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ASSOCIATION OF THYROID FUNCTION AND POST TRAUMATIC STRESS DISORDER: A SYSTEMATIC REVIEW

[1]Pretika Prameswari, [2]Ririn Azhari

[1]Faculty of Medicine, Trisakti University, Jakarta, Indonesia
[2]H Bakri Sungai Penuh General Hospital, Jambi, Indonesia

Corresponding Author:
pretika_p@yahoo.com

ABSTRACT

Background: *Numerous studies conducted over the last few decades have shown a negative correlation between post-traumatic stress disorder PTSD and physical health and wellbeing. Thyroid dysfunction may be related to a variety of mental disorders, including PTSD. However, it is still debatable.*

The aim: *This study aims to investigate association between thyroid function and post-traumatic stress disorder.*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and ScienceDirect, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Results: *In the PubMed database, the results of our search brought up 42 articles, whereas the results of our search on ScienceDirect brought up 163 articles. The results of the search conducted by title screening yielded a total 15 articles for PubMed and 10 articles for ScienceDirect. We compiled a total of 14 papers, 11 of which came from PubMed and 3 of which came from ScienceDirect. We excluded 3 review articles, 3 duplicate articles, 1 animal study, and 2 articles having ineligible outcomes data. In the end, we included five research that met the criteria.*

Conclusion: *PTSD may alter thyroid function but there is scanty evidence regarding their relationship.*

Keywords: *Posttraumatic stress disorder, PTSD, thyroid*

INTRODUCTION

A severe anxiety disorder resulting from trauma that manifests as both physical and psychological signs and symptoms is called post-traumatic stress disorder (PTSD).[1] PTSD comprises four symptom clusters: 'avoidance', 'numbing', 'hyper-arousal' and the hallmark 're-experiencing' or 'intrusive symptoms', which include unwanted thoughts, flashbacks and nightmares.[2] Numerous studies conducted over the last few decades have shown an adverse association between PTSD and physical health and wellbeing. PTSD is independently linked to worsened physical functioning, increased healthcare consumption and expenses, and higher rates of disability, even after controlling for sociodemographic and lifestyle factors.[3]

PTSD may occur in individuals of any age, ethnicity, nationality, or culture. High-risk professional populations, such as military service workers, are more likely to suffer from PTSD, and some ethnic groups are disproportionately impacted and have higher rates of PTSD than non-Latino Whites.[4] In the last five years, masculinity in male war veterans has been the gender-related issue that has gained the greatest attention.[5] Recent epidemiological studies suggest that the lifetime prevalence of PTSD among veterans ranges from 8% to 22%.[3] Its prevalence is estimated to be 5–8% in men and 10–14% in women; so, women are twice as likely as men to develop PTSD.[4] Lifetime prevalence is similar in South Africa (2.3%), Spain (2.2%), and Italy (2.4%), whereas the prevalence was lower in Japan (1.3%). Northern Ireland, in contrast, reported the highest lifetime PTSD prevalence of 8.8%.[6]

Many endocrine illnesses, including Cushing syndrome, are known to be correlated with mental health issues, such as depression, hallucinations, suicidal thoughts, etc. It is still debatable, though, whether thyroid deficiency and specific neuropsychiatric conditions are related.[7] Thyroid dysfunction may be related to a variety of mental disorders. Thyroid dysfunction may present with symptoms such as depression, for example, a mental illness. Patients whose symptoms are actually caused by hyperthyroidism or hypothyroidism may be mistakenly diagnosed as having a serious mental illness. A wide range of mental illnesses and symptoms can arise from abnormal thyroid activity. Among them include phobias, panic attacks, obsessive-compulsive disorder, irritability, aggression, bipolar disorder, sadness, anxiety, and even schizophrenia. There are indications of mild or overt hypothyroidism in up to 15% of people receiving depression treatment. Graves' disease with stress, myxedema, and cretinism are conditions that are frequently associated with mental issues.[8] This study aims to investigate association between thyroid function and post-traumatic stress disorder.

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this systematic review, we determine association between thyroid function and post-traumatic stress disorder. It is possible to accomplish this by researching or investigating the thyroid panel test and PTSD. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine association between thyroid function and post-traumatic stress disorder. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published within the last 10 years. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used "posttraumatic stress disorder"; "PTSD", and "thyroid" as keywords. The search for studies to be included in the systematic review was carried out from December, 7th 2023 using the PubMed and ScienceDirect databases by inputting the words: "stress disorders, post traumatic"[MeSH Terms] OR "stress"[All Fields] AND "disorders"[All Fields] AND "post traumatic"[All Fields]) OR "post-traumatic stress disorders"[All Fields] OR ("posttraumatic"[All Fields] AND "stress"[All Fields] AND "disorder"[All Fields]) OR "posttraumatic stress disorder"[All Fields] OR ("stress disorders, post traumatic"[MeSH Terms] OR ("stress"[All Fields] AND "disorders"[All Fields] AND "post traumatic"[All Fields]) OR "post-traumatic stress disorders"[All Fields] OR "ptsd"[All Fields] AND ("thyroid gland"[MeSH Terms] OR ("thyroid"[All Fields] AND "gland"[All Fields]) OR "thyroid gland"[All Fields] OR "thyroid"[All Fields] OR "thyroid usp"[MeSH Terms] OR ("thyroid"[All Fields] AND "usp"[All Fields] OR "thyroid usp"[All Fields] OR "thyroids"[All Fields] OR "thyroid s"[All Fields] OR "thyroidal"[All Fields] OR "thyroideal"[All Fields] OR "thyroidism"[All Fields] OR "thyroiditis"[MeSH Terms] OR "thyroiditis"[All Fields] OR "thyroiditides"[All Fields] AND (y_10[Filter]) AND (english[Filter]) used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

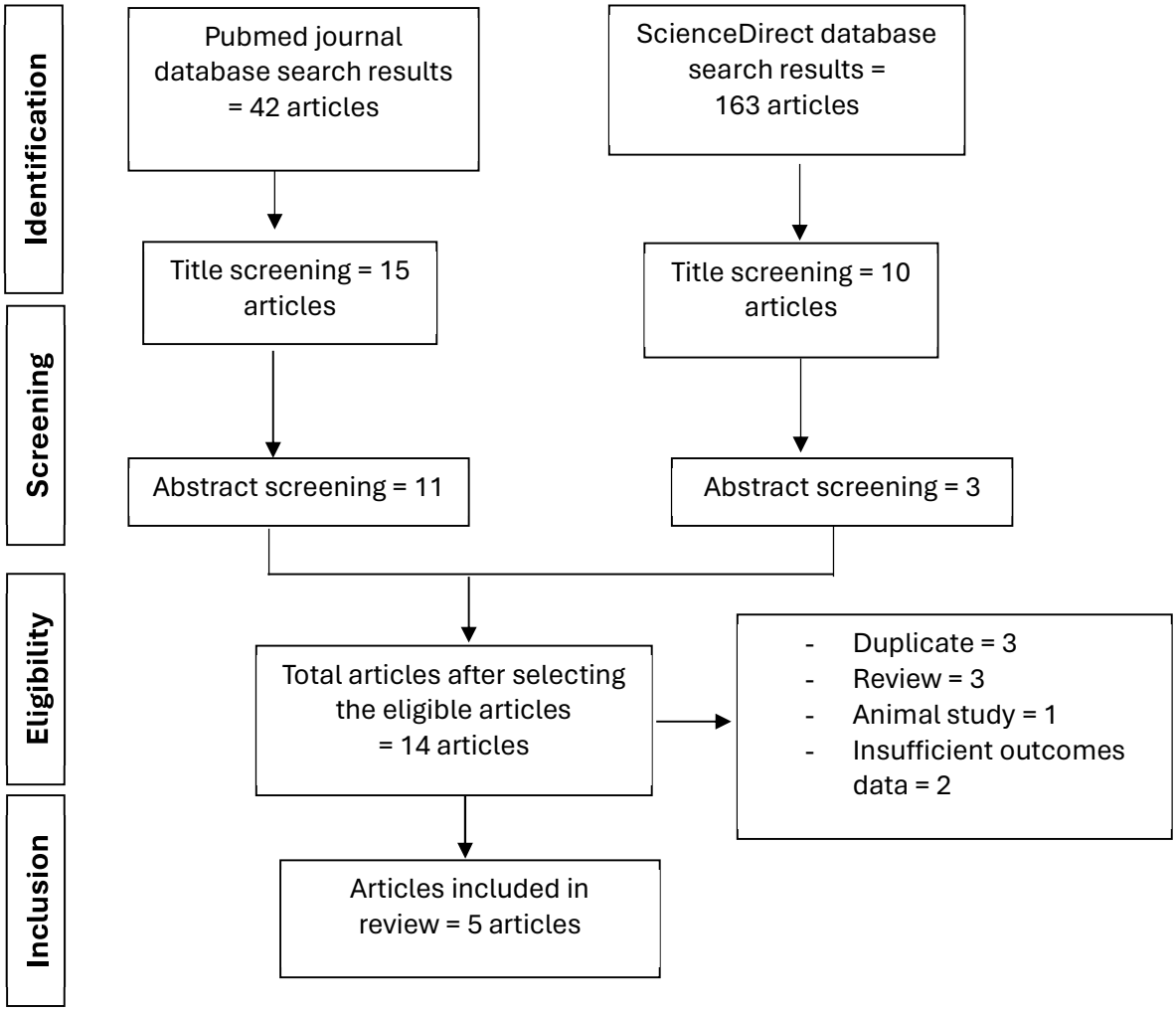

Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 42 articles, whereas the results of our search on ScienceDirect brought up 163 articles. The results of the search conducted by title screening yielded a total 15 articles

for PubMed and 10 articles for ScienceDirect. We compiled a total of 14 papers, 11 of which came from PubMed and 3 of which came from ScienceDirect. We excluded 3 review articles, 3 duplicate articles, 1 animal study, and 2 articles having ineligible outcomes data. In the end, we included five research that met the criteria.

Feklicheva, et al. (2021)[9] showed that no significant differences were present between the studied groups in the levels of the thyroid hormones and thyroid stimulating hormone, which casts doubt on their significance as a biomarker at least in this group of military. Mean levels of T3 (triiodothyronine), T4 (thyroxine) and TSH (thyroid-stimulating hormone) did not differ between groups ($F(2, 85) = 1.15$, $p = 0.321$; $F(2, 85) = 1.92$, $p = 0.153$; $F(2, 85) = 1.3$, $p = 0.277$, respectively). In this study, there were only men (n = 108, 100%). There were no significant differences in the age of participants between the groups. The mean values of CAPS sum scores were 27.7 (SD = 19.76) for PTSD group and 5.22 (SD = 4.76) for resistant group.

Jung, et al. (2019)[10] found significant results between PTSD and hypothyroidism but found no significant results for hyperthyroidism. Over 24 years of follow-up, 7993 women developed hypothyroidism, and 847 women developed Graves' hyperthyroidism. Overall, women with PTSD symptoms had a higher incidence of hypothyroidism in a dose–response pattern. In the final model, women with the highest number of PTSD symptoms had an HR of 1.26 (95% CI 1.14– 1.40, p-trend <0.001) for hypothyroidism, compared with women without any trauma exposure. For women with the highest number of PTSD symptoms (4+ symptoms), the HR for hypothyroidism was 1.21 (95% CI 1.03–1.42, p-trend = 0.012). When we evaluated expo- sures lagged by an additional 2 or 4 years, there was little difference from the main model for the relationship between PTSD symptoms and thyroid dysfunction. In models evaluating whether thyroid conditions as an exposure were associated with subsequent PTSD symptoms as the outcome, we found that hypothyroidism was associated with modestly higher risk of clinical PTSD symptoms [for more than four PTSD symptoms: HR 1.17 (95% CI 0.99–1.38)].

Musheyev, et al. (2022)[11] reported that a 33-year-old female diagnosed with panhypopituitarism. This patient has diagnosed with PTSD because of her combat history when served in the United States military. Thyroid panel was ordered, and TSH and T3 levels were low. In short, the majority of the pituitary hormones were abnormally low, except for cortisol, which is produced by the adrenal glands. For a patient presenting with a deficiency of a collection of anterior pituitary hormones, the diagnosis is hypopituitarism and possibly panhypopituitarism.

O'Donovan, et al. (2015)[12] showed that PTSD may increase risk for autoimmune disorders. PTSD with and without other psychiatric diagnoses was diagnosed in 203,766 (30.6%) veterans, and psychiatric disorders other than PTSD were diagnosed in an additional 129,704 (19.5%) veterans. Veterans with psychiatric disorders were younger ($p < .001$), more likely to be male ($p < .001$) and non-white ($p < . 001$), and had a higher number of visits to primary care in the prior year ($p < .001$) than veterans with no psychiatric disorders. The most prevalent autoimmune disorders included thyroiditis, rheumatoid arthritis, inflammatory bowel disorders, multiple sclerosis, and lupus erythematosus.

Sinai, et al. (2014)[13] showed that there were no significant differences in thyroid hormone levels in female borderline personality disorder (BPD) patients with and without comorbid PTSD diagnosis. The mean age of the patients was 29.5 years (SD = 7.6; range 19-50). Sixty-seven percent of patients reported medium high or high level of exposure to interpersonal violence as a child. The FT3/FT4 ratio showed a significant negative correlation with exposure to violence as a child. Forty nine out of 92 (53%) patients met the criteria of PTSD.

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Feklicheva, 2021[9]	Russia	Cross sectional	108 men	This findings suggested that no significant differences were present between the studied groups in the levels of the thyroid hormones and thyroid stimulating hormone. However, cortisol and to some extent testosterone may serve as biomarker of war zone stress per se, even if trauma was experienced at least ten years before, rather than of only PTSD or resistance to PTSD. GABA, in contrast, can be considered a potential marker of the protracted nature of PTSD.

Jung, 2019[10]	USA	Prospective cohort	116,429 women	This findings suggested that thyroid health warrants clinical attention in women with PTSD symptoms. PTSD was associated with higher risk of hypothyroidism in a dose-dependent fashion. Highlighted awareness for thyroid dysfunction may be especially important in women with PTSD.
Musheyev, 2022[11]	USA	Case report	One woman	A 33-year-old female who served in the United States military presents to her OBGYN with complaints of irregular menses. This patient has PTSD because of her combat history. On the first visit, the OBGYN ordered a thyroid panel, female hormone evaluation, lipid panel, and a CBC. The results revealed high serum cortisol levels as well as low serum levels for estradiol, FSH, LH, TSH, and T3. The patient was further referred to an endocrinologist and the diagnosis of panhypopituitarism was confirmed.
O'Donovan, 2015[12]	USA	Retrospective cohort study	666,259 male and female veterans	Trauma exposure and PTSD may increase risk for autoimmune disorders, including thyroiditis.

Sinai, 2014[13]	Sweden	SKIP project (RCT)	162 women with BPD (53% with comorbid PTSD)	This study showed that severe childhood trauma-related stress may promote lasting altered thyroid levels and/or contribute to the development of psychopathology associated with BPD traits or PTSD. This study found a negative relationship between exposure to interpersonal violence in childhood and the FT3/FT4, among 92 women with BPD. Comorbid diagnosis of PTSD was related to a more pronounced neuroendocrine dysregulation.

DISCUSSION

The purpose of this research was to review studies published after January of 2013 and up to December of 2023 that investigated the association between thyroid function and post-traumatic stress disorder. Three of five identified studies showed impaired thyroid function in patient with PTSD. Nevertheless, two of identified studies suggested that no significant differences of in thyroid hormone levels in patient with PTSD.

There is proof that thyroid function and mental health issues. Thyroid dysfunction symptoms can occasionally even confused with mental health conditions. Patients with Hashimoto's thyroiditis have been mistakenly diagnosed as psychotic depression, mania, and paranoid schizophrenia. Anxiety, bipolar illness, sadness, irritability, aggression, obsessive-compulsive disorder, panic attacks, schizophrenia, and a host of phobias have all been associated with imbalanced THs.[8,14] A study reported the rate of autoimmune thyroiditis in depressive disorders as 8.9 per cent comparable to our finding of 5.6 per cent.[15]

Nevertheless, it is less evident how adult thyroid illness affects the brain and mental functions. Patients with hyperthyroidism still struggle with mood disorders and a reduced quality of life even when their euthyroidism is restored. Furthermore, it is widely known that thyroid hormones cause psychiatric problems through their interaction with serotonin and norepinephrine. This raises the possibility that mental disease and hyperthyroidism are related.[14]

PTSD is associated with changes in several neuroendocrine systems beyond the HPA axis, as supported by numerous studies. Abnormalities in noradrenergic, dopaminergic, and serotonergic pathways have been documented in PTSD, as well as changes in other endocrine systems such as the hypothalamic–pituitary–thyroid (HPT) axis and the hypothalamic–pituitary–gonadal (HPG) axis. These alterations are thought to contribute to the diverse symptomatology of PTSD, including emotional dysregulation, hyperarousal, and sleep disturbances. Moreover, these findings suggest that PTSD is a complex disorder that involves dysregulation of multiple neuroendocrine systems rather than being solely related to HPA axis dysfunction.[4]

Thyroid hormones play a key role in the development, metabolism and the functioning of many organs.[16] Pituitary thyrotropin regulates thyroid hormone secretion; it is increased by hypothalamic thyrotropin-releasing hormone (TRH) and repressed by the negative feedback from serum thyroid hormones. In serum, more than 99% of thyroid hormones are bound to specific proteins; only free hormones are active. The thyroid gland secretes several hormones, including thyroxine (T4), triiodothyronine (T3), and reverse T3 (rT3). T4 is the primary hormone secreted by the thyroid gland, and it comes from nowhere else. On the other hand, the thyroid gland secretes no more than 20% of the more physiologically active hormone T3. Enzymes called deiodinases, which come in various forms and are found in cells, extract iodine from the T4 molecule to make the remaining amount of T3, which is then produced in other tissues.[17]

TRH plays a key role in controlling the HPT axis, which regulates blood levels of thyroid hormones to control metabolism and other homeostatic processes. Thyroid disorders have been linked to trauma, and research has indicated a potential link between PTSD and the HPT axis. Studies have demonstrated that veterans of both World Wars II and the Vietnam War, as well as other PTSD sufferers, have higher baseline levels of T3 and T4, with T3 levels being disproportionately higher than T4, suggesting an increase in the peripheral deiodination process. To completely comprehend the association between the HPT axis and PTSD, particularly the direction of causality and the potential processes underlying this relationship, additional research is necessary as there is currently disagreement about it.[4]

Many multidisciplinary investigations showed that patients with thyroid dysfunction have a significant prevalence of mood problems, especially depression. It has been proposed that slight variations in thyroid hormone levels, especially those that fall within the normal range, may be connected to the altered brain function associated with depression, even if the exact role thyroid hormones play in the pathophysiology of mental diseases is unclear.[16]

CONCLUSION

PTSD may alter thyroid function but there is scanty evidence regarding their relationship.

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