HTN,” “risk factors of CVD,” and “risk factors of diabetes.” The selected studies are represented in Table 1 [10-16]. We search literature available from MEDLINE, PubMed, and Embase from 2015 to 2021 during the period from October 2022 to February 2023.

**Selection and eligibility criteria of study**

Two individual co-authors were assigned to review the revealed literature based on the study criteria like the longitudinal observational study, available investigation report of blood pressure, lipid profile, HbA1c, body mass index, complications of diabetes, and HTN. All English written literature was selected.

**Collection and quality assessment of data**

Two authors extracted the required data from the literature to the predesigned data collecting sheet. The data information included authors’ names, type of study, publication years, study population, sample size, and study design. Finally, all data were separately cross-matched by another author and transferred to the Excel sheet. The assessment of the quality by using the Newcastle-Ottawa quality assessment scale (NOS) was tested [17] (Figure 1).

**Result**

**Selection of study**

The selection of studies was done according to the PRISMA checklist [9]. A total of 170 articles were determined from PubMed, MEDLINE, and Embase.

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**Table 1. Identification and characteristics of included studies (n = 7).**

<table>
<thead>
<tr>
<th>Year and country</th>
<th>Study design</th>
<th>Study conducted on</th>
<th>Sample size</th>
<th>Exposure</th>
<th>Outcomes</th>
<th>Mean age (Years)</th>
<th>Male (%)</th>
<th>Duration of follow-up/years</th>
<th>Mean (median) DM duration at baseline, years</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017, United States [10]</td>
<td>Post-hoc analysis for RCT</td>
<td>HTN</td>
<td>39,763</td>
<td>SBP (&lt;140 mmHg)</td>
<td>CVD</td>
<td>67</td>
<td>53.8</td>
<td>1.5</td>
<td>-</td>
</tr>
<tr>
<td>2017, Singapore [11]</td>
<td>Prospective cohort study</td>
<td>T2DM</td>
<td>5,513</td>
<td>HbA1c (138 mmHg)</td>
<td>CVD, Mortality</td>
<td>62</td>
<td>48.6</td>
<td>9-11</td>
<td>9</td>
</tr>
<tr>
<td>2016, Australia [12]</td>
<td>Prospective cohort study</td>
<td>T2DM</td>
<td>531</td>
<td>HbA1c (138 mmHg)</td>
<td>CVD, Mortality</td>
<td>62</td>
<td>54.2</td>
<td>16</td>
<td>0.6 for group 1, 3.1 for group 2, 9.2 for group 3</td>
</tr>
<tr>
<td>2016, United States [13]</td>
<td>Retrospective cohort study</td>
<td>T2DM</td>
<td>25,732</td>
<td>HbA1c (138 mmHg)</td>
<td>Mortality</td>
<td>56</td>
<td>53.7</td>
<td>13.6</td>
<td>Newly diagnosed DM</td>
</tr>
<tr>
<td>2016, China [14]</td>
<td>Prospective cohort study</td>
<td>DM with HTN</td>
<td>3,159</td>
<td>SBP (120 to 139 mmHg)</td>
<td>CVD, Mortality</td>
<td>54</td>
<td>81.4</td>
<td>8</td>
<td>-</td>
</tr>
<tr>
<td>2016, Australia [15]</td>
<td>Prospective cohort study</td>
<td>T2DM</td>
<td>532</td>
<td>GFR (&gt;60 ml/minute/1.75 m²)</td>
<td>Mortality</td>
<td>62</td>
<td>48.6</td>
<td>16</td>
<td>3.9</td>
</tr>
<tr>
<td>2015, The Netherlands [16]</td>
<td>Prospective cohort study</td>
<td>T2DM</td>
<td>5,711</td>
<td>SBP (120-139 mmHg)</td>
<td>CVD, Mortality</td>
<td>61</td>
<td>50.8</td>
<td>9</td>
<td>1</td>
</tr>
</tbody>
</table>

T2DM = Type 2 Diabetes Mellitus, DM = Diabetes Mellitus; HTN = Hypertension; SBP = Systolic Blood Pressure, GFR = Glomerular Filtration Rate, HbA1c = Hemoglobin A1c, and CVD = cardiovascular disease.
after discarding the duplication. After the close screening of the title and abstract, the 87 articles were eliminated for related outcomes, exposure, and types of articles subsequently, 83 studies were selected but only 45 were prepared for full-text review. At the time of the full-text review, 38 studies were excluded due to wrong inclusion or mismatches, not being written in English, and incomplete outcomes. However, the excluded articles did not mention any complication related to CVD, no measurement of blood pressure, GFR, or HbA1c, and among some articles, there was no history of HTN and diabetes in the patients. In the end, a total of seven articles were included in this systematic review, and all relevant data was extracted carefully. Conversely, all seven selected articles were assessed as an acceptable quality based on the criteria of NOS.

**Characteristics and results of the study**

A total of three studies detected HbA1c [11-13], three studies [10,14,16] measured systolic blood pressure (SBP), and one study revealed GFR as an exposure to the patients [15]. No studies evaluated body mass index, and lipid profile. Besides, no studies estimated individual diastolic blood pressure. Six studies were performed among which five patients were diagnosed with type 2 DM [11-16] and one study did not mention the type of diabetes [14]. Besides one study included diabetic patients associated with HTN. While one study was performed on hypertensive patients (Figures 2 and 3).

**HbA1c**

A total of three studies which were performed in Singapore, the United States, and Australia were...
Major risk factors for CVD

The duration of follow-up was from 6 to 16 years and the duration of mean DM patients ranged from 1 to 10 years. The mean age ranged from 56 to 62 years, and the mean proportion of males ranged from 47% to 54%. Furthermore, in these three studies, patients had complications and progressed to the development of CVD and death due to CVD.

**SBP**

The three studies reported SBP as exposure, of which, one study showed patients with diabetes along with HTN, one study showed diabetes only, and one with HTN only, respectively. All patients enrolled were from the United States, China, and the Netherlands with a study design of prospective cohort study and post-hoc analysis for randomized controlled trial (RCT). The follow-up duration was 8 to 9 and 1.5 years, respectively. The mean age ranged from 54 to 67 years with the mean proportion of male patients ranging from 51% to 81%. The outcome of their studies patients subsequently developed CVD and higher mortality due to CVD. Therefore, it indicates higher SBP is considered a risk for leading to CVD among diabetes and HTN patients.

**GFR**

One study included T2DM patients in Australia with a follow-up of 16 years, the mean age was 62 years with the mean proportion of 49% males. The outcome was higher mortality, and hence, GFR is considered a higher risk for CVD and death (Figure 4).

CVD = Cardiovascular disease, HR = hazards ratio, DM = Diabetes mellitus, and HTN = Hypertension.

**Discussion**

This systematic review revealed the factors that are considered risk for the development of CVD among patients with diabetes and HTN.

In the present study, the articles from PubMed, MEDLINE, and Embase were searched. Initially, a total of 170 pieces of literature were reviewed. After proper evaluation, 163 studies were excluded for a variety of deficiencies that were not matched with the inclusion criteria of the current study. After evaluation to the end, only seven studies were included in the current systematic review.
Previous studies evidenced that CVD accounts for a maximum of 80% of deaths occurring in patients with T2D [18]. Similar results from another study supported that there is a three-time fold increased death rate due to CVD among T2D patients compared to those without diabetes [19].

In the present study, the total sample size was 80,941, and HbA1c, SBP, and GFR were examined. Besides, the effects of CVD were evaluated among them. Of all diabetes patients in total, six studies were exposed to higher levels of HbA1c, and three studies relatively showed high SBP, with low and decreased GFR which might subsequently risk for the development of CVD or death, the similar results were reported by other studies [20, 21].

In the United Kingdom, a survey on diabetes patients reported that there is an association between HbA1c and the risk of CVD [22]. Conversely, it has been determined that increased HbA1c leads to an increased risk of CVD [23]. However, it clearly indicates that higher HbA1c is positively associated with the risk of CVD. Moreover, it was found that increased SBP positively affects the development of CVD, thus indicating that association between systolic HTN with higher risks of CVD [23, 24]. These complications might be due to dose adjustment and complications of the disease. Furthermore, decreased or increased GFR in diabetic patients might be a serious complication of CVD or mortality.

Conclusion

This systematic review revealed the associated risk for the development of CVD among patients with HTN and diabetes. Therefore, it is essential to identify strategies to reduce the risk of diabetes and HTN among patients that in turn will help to reduce the development of CVD.

List of Abbreviations

CAD Coronary artery disease
CVD Cardiovascular diseases
DM Diabetes mellitus
GFR Glomerular Filtration rate
HbA1c Hemoglobin A1c
HTN Hypertension
NOS Newcastle-Ottawa quality assessment scale
SBP Systolic blood pressure
T2DM Type 2 diabetes mellitus

Conflict of interest

The authors declared that there is no conflict of interest regarding the publication of this article.

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Consent to participate

Not required.

Ethical approval

Not required.
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