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Unveiling the Nexus: Depressive Symptoms and Medication Adherence in Hypertensive Patients' Self-care: A Systematic Review

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ABSTRACT

Background: Hypertension, a significant public health concern, is frequently linked to emotional disorders like depression. Research shows a reciprocal link between depression and hypertension, potentially influencing patients' adherence to self-care routines. **Objective:** This systematic review aimed to examine the association between depressive symptoms and aspects of self-care, with a focus on medication adherence in individuals diagnosed with hypertension. **Methods:** Following PRISMA guidelines, a systematic review was conducted by searching PubMed, PsycINFO and Scopus until March 17, 2023. The included studies involved quantitative primary research conducted in English, focusing on adults (≥18 years) diagnosed with hypertension and experiencing depressive symptoms. Observational studies were assessed using the Newcastle-Ottawa Scale, and randomized controlled trials were evaluated using the revised Cochrane Risk of Bias Tool (RoB 2.0). Due to the great diversity of these studies, a narrative synthesis of the results was undertaken. **Results**: A total of 18 studies involving 6,131 people with hypertension, that met our eligibility criteria were ultimately included. The reported rates of depressive symptoms ranged from 4% to 43%. Of these studies, nine reported a statistically significant association, showcasing an adverse impact of depressive symptoms on medication adherence. The remaining nine did not confirm the above. **Conclusion:** This systematic review highlights the diverse body of research exploring depressive symptoms and medication adherence among individuals with hypertension. The review suggests a need for increased attention to self-care practices, particularly in relation to adherence to antihypertensive medication. However, it recommends the conduction of more robust longitudinal studies to comprehensively explore this relationship.

Keywords: depressive symptoms, hypertension, medication adherence, self-care, systematic review.

1. BACKGROUND

Hypertension, often referred as the silent killer (1), is globally recognized as one of the leading causes of premature death, cardiovascular disease, kidney disease, and stroke (2–4). According to the World Health Organization (5), an estimated 1.28 billion adults between the ages of 30 and 79 suffer from hypertension worldwide, with the prevalence expected to reach 29% by 2025 (6).

Individuals with chronic hypertension face an increased risk of experiencing psychological comorbidities, including depression, anxiety, and stress (7). Depressive symptoms are commonly observed in hypertensive patients (8,9), with several studies highlighting this significant relationship (7, 10). Moreover, the association between depressive symptoms and hypertension is recognized as reciprocal, as depressive symptoms can both result from hypertension and increase the risk of its development and treatment (11).

On the one hand, hypertension can exacerbate and intensify the symptoms of depression (12). Living and coping with a chronic

medical condition like hypertension can be emotionally challenging and have a negative impact on a person's overall well-being (13). The burden of managing the condition, regarding potential complications, and the need for long-term medication adherence can contribute to feelings of stress, anxiety, and depression (14). There is a growing body of evidence indicating that hypertension is a significant modifiable risk factor for small vessel brain disease (15). Consequently, this condition can give rise to a wide range of symptoms, including mild to progressive cognitive decline, dementia, and depression (16).

On the other hand, the presence of depressive symptoms can be a contributing factor that increases the risk of developing hypertension (17). The physiological effects of these symptoms, such as increased sympathetic nervous system activity and dysregulation of the hypothalamic-pituitary-adrenal axis, can directly impact blood pressure regulation and contribute to the pathophysiology of hypertension (15). Additionally, the psychological distress associated with depression may lead to unhealthy lifestyle behaviors, such as poor diet, physical inactivity, especially medication non-adherence, making it difficult for individuals to set priorities and consistently adhere to prescribed treatment plans (18, 19).

Depressive symptoms, for instance, can hinder adherence to medication, which is crucial for blood pressure control, as well as self-care behaviors (20,21). Adherence is often defined as the patient's active collaboration in mutually agreed-upon behavior for a therapeutic outcome, including the timing, dosage, and frequency of medication use (22, 23). the apathy, lack of motivation and difficulty concentrating that may be found in the presence of depressive symptoms could affect their adherence to medication (24, 25)

Despite the extensive research examining the interplay between hypertension, depressive symptoms, and self-care, a systematic review summarizing the association between depressive symptoms and medication adherence within the concept of self-care is notably missing from the existing literature.

2. OBJECTIVE

The aim of the systematic review was to examine and evaluate the association between depressive symptoms and medication adherence as a component of self-care in people with hypertension. Our primary focus was to evaluate and synthesize findings from various studies examining the impact of depressive symptoms on medication adherence in the treatment of these people. In doing so, we also sought to provide valuable insights into the nature and significance of this relationship by identifying and summarizing correlations, trends, and disparities to guide future research and clinical practice.

3. MATERIAL AND METHODS

The systematic review was conducted in accordance with the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) (26). Specifically, we followed the PRISMA checklist and the PRISMA checklist for abstracts (27), available in the supplementary material (see Tables 5 and 6). Additionally, the protocol for this systematic review was preregistered with the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42023411857. Differences between the protocol and the final review are discussed below.

Search strategy

A thorough and comprehensive literature search was conducted to identify relevant studies for this review. PubMed, Scopus, and APA PsycINFO databases were searched from their inception until March 7th, 2023, ensuring a broad range of literature was considered. The search strategy was carefully developed for each database, employing appropriate keywords such as hypertension, depression, medication adherence and self-care. Boolean operators were used to refine the search and maximize the retrieval of relevant articles. The complete search algorithms can be found in the supplementary material, specifically in Box 1.

No restrictions were imposed on the eligibility criteria for studies based on factors such as publication year, country of origin, or nationality. This approach ensured a comprehensive examination of the available literature, encompassing diverse studies from various regions and time periods. Furthermore, to ensure a comprehensive review, the reference lists of identified publications were manually screened for additional relevant studies, expanding the scope of the literature search.

Selection and eligibility criteria

Two independent reviewers (TS and ED) assessed the titles and abstracts of the studies to determine whether they met the selection criteria. In cases where a study met the selection criteria, the full article was downloaded for further evaluation. Details regarding the exclusion of full-text articles for various reasons can be found in Box 2 of the supplementary material. Any discrepancies between the two reviewers were resolved through discussions with the research team.

We included observational studies (cohort, case-control, cross-sectional) and/or randomized controlled trials (RCTs) in adult populations (aged 18 years and older) with hypertension reported on medication adherence (outcome variable) and depressive symptoms (exposure of interest). The diagnoses of depression were based on well-defined standard diagnostic criteria, specific requirements, established diagnostic research criteria, or validated assessment instruments commonly utilized in clinical practice or research settings. We excluded qualitative studies, meta-analyses, letters to the editor, doctoral theses, and studies that do not establish a link between self-care and depression. In addition, articles in languages other than English were excluded because their selection would reduce the time and cost associated with translating and evaluating articles in other languages.

Quality assessment

We used the Newcastle-Ottawa Scale (NOS) to assess the quality of observational studies. The NOS was applied for cohort, case-control, and cross-sectional studies by

allocating a star scoring system ranging from 0-10 in the three following domains: a) Selection, b) Comparability, and c) Outcome per study design (28).

The revised Cochrane Risk of Bias Tool (RoB 2.0) was used to evaluate the quality of the randomized controlled trials. The tool assesses the following domains: randomization process, deviations from intended intervention, missing outcome data, outcome measurement, and selective reporting of results. Based on pre- established criteria for each domain, each study is then categorized as having a low risk of bias, moderate concerns, or a high risk of bias (29).

The assessment of quality was performed by one author (TS) and subsequently reviewed by the other three team members (MG, SM and MK). Any disagreements that arose during the quality assessment of the studies were also resolved by consensus among the researchers involved in the systematic review.

Data extraction

After the search was completed, Zotero (30) -an open-source reference management software–was used to compile all citations and duplicate entries were removed. Subsequently, the authors systematically extracted pertinent data from the articles and documented it in a predefined Excel spreadsheet. This data encompassed the study's reference details, publication year, study location, research design, sample size, proportion of female participants, mean age, prevalence of depression among hypertensive patients, tools employed to assess depressive symptoms and medication adherence, alongside the primary research hypothesis and key findings pertaining to the relationship between medication adherence and depressive symptoms in each study.

Data synthesis

While the eligible studies conformed to the search criteria, they exhibited variations in numerous parameters concerning their design and the correlation between medication adherence and depressive symptoms. Additionally, despite a consistent focus on the impact of depressive symptoms on treatment adherence, differences in data collection methods were evident. Some studies employed continuous scales, such as weighted measures for total depression scores, whereas others relied on dichotomous assessments, indicating depression presence or absence through impromptu questionnaires. Notably, these discrepancies extended to concepts of compliance, patients' age ranges, and inclusion criteria.

Consequently, due to the diversity among these studies, performing a quantitative synthesis (meta-analysis) was unfeasible. Instead, a narrative approach was utilized to amalgamate the principal attributes and significant findings across these studies.

Differences with the protocol

There were some differences between the protocol and the final review. Initially, the online database searches targeted the correlation between depressive symptoms and overall self-care in hypertension. However, due to the variations in how the two variables were associated and measured across studies, it was deemed more appropriate to focus solely on the relationship between depressive symptoms and medication adherence, considering it as a constituent of self-care, in individuals living with hypertension, for the purpose of this systematic study.

4. RESULTS

Study selection process

As shown in Figure 1, which illustrates the PRISMA flowchart (31), the initial search of the electronic databases yielded 926 results, of which 384 duplicate and non-English articles were removed. Following this, 509 articles were excluded after a thorough inspection of their titles and abstracts. Subsequently, a rigorous assessment of the full text was conducted for 33 studies against the eligibility criteria. Of these, 13 articles aligned with the selection criteria and were included in the systematic review. Additionally, five more studies were identified through an extensive search of references and citations. Hence, the overall sample size of the final included studies was 18. The supplementary material (Box 2) provides insight into the reasons for excluding articles after the full text review.

Characteristics of the included studies

The main characteristics of the included studies are presented in Table 1 included. Of the 18 studies published from 2002 to 2022, nine were conducted in the USA (32–40), two in Korea (41,42), and one study each was conducted in Mexico (43), Pakistan (44), China (45), Ethiopia (46), Ghana (47), Germany (48), and the UK (49). The predominant study design was cross-sectional, present in the majority of studies (32, 35, 39–47, 49), while two were RCTs (34, 38), two were cohort studies (33,36), one involved baseline cross-sectional analyses derived from an RCT (37), and one was a retrospective study (48).

The collective sample across these studies comprised 6,131 people with people with hypertension. The duration of hypertension showed substantial variation between studies reporting this particular factor. Notably, certain studies indicated diagnoses established a minimum of 2-12 months (41,45,47), whereas other studies (36,43) encompassed patients with a documented history of hypertension spanning at least 3-10 years. In 12 studies (32, 35–39, 41, 43–45,47,49) the majority of the participants were females, one study reported an equal gender distribution (48) and one study exclusively involved male participants (34). Fourteen studies (32–39,41–46) provided data on mean age of the participants, which varied from 41.7 (34) to 75.0 years (36).

Furthermore, only 13 studies (33,34,36–38,42–49) provided the prevalence rate of depressive symptoms, ranging from 4% (47) as the lowest to 43% (44) as the highest. Figure 2 presents a bar chart displaying the rates of depressive symptoms observed in each study.

Measurements of depressive symptoms

A total of 10 different instruments were used to evaluate depressive symptoms (Table 1). Specifically, the Patient Health Questionnaire-9 items (PQ9) was used in two studies (37, 46), the Geriatric Depression Scale (GDS) in two (32, 42), the Beck Depression Inventory (BDI) in two (33, 39), the Center for Epidemiological Studies Depression Scale (CES-D) in five (34, 36, 38, 41, 49), the Hospital

Anxiety and Depression Scale (HADS) in two (43, 45), and one study each utilized the Kim Depression Scale for Korean Americans (KDSKA) (35), the DSM-IV Composite International Diagnostic Interview (DIA-X-CIDI) (48), the Depression Anxiety Stress Scale (DASS) (47), the Depression Symptom Inventory (40), and the Aga Khan University Anxiety and Depression Scale (AKU-ADS) (44).

Measurements of medication adherence

Regarding the measurement of medication adherence self-care, 12 different instruments were employed (Table 1), including the Hypertension Self-Care Activity Level Effects (H-scale) (46), Beliefs about Medicines Questionnaire (BMQ) (32), Hill Bone Compliance to High Blood Pressure Therapy Scale (34, 35, 39), Medication Adherence Self-Efficacy Scale-Short Form (MMAS) (36, 42, 44, 47), Reported Adherence to Medications scale (RAM) (49), Medication Adherence Self-Efficacy Scale Self-care (MASES) (38), Behavior Questionnaire (41) and Blood Pressure Self-Care scale (32). Five studies (37, 40, 43,45, 48) utilized self-report questionnaires, and one study (33) involved enrollment and follow-up visits.

Quality assessment of included studies

Out of the 15 observational studies, (Table 3 in the supplementary material), only two (13%) scored high on the NOS scale (36, 48), 12 studies (80%) demonstrated moderate quality (33, 35, 39–47, 49), and one study (7%) displayed low quality (32).

Regarding the RoB 2.0 assessment (Table 4 in the supplementary material), one RCT (38) was rated as having low risk, while some concerns were noted in two other RCTs (34, 37).

Main findings of the relationship between depressive symptoms and antihypertensive medication adherence

Studies that supported an association between depressive symptoms and antihypertensive medication adherence

Overall, half of the included studies (n=9) demonstrated a significant association between depressive symptoms and medication adherence in individuals dealing with hypertension.

Specifically, research by Abdisa et al. (2022) revealed that patients without depressive symptoms displayed higher tendencies for favorable self-care practices, inclusive of medication adherence, in contrast to those experiencing depressive symptoms (adjusted OR = 1.63, 95% CI: 1.23, 3.92). Bautista et al. (2012) reported an odds ratio (OR) of 2.48 (95% CI: 1.47, 4.18), signifying a higher likelihood of non-compliance with medication among individuals with mild depressive symptoms. Similarly, Cene´ et al. (2012) [Beta = 0.81; p <0.01], Hashmi et al. (2007) [Beta = 0.34 (95% CI: 0.1, 0.6)], Chang et al. (2015) [Beta = -0.44; p <0.001], Morris et al. (2006) [OR = 0.48 (95% CI: 0.32, 0.72)], and Wang et al. (2002) [OR = 0.93 (95% CI: 0.87, 0.99)] reported significant adverse impacts of depressive symptoms on adherence to antihypertensive medication.

Moreover, Krousel-Wood et al. (2010) demonstrated that depressive symptoms substantially contributed to lower adherence rates (MASS <6), indicating odds ratios of 2.09 (95% CI: 1.53, 2.86; p <0.01) and 1.96 (95% CI: 1.43, 2.70; p <0.01) for models with and without adjustment for social support, respectively. Son and Won's (2016) study depicted a statistically significant impact of depressive symptoms on adherence, either directly or mediated by the 'Self-efficacy' parameter, with values of b= -0.28; p<0.001 and b= -0.16; p=0.009, respectively.

Studies that did not support an association between depressive symptoms and antihypertensive medication adherence.

The remaining half of the studies did not demonstrate any statistically significant association between depressive symptoms and adherence to antihypertensive medication. These studies include Adinkrah et al. (2020) [p=0.853], Doubova et al. (2017) [PR = 0.92 (95% CI: 0.65, 1.30)], Kinley et al. (2015) [OR = 0.91 (95% CI: 0.63, 1.30)], Kretchy et al. (2014) [OR = 0.81 (95% CI: 0.1, 6.29, p=0.837], Maguire et al. (2008) [OR = 1.00 (95% CI: 0.96, 1.05), p=0.92], and Spikes et al. (2018) [OR=0.99 (95% CI: 0.94, 1.05, p=0.95)].

Moreover, in the study by Hu et al. (2014), no statistically significant impact of depressive symptoms on medication adherence in antidepressant therapy was identified across two different weighted models (OR=1.11 [95% CI: 0.57, 2.12] and OR=1.41 [95% CI: 0.65, 3.03]). Similarly, Kim et al. (2007) classified non-adherence to antihypertensive medication into intentional or unintentional categories, but neither approach revealed a statistically significant effect of depressive symptoms (OR=1.01 [95% CI: 0.95, 1.07] for intentional non-adherence and OR=1.02 [95% CI: 0.96, 1.07] for unintentional non-adherence).

Conversely, in the randomized clinical trials by Schoenthaler et al. (2009), the initially observed statistically significant effect of depression on adherence became non-significant following the examination of the 'Self-efficacy' parameter, presenting a value of b=0.010; p=0.087.

5. DISCUSSION

The systematic review aimed to explore the association between depressive symptoms and self-care among individuals with hypertension, specifically focusing on the relationship between depressive symptoms and medication adherence. Out of the 18 studies reviewed, nine demonstrated a significant association between depressive symptoms and medication adherence (33, 34, 36, 37, 40–42, 44, 46) while the remaining nine did not indicate such an association (32, 35, 38, 39, 43, 45, 47–49). This discrepancy underscores the complexity of the relationship between depressive symptoms and adherence to hypertension medication, indicating a need for further investigation or consideration of various factors that could influence this association.

Various studies (50–52) within the literature examining the association between depression and or depressive symptoms and medication adherence in conjunction with factors related to metabolic syndrome such as elevated glucose levels, triglycerides, and low high-density lipoprotein (HDL), indicate that depression plays a role in suboptimal medication adherence. This association

potentially amplifies the risk of cardiovascular complications. In addition, in individuals with hypertension, experiencing depressive symptoms is linked to a decline in overall health status, notably impacting their quality of life. The exacerbation of these symptoms contributes to diminished self-efficacy, a negative outlook, and a lack of motivation to adopt beneficial lifestyle changes. Moreover, it might hinder patients from adhering to medical recommendations (53). The study by Souza et al. (2016) emphasized that the quality of life in patients with hypertension was influenced by adherence to pharmacological treatment. According to the authors, adherence had positive effects on both the mental and physical domains, enhancing the overall quality of life and the physical well-being of individuals with arterial hypertension (54).

Furthermore, Van der Laan et al.'s systematic review (2017) identified several statistically significant factors linked to nonadherence to antihypertensive medications, notably side effects and suboptimal patient-provider relationships. While some factors, like low self-efficacy, discrimination, marital status, depression, history of cardiovascular disease, and dissatisfaction with healthcare provider communication, exhibited varying degrees of association, numerous studies indicated substantial connections with medication nonadherence. These identified factors hold potential as markers for assessing the risk of non-adherence (55). Additionally, Al-Noumani et al. (2019) systematic review investigated the link between health beliefs and medication adherence in hypertensive patients, highlighting that greater medication adherence was notably linked to fewer perceived barriers, notably side effects. Moreover, it underscored a positive correlation between higher self-efficacy and increased medication adherence (56).

In our systematic review, while examining the relationship between depressive symptoms and medication adherence, Son and Won's study (2016) revealed a statistically significant relationship, particularly when self-efficacy played a mediating role. In contrast, Schoenthaler et al.'s study (2009) indicated the opposite trend. The need for an integrated strategy to manage medication adherence in hypertension is evident due to its wide-ranging, ever-evolving, and multifaceted nature, which significantly impacts patient well-being (57,58). Embedding this aspect within health policies becomes crucial. Healthcare providers can leverage patient information to make informed decisions, selecting tailored interventions to bolster medication adherence in hypertension. Integrating services that encompass screening, diagnosing, treating, and monitoring depressive symptoms in hypertensive individuals shows potential for enhancing both blood pressure control and treatment adherence (59).

This systematic review represented the inaugural endeavor that scrutinized the association between depressive symptoms and self-care in hypertensive patients. It underscored the variance in data concerning diverse facets of self-care documented in the literature, primarily centering around medication adherence.

However, this systematic review encountered several limitations. Firstly, there existed a potential risk of language bias due to the restriction of the search to studies published solely in English. Secondly, the inclusion criteria encompassed only 18 studies, resulting in a restricted sample size, with the majority of these studies exhibiting moderate quality. Thirdly, deviations in the methodological design from the prescribed protocol were noted, elaborated upon in the 'Methods' section. Moreover, the substantial heterogeneity in the studies' data rendered the conduction of a meta-analysis unfeasible. It's essential to note that the studies included in this systematic review were predominantly cross-sectional in nature. Consequently, while these studies provided valuable insights into the association between depressive symptoms and medication adherence in hypertensive patients, it's important to highlight that being cross-sectional in design, they inherently lack the capacity to establish causation (60). Cross-sectional studies offer a snapshot at a particular point in time, providing associations between variables but not determining the direction or cause of these relationships (61). Therefore, although these studies offer significant observations, inferring causation from their findings should be approached with caution, as causality cannot be determined solely from cross-sectional data (60, 61).

Finally, the recommendations gleaned from this systematic review target healthcare professionals, urging them to integrate the assessment of medication adherence and its influential factors, including the existence of depressive symptoms, as integral elements of hypertensive patient care. Additionally, it is suggested that further research be undertaken to delve deeper into the relationship between depressive symptoms and medication adherence, as well as broader aspects of self-care, among individuals coping with hypertension.

6. CONCLUSION

In conclusion, this systematic review urges healthcare professionals to incorporate the assessment of medication adherence, including factors such as depressive symptoms, into the comprehensive care framework for hypertensive patients. Additionally, it advocates for further research to thoroughly investigate the relationship between depressive symptoms and medication adherence, as well as broader aspects of self-care among individuals managing hypertension. However, this review faced limitations, including potential language bias, a limited sample size, methodological variations, and predominantly cross-sectional study designs. Consequently, caution is necessary when inferring causation solely from cross-sectional data.

- **Author's Contribution:** TS and ED conducted the literature review in electronic databases and selected the appropriate studies. MG, SM, and MK assessed the quality of the included studies. All authors contributed to the writing and made necessary changes to the systematic review. Any disagreements were resolved through discussions involving all team members.
- **Conflicts of interest:** There are no conflicts of interest.

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