REVIEW ARTICLE

THE FEATURES OF POSTTRAUMATIC STRESS DISORDER DEVELOPMENT IN PATIENTS WITH DIABETES MELLITUS 2 TYPE

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ABSTRACT

The aim: The revealing of the development of stress-related disorders in patients with type 2 diabetes mellitus (DM 2) to: identify the prevalence of stress-related disorders, particularly, posttraumatic stress disorder (PTSD); study the influence of psychosocial factors on the occurrence and course of stress-related disorders and increase the effectiveness of treatment in DM 2.

Materials and methods: Research papers have been found by searching the PubMed database using the keywords ``ptsd and diabetes 2 type" with the result of 74 studies. Totally 25 of selected publications were analysed based on our criteria about the mechanisms through which the influence of psychosocial factors, permanent stressful or traumatic events on the probable risk of PTSD development and their analysis and relationships for the improvement of treatment effectiveness in DM 2 patients who have not been the veterans.

Conclusions: Given the complex neurophysiological relationships between the long-term stress and pathophysiological mechanisms of DM 2 — this group of patients has the higher risk of developing stress-related disorders, including PTSD.

KEY WORDS: trauma, stress, stress related disorders

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INTRODUCTION

The Ukrainian population has faced many challenges over the past few years, including the COVID-19 pandemic, military events in Ukraine, and numerous consequences that have affected the overall mental health of the patients. The most vulnerable groups have also been affected – patients with permanent and comorbid diseases, including type 2 diabetes mellitus (DM 2), which is currently one of the most common diseases, so there is an urgent need for high-quality medical and social care for this group of patients. It is known that a group of DM 2 patients is characterised by the number of specific features that distinguish them and create certain difficulties for physicians in the treatment process. For example, the relationship between glycemic profile, psychosomatic aspects and compliance with treatment has been established. Glycemic control largely depends on the adherence to the process of medication therapy. Some specific psychological characteristics to DM 2 patients may be directly useful in the assessing of the impact of psychosocial factors on the glycemic control to achieve glycemic targets. One of the challenges in finding ways to improve the treatment outcomes of DM 2 patients is clearly understanding the relationships between the treatment efficiency and influence factors [1-5].

The population in difficult humanitarian emergencies has the higher risk of developing comorbidities, including mental disorders and cardiometabolic diseases. Various models of post-traumatic stress disorder (PTSD) and concomitant depression have been studied. Furthermore, it has been detected the increasing number of DM 2 new cases during the outbreak of political violence and population displacement. For example, the syndemic theory could be an approach for conceptualising diseases and social determinants for understanding the different models of the multimorbidity phenomenon and underlying mechanisms for the better planning of future interventions [6-8]. PTSD has been declared such as the "life sentence" based on the evidence that it has caused many health problems. Some of the studies have shown that PTSD involves the higher risk of the development of cardiometabolic diseases, including DM 2. Also about the relationships between the PTSD with certain behaviours and biological processes, and assessing whether they can serve as the mechanisms by which PTSD leads to cardiometabolic diseases. As well as the more comprehensive view of the PTSD phenotype, it should be answered whether the specific aspects of PTSD phenomenology are particularly relevant for cardiometabolic diseases. Finally, new areas of research have been discussed that are possible and can improve the understanding of the relationships between PTSD and cardiometabolic diseases, such as examining whether PTSD treatment can stop or even alter cardiometabolic risk factors causally related to DM 2 [9].

Therefore, it has been found that PTSD has been the risk factor for DM 2 development. It is equally important to study the contrary relationships and consider the presence of the consequences by the traumatic events or even the development of stress-related disorders, including PTSD due to military events and their impact on the treatment effectiveness of patients with DM 2.

THE AIM

The revealing of the development of stress-related disorders in patients with type 2 diabetes mellitus to: identify the prevalence of stress-related disorders, particularly, post-traumatic stress disorder; study the influence of psychosocial factors on the occurrence and course of stress-related disorders and increase the effectiveness of treatment in patients with type 2 diabetes mellitus.

MATERIALS AND METHODS

This review was based on the unstructured and comprehensive searching of scientific literature in PubMed. All of the abstracts were checked in accordance with the purpose of methodology by searching the text words in the PubMed search bar (https://pubmed.ncbi.nlm.nih.gov/). The purpose of the search methodology was to determine and identify the abstract essence of full-text contents researching materials in accordance with the established search criteria in the process of studying. Research papers have been found by searching the PubMed database using the keywords "ptsd and diabetes 2 type" with the result of 74 studies. The scoping review research method has been used, which allows to define the particular goals of research. In the review part of this paper it has been cited the related articles. From the relevant literature, we excluded studies which did not meet our inclusion criteria and particularly described veterans who have been included into research samples of the studies. Totally 25 of selected publications were analysed based on our criteria.

Based on the results of the literature review – it would be discuss the mechanisms through which the influence of psychosocial factors, permanent stressful or traumatic events on the probable risk of the development of stress-related disorders, particularly, PTSD and their analysis and relationships for the improvement of treatment effectiveness in DM 2 patients whose have not been the veterans, by the review results. Promising further research would have been the studying of this question.

REVIEW AND DISCUSSION

According to the results of studies conducted to determine the prevalence and predictors of DM 2 in people with PTSD – the overall prevalence of DM 2 was 10.0%. The relative risk meta-analysis comparing the control group with PTSD patients showed the significantly increased risk of DM 2. Therefore, people with PTSD have a higher risk of developing DM 2 in the future [10]. Also, the symptoms of depression and PTSD accounted for 10-40 percent of the variance in results associated with DM 2. Symptoms of PTSD have been associated with increased distress in DM and blood glucose analysis (R2 ~ 3%). The potential relationships between PTSD and the consequences of DM were assessed. Symptoms of PTSD can be poorly diagnosed in DM 2 among patients without the formal diagnosis of mental disorder, and they require special attention. In addition to the role of depressive symptoms, PTSD symptoms (intrusion, avoidance and hyperexcitability) have been the aspects of psychiatric functioning in DM that deserves increased attention in clinical care and research [11]. PTSD is associated with the 2-4 fold increased risk level of developing DM 2. Case-control studies were analysed to determine whether people with PTSD had the abnormal response to glucose or insulin by the Oral Glucose Tolerance Test, compared to the control group. Potential indicators such as sleep, cortisol, and adiponectin were evaluated, and individuals with PTSD had the hyperinsulinemic response to oral glucose versus controls, indicating insulin resistance. Therefore, the results indicate the presence of insulin resistance during the oral glucose loading in individuals with PTSD [12]. Early life experiences can have long-term health effects. For example, among those who had the traumatic experience of separation in early childhood have been at risk for the development of cardiometabolic diseases in the future. The impact on morbidity was not explained by the age or socioeconomic circumstances in childhood or adulthood. Traumatic events in early life can continue to affect health throughout life and predict the higher prevalence of cardiovascular disease and DM 2 in late adulthood, according to longitudinal clinical trials [13]. As well as, changes in serum HbA (1c) levels were studied according to the rate of deterioration in diet and living conditions and the significant temporary increase in mean HbA (1c) levels was found [14]. By results of studies, for example, the logistic regression and generalised multilevel growth models were used to assess the association between PTSD measured at enrollment and subsequent DM. Therefore, it was found that PTSD has been the risk factor for diabetes [15-20]. Relationships have been found between trauma and the manifestation of diseases in the refugee category. There is growing evidence that traumatised people have an increased prevalence of medical conditions. Diabetes and hypertension were higher in the high-trauma groups than the low-trauma groups. Asylum seekers with PTSD had the higher prevalence of DM compared with those who did not have post-traumatic stress disorder [21-23].

The relationship between stress-related disorders, including PTSD and permanent diseases, such as DM, cardiovascular and metabolic disorders, and other diseases, has been studied. In addition, the biological pathways through which stress-induced diseases can be pathologically pronounced have been investigated. In particular, the hypothalamic-pituitary-adrenal (HPA) and sympatho-adrenal-cerebral (SAC) stress axes have been the key processors in this pathogenic process, as well as genetic and behavioural or

psychological risk factors. Patients with severe PTSD have significantly higher levels of circulating T-cell lymphocytes and lower levels of cortisol in the blood [24]. The stress hormones released affect glucose metabolism, can activate immune cells and modulate subclinical inflammation. For example, after stress – cortisol levels and heart rate tend to increase, and it has been detected the increase in blood glucose and insulin level after exposure to stress. Systemic levels of the chemokines interferon-gamma-inducing protein-10 and macrophage chemoattractant protein-1 were reduced, and the expression of the proinflammatory regulator IKK-beta is significantly reduced after exposure to stress. Acute stress also causes postprandial blood glucose peaks and elevated insulin levels and the selective decrease in the systemic immune markers and proinflammatory NF kappaB cascade regulators associated with DM 2. This indicates the independent effect of the acute psychological stress on glucose metabolism and inflammation [25]. C-reactive protein (CRP) has been the marker of systemic inflammation which is associated with PTSD that could be also associated with permanent inflammation in the brain. CRP has been easily measured and has been the significant predictor of the risk of serious physical conditions such as cardiovascular diseases [26]. It is known that reactions to acute stressful events have also been protective and adaptive. However, the permanent stress can cause neurochemical, neuroanatomical, and cellular changes that could have detrimental effects on higher brain functioning. When the effects of acute stress contribute to the formation and consolidation of memory, the permanent effects of glucocorticoids may impair cognitive function. It is likely that permanent stress and dysfunction of HPA may contribute to the occurrence of including PTSD. Dysfunction of the HPA axis, disturbances of stress responses and increased levels of glucocorticoids are also characteristic features of DM 2. Therefore, the level of stress in patients with DM 2 is the risk factor for the development of neurological complications. In addition, most changes in the brain mediated by hyperglycemia are similar to those observed in experimental models of permanent stress. These results suggest that common mechanisms may be involved in the development of neurological complications associated with depressive disorders and DM 2. So, it is extremely important to study the mechanisms by which the limbic structures, hippocampus and amygdala — could respond and adapt to the harmful effects of hyperglycemia and permanent stress [27]. Early exposure to permanent stress leads to the long-term improvements in the insulin sensitivity, oxidative metabolism and adipose tissue remodelling, accompanied by the tissue-specific adaptations of lipid and glucose metabolism, and these changes may occur long after stressors [28]. It has been detected that the aberrant susceptibility of emotion- and fear-related neurocircuits, including the amygdala, prefrontal cortex, and hippocampus could contribute to the development and retention of PTSD symptoms. [29]. For example, in the study of dipeptidyl peptidase 4 inhibitors (DPP4), better glucose tolerance was confirmed in functionally DPP4-deficient congenital rats (DPP4mut), as well as immunological changes and the stress resistance phenotype. DPP4 showed the highest affinity for neuropeptide Y (NPY), the endogenous anxiolytic neurotransmitter that is offered as the biomarker in PTSD and depression and found the significantly higher peptide concentration in the cerebrospinal fluid of DPP4mut. It was also positively correlated with the blunt stress phenotype measured on the analgesiometer and in the study of the classical paradigm of fear conditioning — the short-term disappearance of fear was significantly enhanced in DPP4mut rats compared with controls, indicating the positive correlation between decreased centre sensitivity and increased sensitivity to NPY in DPP4mut. Also, the behavioural phenotype extends to facilitating the extinction of fear [30]. It is also important to study the genetic links between PTSD and DM 2 in future studies [31]. Given the complex neurophysiological relationships between the long-term stress and pathophysiological mechanisms characteristic of DM 2 — this group of patients has the higher risk of developing stress-related disorders, including PTSD [32-35].

CONCLUSIONS

- By the results of studying – the mechanisms of the development of stress-related disorders in patients with DM 2 with prolonged exposure to stress, can lead to: the abnormal response to glucose and insulin; insulin resistance; hyperglycemia; dysfunctions in the HPA and SAC stress axes, as well as genetic and behavioural or psychological risk factors; increased levels of circulating T-cell lymphocytes and CRP as the marker of permanent inflammation in the brain; neurochemical, neuroanatomical, and cellular changes that affects the higher brain functioning by levels of glucocorticoids; the tissue-specific adaptations of lipid and glucose metabolism; the aberrant susceptibility of the emotion- and fear-related neural circuits with limbic structures, including the hippocampus, amygdala, prefrontal cortex and neurotransmitters.
- The solution of this problem could be the multidisciplinary approach for the patients` care and therapy goals, which impact on the treatment effectiveness and quality of life of patients with DM 2. An association between glycemic levels and psychological aspects in patients with DM were also found. Patients are at increased risk of treatment failure and need qualified mental health care assistance in collaboration with professionals to provide the multidisciplinary approach. This is the wide scope for research in the both of medical and social sciences. Multidisciplinary and multicenter studies may be promising in the future to address the problem of comorbidity in order to improve patients` outcomes.

REFERENCES

1. Mogre V., Johnson N.A., Tzelepis F. et al. Adherence to self-care behaviours and associated barriers in type 2 diabetes patients of low- and middle-income countries: a systematic review protocol. Syst Rev. 2017;6(1):39. doi:10.1186/s13643-017-0436-4.

2. Indelicato L., Dauriz M., Santi L. et al. Psychological distress, self-efficacy and glycemic control in type 2 diabetes. Nutr Metab Cardiovasc Dis. 2017;27(4):300-306. doi:10.1016/j.numecd.2017.01.006.
3. Esmaeilinasab M., Ebrahimi M., Mokarrar M.H. et al. Type II diabetes and personality; a study to explore other psychosomatic aspects of diabetes. J Diabetes Metab Disord. 2016;15:54. doi:10.1186/s40200-016-0281-3.
4. Shamsi A., Khodaifar F., Arzaghi S.M. et al. Is there any relationship between medication compliance and affective temperaments in patients with type 2 diabetes?. J Diabetes Metab Disord. 2014;13(1):96. doi:10.1186/s40200-014-0096-z.
5. Conti C., Di Francesco G., Fontanella L. et al. Negative Affectivity Predicts Lower Quality of Life and Metabolic Control in Type 2 Diabetes Patients: A Structural Equation Modeling Approach. Front Psychol. 2017;8:831. doi:10.3389/fpsyg.2017.00831.
6. Kourkouta L., Koukourikos K., Papathanasiou I.V. et al. Immigration And Mental Disorders. Mhgcj. 2019;2(2):36. doi:10.32437/MHGCJ-2019(2).59.
7. Kohrt B.A., Carruth L. Syndemic effects in complex humanitarian emergencies: A framework for understanding political violence and improving multi-morbidity health outcomes. Soc Sci Med. 2022;295:113378. doi:10.1016/j.socscimed.2020.113378.
8. Flaherty M.P., Sikorski E., Klos L. et al. Peacework and mental health: From individual pathology to community responsibility. Intervention. 2020;18(1):28–36. doi: 10.4103/INTV.INTV_59_18.
9. Koenen K.C., Sumner J.A., Gilsanz P. et al. Post-traumatic stress disorder and cardiometabolic disease: improving causal inference to inform practice. Psychol Med. 2017;47(2):209-225. doi:10.1017/S0033291716002294.
10. Vancampfort D., Rosenbaum S., Ward P.B. et al. Type 2 Diabetes Among People With Posttraumatic Stress Disorder: Systematic Review and Meta-Analysis. Psychosom Med. 2016;78(4):465-473. doi:10.1097/PSY.0000000000000297.
11. Arigo D., Juth V., Trief P. et al. Unique relations between post-traumatic stress disorder symptoms and patient functioning in type 2 diabetes. J Health Psychol. 2020;25(5):652-664. doi:10.1177/1359105317727839.
12. Rao M.N., Chau A., Madden E. et al. Hyperinsulinemic response to oral glucose challenge in individuals with posttraumatic stress disorder. Psychoneuroendocrinology. 2014;49:171-181. doi:10.1016/j.psyneuen.2014.07.006.
13. Alastalo H., Raikkonen K., Pesonen A.K. et al. Cardiovascular health of Finnish war evacuees 60 years later. Ann Med. 2009;41(1):66-72. doi:10.1080/07853890802301983.
14. Kirizuka K., Nishizaki H., Kohriyama K. et al. Influences of The Great Hanshin-Awaji Earthquake on glycemic control in diabetic patients. Diabetes Res Clin Pract. 1997;36(3):193-196. doi:10.1016/s0168-8227(97)00030-2.
15. Miller-Archie S.A., Jordan H.T., Ruff R.R. et al. Posttraumatic stress disorder and new-onset diabetes among adult survivors of the World Trade Center disaster. Prev Med. 2014;66:34-38. doi:10.1016/j.ypmed.2014.05.016.
16. Scherrer J.F., Salas J., Norman S.B. et al. Association Between Clinically Meaningful Posttraumatic Stress Disorder Improvement and Risk of Type 2 Diabetes. JAMA Psychiatry. 2019;76(11):1159-1166. doi:10.1001/jamapsychiatry.2019.2096 .
17. Vaccarino V., Goldberg J., Magruder K.M. et al. Posttraumatic stress disorder and incidence of type-2 diabetes: a prospective twin study. J Psychiatr Res. 2014;56:158-164. doi:10.1016/j.jpsychires.2014.05.019.
18. Aronson B.D., Palombi L.C., Walls M.L. Rates and consequences of posttraumatic distress among American Indian adults with type 2 diabetes. J Behav Med. 2016;39(4):694-703. doi:10.1007/s10865-016-9733-y .
19. Roberts A.L., Agnew-Blais J.C., Spiegelman D. et al. Posttraumatic stress disorder and incidence of type 2 diabetes mellitus in a sample of women: a 22-year longitudinal study. JAMA Psychiatry. 2015;72(3):203-210. doi:10.1001/jamapsychiatry.2014.2632 .
20. Lukaschek K., Baumert J., Kruse J. et al. Relationship between posttraumatic stress disorder and type 2 diabetes in a population-based cross-sectional study with 2970 participants. J Psychosom Res. 2013;74(4):340-345. doi:10.1016/j.jpsychores.2012.12.011 .
21. Kinzie J.D., Riley C., McFarland B. et al. High prevalence rates of diabetes and hypertension among refugee psychiatric patients. J Nerv Ment Dis. 2008;196(2):108-112. doi:10.1097/NMD.0b013e318162aa51.
22. Agyemang C., Goosen S., Anujuo K. et al. Relationship between post-traumatic stress disorder and diabetes among 105,180 asylum seekers in the Netherlands. Eur J Public Health. 2012;22(5):658-662. doi:10.1093/eurpub/ckr138.
23. van Melle M.A, Lamkaddem M., Stuiver M.M. et al. Quality of primary care for resettled refugees in the Netherlands with chronic mental and physical health problems: a cross-sectional analysis of medical records and interview data. BMC Fam Pract. 2014;15:160. doi:10.1186/1471-2296-15-160.
24. Boscarino J.A. Posttraumatic stress disorder and physical illness: results from clinical and epidemiologic studies. Ann N Y Acad Sci. 2004;1032:141-153. doi:10.1196/annals.1314.011.
25. Nowotny B., Cavka M., Herder C. et al. Effects of acute psychological stress on glucose metabolism and subclinical inflammation in patients with post-traumatic stress disorder. Horm Metab Res. 2010;42(10):746-753. doi:10.1055/s-0030-1261924.
26. Powers A., Michopoulos V., Conneely K. et al. Emotion Dysregulation and Inflammation in African-American Women with Type 2 Diabetes. Neural Plast. 2016;2016:8926840. doi:10.1155/2016/8926840 .
27. Reagan L.P., Grillo C.A., Piroli G.G. The As and Ds of stress: metabolic, morphological and behavioral consequences. Eur J Pharmacol. 2008;585(1):64-75. doi:10.1016/j.ejphar.2008.02.050.
28. Jelenik T., Dille M., Müller-Lühlhoff S. et al. FGF21 regulates insulin sensitivity following long-term permanent stress. Mol Metab. 2018;16:126-138. doi:10.1016/j.molmet.2018.06.012.
29. Yabuki Y., Fukunaga K. Clinical Therapeutic Strategy and Neuronal Mechanism Underlying Post-Traumatic Stress Disorder (PTSD). Int J Mol Sci. 2019;20(15):3614. doi:10.3390/ijms20153614.
30. Canneva F., Golub Y., Distler J. et al. DPP4-deficient congenic rats display blunted stress, improved fear extinction and increased central NPY. Psychoneuroendocrinology. 2015;53:195-206. doi:10.1016/j.psyneuen.2015.01.007.
31. Schultz L.M., Merikangas A.K., Ruparel K. et al. Stability of polygenic scores across discovery genome-wide association studies. HGG Adv. 2022;3(2):100091. doi:10.1016/j.xhgg.2022.100091.
32. Bobryk M., Tutchenko T., Sidorova I. et al. Insulin resistance in the XXI century: multimodal approach to assessing causes and effective correction. Reproductive endocrinology. 2021;62:97–103. doi:10.18370/2309-4117.2021.62.97-103.
33. Ciocca G., Carosa E., Stornelli M. et al. Post-traumatic stress disorder, coping strategies and type 2 diabetes: psychometric assessment after L'Aquila earthquake. Acta Diabetol. 2015;52(3):513-521. doi:10.1007/s00592-014-0686-8 .

34. Dixon H.D., Michopoulos V., Gluck R.L. et al. Trauma exposure and stress-related disorders in African-American women with diabetes mellitus. Endocrinol Diabetes Metab. 2020;3(2):e00111. doi:10.1002/edm2.111.
35. Livneh H., Martz E. On structure of trauma-related stress reactions among people with diabetes mellitus. Psychol Rep. 2006;99(1):209-212. doi:10.2466/pr0.99.1.209-212.

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