ASSOCIATION BETWEEN TRAUMA AND OCCURRENCE OF DIABETES MELLITUS AT THE AGE OF LESS THAN 40 YEARS

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ARTICLE INFO

ABSTRACT

Although there is extensive research on diabetes and associated factors, there is still a deficiency in the literature investigating the link between trauma and diabetes prevalence. Gaining insight into this association will enhance clinicians' understanding of the condition and inform the strategies adopted to ensure effective management. Therefore, the study will provide information on the prevalence and presentation of the condition within the population of interest, while providing an in-depth analysis of its association with trauma. To assess the relationship between diabetes mellitus and trauma in adolescents and young adults below the age of 40. A review of primary studies on trauma and diabetes in younger populations was conducted. To identify the studies to be included in the review, the researcher utilized PubMed and EBSCOhost databases due to their extensive research article records. The search was limited to studies published within the past five years (2017-2022) to obtain the most recent data available. The selected studies were assessed for quality and scanned for relevance to the topic before being included in the review. 9 articles were eventually selected for inclusion in the review. These primary studies addressed various aspects of and its association with trauma. The analysis revealed a rise in the condition's prevalence facilitated by multiple risk factors, including trauma. The findings' implications for clinical practice were also discussed.

Introduction

Diabetes mellitus is a lifestyle condition characterized by abnormalities in insulin secretion or its action within the body, thereby causing a chronic state of hyperglycemia [1-3]. Given insulin's multiple sites of action, any disruption to its normal functioning or utilization by the body means that there will be an imbalance in the levels of blood glucose, which is the basis of a diabetes diagnosis. Glucose is crucial for a person's health since it is a vital energy source for the cells that constitute the muscles and tissues. Nonetheless, glucose levels above 140mg/dL translate to excess sugar in the blood and can lead to severe health problems. According to [4, 5], the global prevalence of diabetes mellitus was 382 million as of 2013 and is expected to reach 592 million by 2035 with type 2 diabetes making up more than 85% of cases. In another study, the global

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burden of the disease was approximated to have hit 462 million cases by 2017 for type 2 diabetes mellitus (T2DM) alone [6, 7]. These statistics show a projected rising trend, especially in the incidence of T2DM, meaning that diabetes will become an even greater public health issue in the future. The World Health Organization (WHO) reports that the condition has, over the past three decades, shown a higher prevalence in low- and middle-income countries (LMICs) compared to high-income countries [8]. Evidence of this trend can be seen in research where four of every five diabetic patients live in LMICs and account for 336 million cases of diabetes [9, 10]. Higher diabetes mellitus prevalence among the LMICs is attributable to various factors that include reduced access to healthcare facilities that promote good health and desirable healthy behaviors, and limited access to social determinants which advance good health like education, good jobs, social networks, and public safety. Based on the present estimates of prevalence and the condition's distribution, it is evident that diabetes is not only a public health concern but also a social justice concern due to its impact on the most vulnerable global populations. The condition's impact becomes even more concerning when one considers the economic burden of the disease.

Given that this systematic review is interested in examining the association between trauma and diabetes, one of the most significant risk factors to examine is trauma. According to the JAMA Editorial Staff (1954), the association between sudden trauma and diabetes had steadily been losing support among researchers but new research had generated more robust evidence to support the thesis [11]. Building on these assertions, recent literature has started to take a keen interest in the influence of trauma on the development of diabetes, although Karrouri (2014) notes that there is still a significant gap in the level of evidence that supports a relationship between the two states [12]. Trauma is of significant public health interest due to the numerous far-reaching consequences it has on an individual's physical and mental health. Roberts *et al*. (2015) define posttraumatic stress disorder (PTSD) as being characterized by "intrusion, avoidance, negative alterations in cognition and mood, and alterations in arousal and reactivity" in response to a potentially traumatic life event [13]. PTSD is the precursor to many other conditions such as depression, anxiety, and eating disorders that adversely impact an individual's health outcomes. Due to its severity, PTSD has been shown to have indirect impacts on the development and progression of diabetes. In their study, Roberts *et al*. (2015) found that PTSD was associated with almost a two-fold increase in the risk of T2DM among civilian women, mediated by neuroendocrine dysfunction, poor dietary habits, physical inactivity, and depression [13]. Each of these risk factors has been mentioned previously in the discussion on the risk factors associated with diabetes. A case study involving a 10-year-old Libyan boy without a familial history of diabetes implicated psychological trauma in the pathogenesis of T1DM [12]. This observation is similar to the conclusion reached by Agyemang *et al*. (2012) who concluded that asylum seekers suffering from PTSD exhibited a higher prevalence of T2DM even after controlling for mediating factors such as comorbid depression [14]. These studies prove that there is a need for further studies on the relationship between traumatic experiences and diabetes. Given trauma's implication in the pathogenesis of T1DM, it is evident that there are physiological changes caused by an individual's response to traumatic life events that facilitate the development of chronic autoimmune conditions, and studying the mechanism by which diabetes results from such changes could generate valuable information on the mechanisms through which trauma influences physical health outcomes.

Study Objectives

The objectives of this study was to discuss the mechanism of action of trauma in the development of diabetes mellitus in addition to discuss the management of the condition.

Materials and Methods

This study employed a systematic review approach that needed neither informed consent from patients nor approval from an Institutional Review Board (IRB). This approach was preferred because systematic reviews – like meta-analyses – provide a high level of evidence on current clinical knowledge to guide the adoption of evidence-based care [15]. The entire study took nine months to complete and publish, giving the researcher ample time to identify appropriate studies and draft the review.

Search Strategy

Since this is a systematic review, eligible studies were selected from two databases: PubMed and EBSCO host. These two databases were settled upon because they were among the most readily accessible through the institution's library and were also the most familiar to the researcher. Given the extensive collection of research articles found in these databases, the researcher was convinced they would find enough studies to fulfill the study's objectives. The initial search was conducted on November 21, 2021, and updated on January 17, 2022. The initial search was meant to provide the researcher with an overview of the topic and determine whether it's a viable research area. Following consultation with the supervisor and further reading up on the topic, the researcher developed more relevant search terms that were used in the updated search. The search terms used in the latest search were "diabetes", "young adults", and "trauma" to make the search as specific as possible to the topic. The different terms were joined using the Boolean operator "AND" to further specify the studies of interest.

Error! Reference source not found. below shows the stepwise strategy employed to identify the studies included in this systematic review.

Table 1. Search strategy developed by the author to identify studies to be included in the review

Step	Description
1	Entered the search terms "diabetes" and "young adults" using the Boolean operator "AND"
2	Filtered the results by the year of publication, study type, and full-text availability
3	Added the search term "trauma" to the search criteria to further specify the results and reduce the number of results
4	Reviewed the abstracts of the returns to identify relevant studies.
5	Searching for the full-text articles of the selected articles and finding replacements for any unavailable articles.
6	Downloading and carefully studying the selected articles to identify the criteria used and their suitability for the present study.

Selection Criteria

Systematic reviews are designed to synthesize literature from primary sources only to generate high-quality knowledge to inform clinical practice. As such, the primary inclusion criteria for the present study were studies published within the past five years (2017-2022), primary studies (those that involved data collection), and those whose full-text articles were available. All studies published before 2017, reviews, unrelated results, and those that only had abstracts were excluded from the study. Upon reviewing the abstracts, the author selected studies that were easier to understand and whose abstracts were well laid-out. Such preference was meant to ensure that they had an easier time analyzing the articles later in the review given their level of research proficiency. As Tawfik *et al.* (2019) note, when a researcher uses more than one database, they should modify the search strategy to suit each database [15]. In the present study, the search strategy described in Error! R eference source not found. above was tailored for the search conducted on PubMed and few adjustments had to be made when conducting the search on EBSCO host although the search terms remained the same. The screening process was by far the most time-consuming given the high number of results from each of the databases. The entire process was made even more challenging by the fact that the researcher was entirely responsible for all aspects of the study. However, focusing only on studies that were easier to interpret given the researcher's proficiency made the process a lot easier and improved the quality of the analysis conducted later on.

According to the WHO (2019), diabetes is a group of metabolic disorders characterized by the presence of hyperglycemia among untreated patients [16]. Therefore, some of the studies selected for this systematic review addressed specific types of diabetes instead of the condition as a whole. In any case, each of the included studies was chosen based on their perceived value to the research topic and their ability to fulfill the different objectives. Since the study topic is concerned with diabetes occurrence in people below the age of 40, the search term "young adults" was preferred as it encompasses the group with which the researcher was interested. Since this systematic review is interested in various aspects of the condition (presentation, management, and prevalence), the included studies had to address at least one of these areas to be selected. Limiting studies to the past five years also ensures that only the latest research findings are considered for the review. Given the rapid pace of research in diabetes management, this approach ensures that the researcher makes their deductions based on the most recent research available within the industry. It also ensures that any practice recommendations made in this systematic review are relevant to the current patient and clinician populations. Kalyani *et al.* (2017) note that the homogeneity in the incidence of diabetes across the population makes it difficult to recommend generalized recommendations for treatment approaches [17]. For this reason, it was crucial to define the age group of interest to the researcher to ensure the synthesis provided herein is as targeted as possible to the types of patients with whom the researcher will interact.

Data Extraction

The student screened the titles and abstracts from the returns to identify all the studies relevant to the study topic and exclude those that did not meet the inclusion criteria. During the second search session (January), the finalized list of articles was shared with a colleague who reviewed the researcher's selection and made recommendations on their suitability for the topic and the stated objectives. After receiving the colleague's feedback, the researcher proceeded with the extraction of data from the selected studies. The extracted data was then verified by the same colleague who had helped with study selection after which the extraction was finalized. The data of interest included: general article information (author, year, and identifier), study characteristics (design, sample, demographic details), and main findings. This data was compiled and will be presented in Error! Reference source not found. in the following chapter. With this data, it was then possible for the researcher to start w orking on the protocol, which was submitted to the supervisor for review and feedback. At this point, the search had been concluded and all the relevant sources had been examined for suitability and it was time to start the synthesis section of the study.

Quality Assessment

The studies ultimately included in the study were evaluated for quality by considering various factors such as the methods used, the validity of data collection methods, and the qualifications of the authors. These criteria ensured that all the data that eventually made its way into the analysis was of the highest quality possible and was robust enough to be of valuable clinical

applications. Moreover, working closely with the research supervisor meant that the student was aware of the qualities to look for in research studies to ensure they only included high-quality evidence.

Data Synthesis

Since the study was meant to be a simple systematic review, there were no statistical analyses included in the synthesis stage. The researcher simply read through articles and identified the data that was suitable for inclusion in the discussion considering the scope of the review. Furthermore, the qualitative nature of the review means there were no expectations of an in-depth statistical analysis. Therefore, synthesis involved the identification of evidence under different subtopics as developed by the student. This synthesis involved bringing together evidence from different sources on various aspects of diabetes within the population of interest to synthesize a cohesive evidence-based discussion of clinical value. The subtopics of interest to the researcher included the prevalence, the role of trauma in diabetes pathogenesis, other relevant risk factors, and effective management practices for trauma-induced diabetes.

Results and Discussion

Following the search strategy described in **Table 1** above, steps 1 and two yielded 1,581 returns in PubMed and 6,335 results in EBSCOhost. These results were based on the inclusion of "young adults" as a search term using "AND" as the Boolean operator. The third search term - "trauma" – was added also using "AND" as the Boolean operator in both databases, which narrowed the search down to 20 results on PubMed and 55 results on EBSCOhost. The titles and abstracts for each of these studies were examined for relevance to the topic and 25 articles were selected for synthesis since they met the inclusion criteria defined above. These studies are summarized in Error! Reference source not found. below.

Study Characteristics

Each of the 9 included studies was a primary study that included data collection and analysis. The most common designs employed in the study were the cross-sectional [18, 19], retrospective [20-24].

Table 2. An overview of the 9 articles included in the systematic review

Citation	Sample Size	Mean Age	Study Design	Main Outcomes
[18]	5786	N/A	Cross-sectional study	• Fasting plasma glucose (FPG) levels • Glycated hemoglobin (HbA$_{1c}$) levels • Fasting insulin levels • BMI • Cardiometabolic risk factors
[19]	184	55.4	Cross-sectional study	• HbA1c levels • Clinical measures of depressive and PTSD symptoms • Self-reported diabetes self-care behavior • BMI
[20]	106,141	N/A	Retrospective cohort study	• Rates of complications associated with diabetes
[21]	1,395	67.1/ 64.4	Retrospective study	• Serum glucose levels • HbA$_{1c}$ levels • Mortality risk levels
[22]	5,916	42.1	Retrospective cohort study	• Clinical diagnosis of T2DM • Clinical diagnosis of PTSD symptom severity
[23]	1,058	12.6/ 14.4	Retrospective study	• In-hospital mortality rate • Length of hospital stay • Rate of admission into the intensive care unit (ICU) • Serum glucose levels • HbA$_{1c}$ levels
[24]	72,604	66	Single-center, retrospective study	• HbA$_{1c}$ levels • PTSD clinical diagnosis • BMI • Hypertension diagnosis • Atherosclerotic cardiovascular disease diagnosis

Stress, Trauma, and Diabetes

One of the risk factors not discussed in the previous subchapter is trauma. Eight articles [19, 21-24] included in this review examine the impact of traumatic experiences on the development of diabetes. Rau *et al*. (2017) defined stress-induced hyperglycemia (SIH) as glucose levels above 250 mg/dL and found it to be associated with a 3.5-fold increase in the risk of mortality compared to patients showing diabetic normoglycemia [21]. Tsai *et al*., (2019) examined the effect of SIH in

children with a history of trauma and found that compared to their non-diabetic counterparts, they experienced longer hospital stays (16.4 days vs. 7.8 days), higher rates of ICU utilization (55.6% vs. 20.9%), and higher levels of in-hospital mortality (5.6% vs. 0.6%) [23]. Moreover, they concluded that pediatric patients with SIH showed different responses to traumatic events than those exhibited by adult patients. On the other hand, Guzman-Martinez *et al*. (2018) found that infectious complications were more common among diabetic patients (31.3%) than their non-diabetic counterparts (11.6) within a sample of 1,134 trauma patients admitted into the TICU [25]. These findings point to the interplay between trauma and other diabetes precursors such as SIH in the development of the condition.

Following the findings by Tsai *et al*. (2019), it is evident that SIH, in response to trauma, results in a higher prevalence of diabetes complications in both pediatric and adult patients, calling for stricter and extensive disease management within these patient populations [23]. On the other hand, there seems to be an inconsistency over the standard cut-off value for glucose levels beyond which a patient is considered to exhibit SIH. As mentioned, Rau *et al*. (2017) concluded that 250 mg/dL provided a better definition of SIH according to their sample [21]. However, Tsai *et al*. (2019) adopted glucose levels ≥200 mg/dL [23]. These discrepancies point to the need for further investigation to establish a standard universally agreed-upon definition for the condition.

The other 3 studies [19, 22, 24] examined various dimensions of the association between diabetes and PTSD. In their study, Arigo *et al*. (2017) concluded that the presence of clinically significant PTSD accounted for the 10-40% variance in T2DM outcomes they observed within their sample since experiencing more severe depressive symptoms was associated with higher HbA_{1c} and diabetes distress levels and lower levels of physical exercise and poor adherence to dietary recommendations [19]. The authors examined the influence of PTSD and depressive symptoms simultaneously since the two conditions typically occur as comorbidities in many patients. When they controlled for depressive symptoms, Arigo *et al*. (2017), found PTSD symptoms to account for approximately 3% of the variance in diabetes outcomes and even observed a positive association between these symptoms and exercise adherence and glucose self-monitoring behavior [19]. In Scherrer *et al*. (2019), the authors were interested in examining the incidence of T2DM among a sample of Veterans with a positive PTSD diagnosis [22]. Their analysis revealed that patients who registered clinically significant reductions in PTSD symptom severity (described as a reduction ≥20 points on the PCL) over the course of the study had a lower incidence of T2DM (at 2.6%) compared to those who failed to attain clinically significant reductions according to the PTSD Checklist (PCL) – who had a cumulative prevalence of 5.6% [22]. These findings align with those of other researchers who showed a positive association between trauma and diabetes development and severity.

Higher BMI is a crucial culprit in the development of complications such as obesity. Yatutu (2022) reported obesity and overweight prevalence rates of 41% and 37%, respectively, among veterans [24]. These conditions are precursors to insulin resistance and diabetes. Within its sample, the study found that 35% of participants progressed from prediabetes to diabetes over the course of the study: a progression mediated by hypertension, high BMI, and atherosclerotic cardiovascular disease (ASCVD). Interestingly, the percentage of those with PTSD who progressed from prediabetes to diabetes was lower (33.55) than those who progressed to diabetes without PTSD (36.4%) showing a complex association between the two conditions [24]. This observation can be explained by looking at the findings from other studies reviewed under this subsection, where depressive symptoms were determined to be the main culprits in causing negative diabetes outcomes in patients with PTSD.

Since the study sought to present a review of the association between trauma and diabetes, the researcher devoted a significant portion of the discussion to addressing the impact of stress and trauma on diabetes development and progression. Multiple studies provided evidence of the critical role SIH plays in elevating diabetes risk and enhancing the severity of its symptoms and complications. It has also been established that PTSD is a significant risk factor for diabetes and that patients suffering from PTSD register poorer diabetes outcomes than their non-PTSD counterparts. However, this analysis of the relationship between PTSD and diabetes revealed some interesting outcomes. In cases where diabetes patients were diagnosed with PTSD alone, researchers observed a positive association between the comorbidity and physical activity and dietary habits. However, where diabetics presented with PTSD and depressive symptoms, they exhibited poor diabetes outcomes, suggesting that depression severity accounts for a majority of the variance seen between PTSD and non-PTSD diabetics. The mechanism through which depression in PTSD increases the risk of diabetes (particularly T2DM) is through lowering the level of physical activity, encouraging poor dietary habits leading to higher BMI values, and increasing the likelihood of smoking. Through these mechanisms, patients start to develop insulin resistance, which manifests as hyperglycemia, prediabetes, and ultimately diabetes. For these reasons, it is critical to adopt effective treatment practices to get the condition under control and reduce the rate of complications.

Due to the severity of the condition, diabetes is known to cause numerous complications if not controlled well. It has been shown to be associated with higher risks for conditions such as hypertension, hyperlipidemia, and CVDs. Diabetes mellitus when improperly managed can have negative impacts on the patient's every body organs including the heart, kidneys, eyes, and nerves. Notably, the associated comorbid conditions can have significant adverse effects on a patient's health outcomes and make diabetes management even more challenging. Where trauma is involved, infections and cardiac complications were shown to be the most common complications that resulted in a higher rate of resource utilization among diabetics compared to their non-diabetic counterparts. Although incurable, diabetes can be controlled through medication and behavioral changes. Insulin is the most commonly prescribed management drug among T1DM patients since their condition results in the destruction of insulin-producing pancreatic β-cells. Other drugs such as metformin have also been tested for effectiveness and proven to be at least as effective as insulin albeit in specific types of diabetes. On the other hand, since

T2DM is characterized by insulin resistance, the administration of insulin alone does not yield optimal outcomes. Therefore, behavioral changes are the most preferred management strategies. These include changes in dietary habits such as reducing carbohydrate intake, increasing physical activity levels, and counseling for those with a history of trauma. The studies also advocate for better patient education to enhance their self-efficacy in managing their condition. Patients with high levels of perceived self-efficacy were shown to register better diabetes outcomes.

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Study Limitations

Despite the robust systematic review process adopted for this study, there are several limitations to the methodology. One of the main drawbacks of this study is the narrative form of the systematic review instead of an analytical one. Also, some of the included studies did not include participants within the age group of interest although they contained findings that were relevant to the discussion. Although the researcher determined the included studies to be of high quality, this determination was based on a non-validated approach. The implication is that some of the included studies may not meet the quality standards for inclusion in a systematic review. Moreover, having only one reviewer enhances the risk of selection bias when choosing the articles to include in the review. The extensive scopes of the studies included in this review might also have potentially made it difficult to address all the relevant aspects of the research topic.

Implications for Clinical Practice

It has already been established that systematic reviews have a significant influence on clinical practice since they bring together numerous studies, identify trends, and inform clinical guidelines. Based on the findings of this study, it is evident that there is a need for more public education on the prevalence, impacts, and prevention strategies of trauma induced diabetes among the populations. The review also emphasizes the need for psychological assessments among diabetics to identify those at risk of depressive symptoms so they can be enrolled in the appropriate care programs to enhance their treatment outcomes. For diabetes patients with a history of trauma, there is a need for greater care to be observed when offering them treatment to ensure they do not experience the many complications that have been discussed in this review.

Conclusion

The researcher set out to examine the association between trauma and diabetes prevalence in people under the age of 40 and provide information on diabetes prevalence, risk factors, and management. Throughout the review, these topics were addressed in great detail. The 25 studies included in the systematic review addressed the different aspects of the condition and provided answers to the research questions. It has been made clear that diabetes is a complex and expensive condition,

with multiple risk factors ranging from genetic predispositions to sociodemographic elements, and individual characteristics. Although there is still no cure for the condition, pharmacological agents such as insulin and behavioral changes that include dietary improvements have been shown to be effective in treating diabetes and enhancing glycemic control. The review ends with a discussion of what the findings mean for professionals in clinical practice. Despite the extensive nature of the review, there are several issues that future studies need to examine. For instance, it has been noted that there is still a significant deficiency of diabetes literature in the developing world. Therefore, researchers should examine trends in diabetes prevalence outside developed nations. Likewise, there seems to be no consensus on the standard definition of SIH with regard to glucose levels, which calls for further investigations to identify the appropriate cut-off point. Finally, there is a need for more extensive research on the effectiveness of drugs such as metformin in the management of diabetes.

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