Prevalence of depression among children and adolescents with type 2 diabetes: a systematic review and meta analysis

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Introduction

The prevalence of depression in children and adolescents with type 2 diabetes (T2D) is a clinical, public and social problem. Research reports that the average annual prevalence rate of depression in children and adolescents with T2D is about 4.8% (1). Compared with T2D in adults, T2D in children and adolescents has significant pathophysiological characteristics, including β the rapid decline of cell function of β cell and the significant increase of insulin resistance (2). Besides, epidemiological report and clinical studies have found that T2D in children and adolescents was significantly associated with age, weight status, family history of diabetes, diabetic ketoacidosis at presentation, ethnicity and diabetes-associated antibodies (3-6). Walders-Abramson et al. found that the failure to maintain a sufficiently normal blood glucose level may be related to the high depression rate of children and adolescents with T2D (7). Besides, Gulley et al. believed that failure to maintain adequate blood glucose control may also lead to various adverse effects on patients (such as changes in drug compliance, eating habits and psychological...
disorders) (8). These depression of T2D in children and adolescents may lead to stress, sadness, and a reduction in quality of life, adding the burden of families and society. Therefore, focusing on the current prevalence of depression in children and adolescents with T2D, and investigating the relationship between depression and T2D is very important for clinical treatment and attention to T2D children and adolescents and their depression. Collecting the prevalence of depression of children and adolescents with T2D can help clinicians plan for diseases prevention and treatment, as to provide evidence-based medical evidence for future clinical practice. We present the following article in accordance with the PRISMA reporting checklist (available at https://jxym.amegroups.com/article/view/10.21037/jxym-22-17/rc).

**Methods**

**Inclusion and exclusion criteria**

- Study type: retrospective study and prospective study.
- Subjects: children and adolescents with T2D (age ≤18 years).
- Outcome measures prevalence of depression.
- Exclusion criteria: (I) non-English literature; (II) research with repeated publication or similar data; (III) there are no relevant outcome to be included; (IV) significant statistical error in article or cannot be extracted, and it is still unavailable after contacting the author; (V) the research design has obvious defects, inappropriate statistical methods and other obvious errors.

**Literature retrieval strategy**

We searched PubMed, EMBASE, the Cochrane Library, CNKI, VIP, Wanfang Data and other databases to collect observational studies and RCTs on the prevalence of depression in children or youth with T2D. The retrieval time limit was from the establishment of the database to April 2022. The computed search is carried out by combining MESH and free words, and adjusted according to the characteristics of each database. At the same time, the references included in the study were searched to supplement and obtain relevant materials. Search terms include: type 2 diabetes, depression, prevalence, epidemiology, randomized controlled trails, etc. Search terms see Appendix 1.

**Literature screening and data extraction**

Two reviewers screened the literature by independently screening the literature and extracting the data. After excluding the obviously irrelevant literature, we read the abstract and full text again to determine whether the article meets the inclusion and exclusion criteria. We extract the following contents: (I) research title, first author and publication date; (II) baseline data included in the study; (III) outcome measurement data.

**Risk assessment of bias included in the study**

NOS score (9) was used for retrospective studies and Jadad’s score (10) was used for randomized controlled studies.

**Statistical analysis**

All analyses were performed using Stata version 14.0 software. The original data in the study is first converted by the double arcsine method to make it conform to the normal distribution, and then analyzed in Stata to draw the final conclusion. Statistical heterogeneity between effective measurement studies will be assessed by mantel Haenzel $\chi^2$ test and $I^2$ statistics. When there is no significant heterogeneity ($I^2<50\%$), we use the fixed effect model. In addition, if there is significant heterogeneity ($I^2\geq50\%$), the random effect model is adopted (11). Different effect models and sensitivity analysis were selected to explore the source of heterogeneity.

**Results**

**Literature search results**

A total of 571 literatures were obtained through the initial search. After initial screening, 8 (12-19) literatures, with a total of 5,948 patients (4,039 cases were included in the analysis) meeting the inclusion and exclusion criteria, were included in this study (Figure 1). The basic characteristics of the literature and the evaluation results of literature quality are shown in Table 1.

**Overall prevalence of depression in children with T2D**

All the included studies reported the overall prevalence of depression in patients with T2D. The prevalence was 19.9% (95% CI: 14.3–26.2%), and there was significant heterogeneity among the studies ($I^2=94.056\%, P=0.000$).
Records identified through database searching (n=568)
Additional records identified through other sources (n=3)

Records after duplicates removed (n=168)

Records excluded (n=147)
- Review (n=14)
- Other intervention (n=47)
- Case reports (n=32)
- The patients did not meet the inclusion criteria (43)
- Letter and comments (n=4)
- Diagnostic test (n=7)

Records screened (n=21)

Full-text articles excluded, with reasons
(I) Focused on patients with venous thrombosis
(II) Didn’t include relevant data
(III) Overlapping cohort studies

Full-text articles assessed for eligibility (n=13)

Studies included in qualitative synthesis (n=8)

Studies included in quantitative synthesis (meta-analysis) (n=8)

Figure 1 Flowchart of study inclusion.

(Figure 2). In addition, we conducted sensitivity analysis to explore potential sources of heterogeneity, but we did not find sources of heterogeneity.

Discussion

The pathogenesis of depression in T2D patients is complex and has not been fully clarified. The mechanism can be explained by the fact that T2D may lead to the functional and structural problems of the peripheral nerves. Blood glucose level is significantly associated with the depression, as Picozzi et al. (19) reported that the use of insulin pump can not only control the blood glucose level of T2D children and adolescents, but also reduce the prevalence of depression (19,20). Based on the mentioned studies, we infer that the depression of T2D children and adolescents may be associated with the glucose level. Besides, the racial differences, obesity and insurance status also have impact on the diabetes distress, depression and glycemic control (20). In addition, the depression of T2D children and adolescents is associated with many other factors such as age, glycosylated hemoglobin, gender, and heredity, suggesting that the depression of T2D children and adolescents is not caused by a single factor and it is associated with social, psychological and their own diseases (10,21), so further investigation is needed to explore the mechanism. Considering the complexity of the disease, the treatment of these patients can not only rely on drugs but need multidisciplinary treatment.

In this study, by collecting and sorting out the relevant studies on the prevalence of depression in T2D children and adolescents, and combining the relevant data, we finally found that the overall prevalence of this part of the population is about 19.9% (95% CI: 14.3–26.2%).
Table 1 Characteristics of studies and patient populations

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>Design</th>
<th>Cases, n</th>
<th>Measuring tools</th>
<th>Age (years)</th>
<th>Sex ratio</th>
<th>Duration of diabetes</th>
<th>Jadad’s score/NOS score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderson et al. (16)</td>
<td>2011</td>
<td>USA</td>
<td>RCT</td>
<td>687&lt;sup&gt;a&lt;/sup&gt;</td>
<td>CDI/BDI-II</td>
<td>14</td>
<td>452/235</td>
<td>0.5</td>
<td>3</td>
</tr>
<tr>
<td>Cullum et al. (17)</td>
<td>2016</td>
<td>USA</td>
<td>Retrospective</td>
<td>31</td>
<td>CES-D</td>
<td>15.3</td>
<td>19/12</td>
<td>2.5</td>
<td>6</td>
</tr>
<tr>
<td>Lawrence et al. (18)</td>
<td>2006</td>
<td>USA</td>
<td>Retrospective</td>
<td>2,637&lt;sup&gt;b&lt;/sup&gt;</td>
<td>CES-D</td>
<td>15.3</td>
<td>1,376/1,261</td>
<td>NA</td>
<td>7</td>
</tr>
<tr>
<td>Picozzi et al. (19)</td>
<td>2019</td>
<td>USA</td>
<td>Retrospective</td>
<td>211&lt;sup&gt;c&lt;/sup&gt;</td>
<td>PHQ-9</td>
<td>15.8</td>
<td>117/94</td>
<td>6.3</td>
<td>7</td>
</tr>
<tr>
<td>Silverstein et al. (12)</td>
<td>2015</td>
<td>USA</td>
<td>Retrospective</td>
<td>600</td>
<td>CDI</td>
<td>14</td>
<td>347/253</td>
<td>NA</td>
<td>8</td>
</tr>
<tr>
<td>Van Buren et al. (13)</td>
<td>2018</td>
<td>USA</td>
<td>RCT</td>
<td>682</td>
<td>CDI/BDI-II</td>
<td>13.9</td>
<td>447/235</td>
<td>NA</td>
<td>3</td>
</tr>
<tr>
<td>Weinstock et al. (14)</td>
<td>2015</td>
<td>USA</td>
<td>RCT</td>
<td>623</td>
<td>CDI/BDI</td>
<td>13.9</td>
<td>395/228</td>
<td>NA</td>
<td>3</td>
</tr>
<tr>
<td>Zeitler et al. (15)</td>
<td>2015</td>
<td>USA</td>
<td>RCT</td>
<td>477</td>
<td>CDI/BDI</td>
<td>13.8</td>
<td>304/171</td>
<td>NA</td>
<td>4</td>
</tr>
</tbody>
</table>

<sup>a</sup>, in this study, only 513 cases received CDI; <sup>b</sup>, in this study, only 371 cases were diagnosed with type 2 diabetes; <sup>c</sup>, in this study, only 55 cases were diagnosed with type 2 diabetes. NOS, Newcastle-Ottawa scale; RCT, randomized control trial; CDI, Children’s Depression Inventory; BDI-II, Beck Depression Inventory II; CES-D, Center for Epidemiological Studies Depression Scale for Children; PHQ-9, Patient Health Questionnaire-9; NA, not available.

Figure 2 Forest of prevalence of depression in children and adolescents with type 2 diabetes.

indicating that the prevalence of depression in this part of the patients is worthy of attention. It is worth noting that Poulsen et al. (22) reported that 84% of T2D patients will be accompanied by depressive symptoms, while 19.9% of the population found in this study have depression, indicating that depressive symptoms and depression in T2D patients are high probability events. Besides, existing study has shown that the prevalence of depression in T2D patients is associated with peripheral neuropathy and adverse events caused by peripheral neuropathy, such as pain and reduction of daily activities, may be the main factors leading to depression (23). Peripheral neuropathy related to T2D may lead to the irregulation of endocrine system and autoimmune system, which leads to the over stimulation of hypothalamic pituitary adrenal axis and the damage of glucocorticoid receptor, making the body enter
the state of high cortisol and leading to the abnormalities of hippocampus, amygdala and other areas associated with depression, this leads to an increase in the prevalence of depression (24-30). Unlike in children and adolescents, the prevalence of depression is 28% in T2D adults (31), which is higher than our results (19.9%). This difference can be explained by the fact that long-term high glucose level, peripheral neuropathy and high HbA1 is an important fact of depression.

There are still some limitations in this study: (I) only eight literatures with a total of 5,948 respondents (4,039 cases were included in the meta-analysis) were included in this study, and the sample size needs to be confirmed by larger sample studies in the future. (II) The included population is affected by the differences of living place and this series of interference factors cannot be analyzed. (III) The population included in this study are all from the United States, so they cannot fully represent the prevalence of the overall population. (IV) The authors included both RCT and retrospective studies. Based on the above limitations, future scholars need to carefully interpret the author's results.

In conclusion, based on the results of this study, it is suggested that children and adolescents with T2D have a high prevalence of depression, but the prevalence of depression in children and adolescents with T2D is the result of multiple factors. Therefore, future studies need to further verify the related factors of these diseases. We need to focus on prevention and treatment, reduce the burden of patients and improve the quality of life.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://jxym.amegroups.com/article/view/10.21037/jxym-22-17/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jxym.amegroups.com/article/view/10.21037/jxym-22-17/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References


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Appendix 1

#1 type 2 diabetes [Mesh Terms]
#2 diabetes [Title/Abstract]
#3 #1 OR #2
#4 depression [Title/Abstract]
#5 depressive diseases [Title/Abstract]
#6 #4 OR #5
#7 randomized controlled trial [Mesh Terms]
#8 controlled clinical trial [Title/Abstract]
#9 randomized [Title/Abstract]
#10 observational studies [Title/Abstract]
#11 randomly [Title/Abstract]
#12 trial [Title/Abstract]
#13 #7 OR #8 OR #9 OR #10 OR #11 OR #12
#14 humans [Mesh Terms]
#15 child [Mesh Terms]
#16 adolescents [Mesh Terms]
#17 #14 OR #15 OR #16 OR
#18 #3 AND #6 AND #13 AND #17