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Systematic Review

Can targeted interventions aimed at improving mental health and reducing symptoms of depression in hypertensive patients, lead to increased medication compliance and improved longevity? A systematic review

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ABSTRACT

Background: Hypertension is identified as a chronic disease leading to complications and untimely deaths if left untreated or undiagnosed.

There are several factors that contribute to the worsening of hypertension either directly or indirectly. Medication noncompliance is one of the direct factors. Depression plays a significant role as an indirect factor which convolutes management goals in hypertension. Correlation of mental health and adherence to medication requires further exploration.

Method: Medical databases such as PubMed, Cochrane library, Science direct were searched for relevant literature ranging between May 2013 and May 2023. The literature found was screened, checked for eligibility and 10 papers were reviewed. This was done using the Preferred Reporting Items for Systemic Review and Meta-analysis (PRISMA) guidelines. The finalized papers investigated the relationship between mental health/ depression and antihypertensive compliance. Improvement in mental health led to reduced blood pressure which was associated with better medication compliance.

Result: The analysis encompassed 10 research papers involving a total of 12,121 patients, excluding 542 individuals who had concurrent chronic conditions. One of the studies had other chronic diseases in addition to hypertension in it. Among these papers, one included patient with additional morbidity alongside hypertension. The studies hailed from diverse locations including Nigeria, Palestine, China, and the USA, with a notable proportion of patients being of Chinese origin. This predominance of Chinese patients reflects the abundance of relevant studies conducted in China on the subject matter.

Conclusion: The studies showed a significant improvement in blood pressure control with depression management. In the studies, other contributing factors to medication compliance were found and incorporated into this systematic review. Different methods were used to measure depression and medication compliance across the studies. All this warrant further research into the topic and how solutions can be implemented globally.

Keywords: Hypertension, medication compliance, depression, mental health, hypertensive patient, anxiety

INTRODUCTION

"Many physical illnesses are associated with depression and anxiety, including heart disease, high blood pressure, diabetes, Parkinson's disease, stroke, kidney disease, lung disease, dementia and cancer." - Liz Miller

Around the world, 1.28 billion persons between the ages of 30 and 79 are projected to have hypertension, with two-thirds of those individuals living in low- and middle-income countries.[1] Adults with hypertension are reportedly 46% less likely to be aware of their condition.[1] Due to its high incidence and the ensuing chronic renal disease, stroke and cardiovascular disease, hypertension is a significant worldwide health concern.[2-3]

Ten percent to 80% of hypertension patients do not follow their antihypertensive treatment regimens, which is one of the major causes of inadequate blood pressure control 4 thereby leading to complications.

It is evident that there is a clear necessity to enhance adherence to antihypertensive medication through counselling. However, for such interventions to be effectively planned, targeted, and economical, it is crucial to comprehend the nuanced causes of nonadherence and to pinpoint those that may be changed.[5]

Depression affects 251-310 million individuals globally.6-7 Several characteristics of depression, such as low motivation, doubt about the success of treatments, declines in attention, memory, and cognition, decreased self-care, intentional self-injury, as well as heightened awareness of unfavorable drug side effects could have a negative impact on adherence with preventive drugs.[5]

Hypertension, once diagnosed usually causes negative emotions in patients due to it being a lifelong disease which can lead to mental health issues such as depression.8-9 Such negative emotions include the loss of one's sense of self, worry and apprehension about the future, the breakup of relationships and social isolation, and guilt.8 Hypertension and mental health diseases have some similar/overlapping symptoms leading to underdiagnosis of mental health disease in patient with hypertension although, both conditions can be separate or inter-related.[8]

Such causes of non-compliance to antihypertensives includes poverty (which include insufficient access to food, lack of money for hospitals/medications, absence or limited access to transportation), insufficient grasps of the function and proper way of using prescribed medication and/or lack of faith in the medical system.[10-12]

This systematic review is to deduce if paying attention to mental health and depressive symptoms in patients and providing the needed care or treatment will improve patient's adherence to antihypertensives thereby reducing complications and sudden death due to cardiovascular diseases.

METHOD

This systematic review was done using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 guidelines.[13]

The following databases were searched from May 14th 2013- May 2023: PubMed, Medline, Cochrane Library and Science Direct for published research using the following keywords: hypertension, ''medication compliance'', depression therapy. In PubMed, keywords were used as well as PubMed MeSH strategy: "Hypertension"[MeSH Major Topic] AND "depression/therapy"[MeSH Major Topic] AND "Medication Adherence"[MeSH Terms]

The table below shows the search strategy, databases used and numbers of papers identified.

TABLE 1: Search strategy

SEARCH STRATEGY without filter	DATABASES USED	Number of papers identified
"Hypertension"[MeSH Major Topic] AND "depression/therapy"[MeSH Major Topic] AND "Medication Adherence"[MeSH Terms]	PubMed MeSH database	3
((hypertension) AND (depression therapy)) AND ('Medication compliance')	PubMed	189
hypertension 'depression therapy' 'medication compliance'	Cochrane trial	88
(depression therapy) and hypertension and (medication compliance)	Science Direct	5809
Total number of research paper identified		6,089

Inclusion and Exclusion criterio

We included literature and articles published within the past decade, involving participants aged 18 years and older, written in English or fully translated into English from their original language.

Excluded from our analysis were grey literature, studies involving participants under 18 years of age, and articles lacking full-text availability.

Selection process

After the inclusion and exclusion criteria was used to filter out the articles, papers from PubMed were transferred to Endnote, Duplicate articles were excluded, and the rest transferred to excel sheet. The other articles from Cochrane were scanned manually for relevant papers that included the keywords related to the topics which were then transferred to excel sheet, one duplicate was found in combination with articles transferred from PubMed and removed. Articles from science direct were also screened and relevant articles were selected as well.

The articles left were further evaluated by reading the full text to extract articles not related to the topic. After this, only 15 articles were accessed for eligibility assessment.

Quality assessment of the studies: The 15 articles left were checked for quality using the quality appraisal tools useful for the various studies. Clinical trials were assessed for quality using Cochrane Risk Bias Assessment tool,14 while observational studies (cohort and cross-sectional studies) were assessed using Newcastle- Ottawa tool.[15] In this systematic review, only 10 studies which met the quality assessment criteria were considered.

Data collection Process
Data was extracted from the articles finalized upon and data was extracted. All authors were involved in the review of the data extracted.

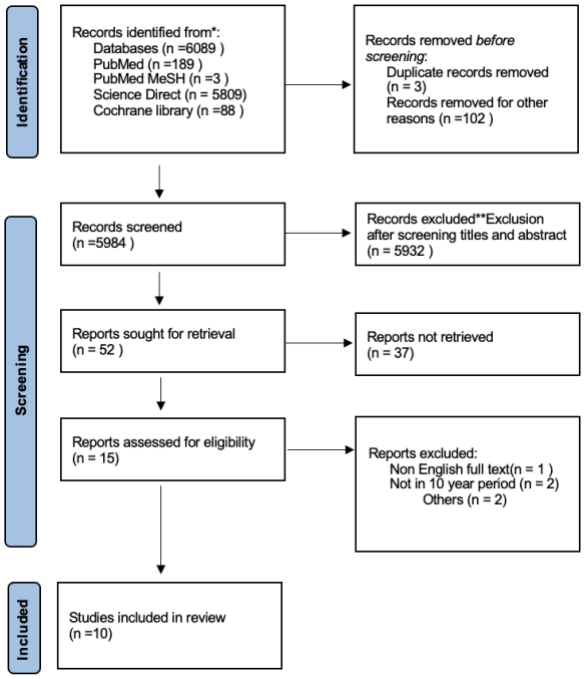
Results

Study Identification and Selection

A total of 6089 articles were identified using all databases. Titles and abstracts were screened to identify eligible articles. The selected articles underwent full text review. Articles that didn't have full text available were excluded. 15 articles were then assessed for eligibility then 10 articles were finally selected.

The selection process is shown in the PRISMA flowchart shown below:

FIGURE 1: PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart



DISCUSSION

In a study conducted in the USA, hypertensive, diabetic, and obese Caucasian patients were collectively examined, with a specific focus on antihypertensive medication adherence. The overall non-compliance rate for medication was found to be 12% (191 out of 1559 patients) among all three groups combined. However, when considering only hypertensive individuals, the non-compliance rate was slightly lower at 10% (99 out of 1,017 patients). Additionally, the study revealed a correlation between depression and reduced medication adherence, resulting in elevated diastolic blood pressure levels.[16]

In a study done in Nigeria, there was a high antihypertensive medication compliance in patient with comorbid depression which was associated with talks given by the nursing staff before the patients were seen by the physician during hospital visits.[17]

In a randomized trial conducted in China, the treatment of depression showed significant effects within the integrated care group. However, there were no discernible clinical distinctions between patients who took antidepressants and those who did not within this integrated group. Conversely, regarding hypertension, there were no notable clinical or non-clinical differences observed. Interestingly, individuals who did not receive antidepressant treatment within the integrated group exhibited better outcomes compared to those receiving usual care.[18] The integrated approach employed in this study was the Chinese Older Adult Collaborations in Health (COACH) intervention, conducted by Chen S in 2022.

The study conducted by Sin W in China,19 although involving a smaller sample size of only 60 participants, was included in this systematic review due to its nature as a clinical trial and its relevance to the topic under investigation. Notably, its integrated group exhibited a significant variance in treatment outcomes. This study bears similarities to the research conducted by Chen S, with the primary distinction lying in the sample sizes: while the Chen S study encompassed over a thousand participants per study group, Sin W's study comprised 30 individuals in each group. In terms of intervention, the Chen S study incorporated a multidisciplinary team consisting of a physician, a part-time worker referred to as an Aging worker responsible for reinforcing disease knowledge, and a psychiatrist accessible via phone.[18] In contrast, the Sin W study involved hospital staff at various levels of care, including physicians, nurses who reinforced knowledge through phone calls and home visits, as well as family members.[19]

In another study in China, which was a cross-sectional study showed the association between income disparities in the population (termed relative deprivation) and hypertension control.[20] It showed it affects poor hypertension control directly but also indirectly through poor medication adherence and poor mental health (depressive symptoms).[20]

A different study done in Philadelphia USA21 similar to Sin W study done in China in terms of the number of participants and purpose of study. It also showed an improvement in depression and hypertension control in the integrated care group compared to the control. The integrated group had a licensed nurse constantly monitoring the participants mental health and bridging the gap between physicians and patients instead of including another external worker that hadn't worked with the participants from the onset as was done in the Chen S study which didn't have nurses working in the primary health care center so it recruited workers from the community and educated them on the knowledge needed to interact with the patients/participants. All the participants in this study were on antihypertensives and antidepressants unlike other studies that had some patients on while others weren't on antidepressants.[18]

Another study conducted exclusively in African Americans in the USA revealed significant findings. It demonstrated that depression indirectly influenced medication adherence. Additionally, self-efficacy directly affected medication compliance, with depression playing a role in shaping self-efficacy. Furthermore, depression was found to be associated with patients' interactions with medical professionals, family members, and the wider community.

In the study, participants in the Counselling African Americans to Control Hypertension (CAATCH) group received monthly educational sessions about high blood pressure and its management from medical personnel (physicians). Patients monitored their blood pressure at home, receiving feedback from physicians. In contrast, the control group received information solely through printed materials.[22]

A cross-sectional study done in USA, which monitored race and sex dependent risk factors for medication non-compliance. Medication noncompliance in black and white women was associated with depression while for men it was noticed predominantly in white males. Other association found with medication noncompliance in the participants was high cost of medication, polypharmacy, comorbidities, not being married (evident mostly in white men).[23]

A study by Xue J et al monitored the connection over time between depressive symptoms, medication compliance and blood pressure control. The study didn't compare patients with and without depression but rather excluded patients without depressive symptoms. The study showed that medication noncompliance can be improved by enlightening the patient on disease and benefit of lifestyle improvement and medication use, employing inspirational techniques, easing dosage schedules as well as employing (using) sophisticated methods to get around patient-specific obstacles.[24]

A cross sectional study done in Palestine excluded patients with depressive symptom or on medications for depression unlike the Xue J et al study which exclude patients without depressive symptoms. This study showed that depressive symptoms were associated with non-compliance with medications, overweight, and having quality health care while those with better mental health had their disease for longer, quality family and community support as well as good rapport between physician and patient.[25]

Limitation:

The studies varied in the scale of measurement used for assessing depression and medication adherence. The studies had a higher number of female participants compared to male participants. Some of the studies exhibited recall bias, as they required participants to answer questions about past events. A combination of factors contributes to medication non-compliance, with depression being one of the primary factors, as evaluated in this systematic review.

CONCLUSION

Patients receiving integrated care experienced a decrease in symptoms of depression, enhanced medication adherence, and improved control of hypertension.

The studies show that consistent check-ups, monitoring patient progress, assessing medication side effects, adjusting management strategies as needed, providing ongoing explanations of medical conditions, offering home or telephone monitoring, providing social support, and addressing income disparities are beneficial in managing hypertension and depression.

The presence of a supportive family and community environment was linked to lower depression scores and improved medication adherence.

The research suggests that enhancing the mental health of patients with chronic diseases such as hypertension leads to improved overall health outcomes. This is because patients are more likely to adhere to medication regimens and adopt healthier lifestyles, ultimately contributing to their longevity.

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TABLE 2: Characteristics of the included study

Author and Year of Publication	Country	Number of participants	Women percentage	Mean Age	Ethnicity
Hennein R 2018[16]	United States	1,559 1017 were hypertensive	53	70	100% White
Okunrinboye 2019[17]	Nigeria	400	62	59.6	100%
Chen S 2022[18]	China	2,365	67	74.5	100%
Shi W 2022[19]	China	60	53.3	65.78 65.64	100%
Qin W 2023[20]	China	2,382	61.3	64.9	100%
Bogner HR 2013[21]	United States	60	65	67.1	50.0% white, 38.3%, black/African-American, 10.0% Hispanic/Spanish, 1.7% Asian/Pacific Islander
Schoenthaler AM 2016[22]	United States	815	70.9	57(56.99)	76.9% African-American, 17.1% West Indian/Caribbean, 1,2% Multi-ethnic, 2.3% Others
Williams LG 2018[23]	United States	2,122	59.2	Not reported	69.3% white, 30.7 blacks
Xue J 2019[24]	China	2,362	66.6(1574)	Controlled HTN 73.6 Uncontrolled HTN 74.8	-
Khadoura KJ 2021[25]	Palestine	538	60.95	57.1	-

TABLE 3: Quality Appraisal using the Newcastle Ottawa tool

Study	Selection	Comparability	Outcome
Hennein R 2018[16]	***	**	**
Okunrinboye 2019[17]	***	**	**
Qin W 2023[20]	***	**	**
Schoenthaler AM 2016[22]	***	**	**
Williams LG 2018[23]	***	**	**
Khadoura KJ 2021[25]	***	**	**

TABLE 4: Summary of the included studies

First Author	Type of study	Purpose of study	Result	Conclusion
Hennein R[16]	Cohort	To access medication compliance risk factors and the correlation between compliance and levels of CVD risk variables in older adults with hypertension, dyslipidemia, and diabetes.	191 of 1559 patients who took blood pressure, lipid and or diabetes control had low medication compliance. 99 out of 1017 had Low compliance to antihypertensives which was associated with High mean diastolic pressure.	The difficulty in taking prescribed medications on account of depressive symptoms may make older persons' CVD risk factors worse.
Okunrinboye[17]	Cross sectional	To study the degree of occurrence of depression in hypertensive patients	A large number of participants had a high medication adherence despite the presence of depression	Constant checkup is recommended for adjusting of antihypertensives to developing depressive symptoms as a complication of antihypertensive medication
Chen S[18]	Randomized control trial	To compare between the outcome of integrated care and usual care in patients with both depression and hypertension in Chinese adults over the age of 59 years	There was better control of Blood Pressure in patient managed with integrated care method compared to usual care irrespective of whether antidepressant was taken or not	The integrated method of management showed a significant change when compared with usual management method in both blood pressure control and depression in comorbid patients
Shi W[19]	Clinical trial	To investigate the effect of integrated management that includes the medical personnels, society and family members cooperation on hypertension control and mental health in hypertensive patients.	Nursing satisfaction, blood pressure, anxiety, and depression, improved after treatment	Medication adherence, mental health and hospital care is able to improve by integrated method of care.
Qin W[20]	Cross sectional study	To access the correlation between hypertension and poverty level in hypertensive patients above 44 years	Hypertension was anticipated to be more likely with greater levels of poverty. The relationship between poverty level and hypertension management was partly influenced by depression and compliance with medication.	Improving the standard of living of citizen will impact blood pressure control positively in addition to healthcare management
Bogner HR[21]	Randomized Control Trial	To determine the extent to which incorporating depression management into hypertension care enhanced the management of hypertension and depressive symptoms.	Participants in the integrated method of management showed improved depression symptoms in addition to better hypertension control when compared with the control group.	In real-world settings with constrained resources and multiple needs, adoptionof integrated method of management will be facilitated by training current primary healthcare staff.
Schoenthaler AM[22]	Cross sectional Study Randomized clinical trial	To determine the effect on medication compliance that good patient-medical personnel interaction and mental health has.	In black* hypertensive patients, self-efficacy is a major indicator of treatment compliance.	Symptoms of depressive disorder and the perceived caliber of interaction between patients and healthcare professionals both have an impact on initial levels of self-efficacy.
Williams LG[23]	Cross-sectional study	To access the gender-ethnic related contributing factor for prescription non-compliance monitored by medication refill.	Medication noncompliance was almost two time worse in black females compared to white, In white males being single and having depression was associated with medication noncompliance	Hypertension control and medication compliance can be achieved by generation and execution of gender-ethnic specific measures to curb blood pressure treatment noncompliance.
Xue J[24]	Randomized Clinical Trial	To assess how medication compliance affects hypertension control in older patients with depressive symptoms.	Noncompliance to medication complicates blood pressure control in elderly patients with depression	Health care professionals in a primary health care setting can improve hypertension control by constant encouragement in treatment compliance.
Khadoura KJ[25]	Cross-sectional study	To ascertain the prevalence of undetected depression among patients with diagnosed high blood pressure at basic healthcare facilities and its contributing variables.	About 25%of all cases of depression were undetected in hypertensive patients, while 50% of these patients had moderate or severe depressive symptoms.	Regular evaluation of depressive symptoms needs to be carried out in hypertensive patients at the basic healthcare facilities.

TABLE 5: Depression and medication assessment.

Study	Depression assessment	Medication compliance measure
Hennein R [16]	Center for Epidemiologic Studies of Depression (CES-D) scale	four-item Morisky Medication Adherence Scale
Okunrinboye [17]	Hamilton Rating Scale for Depression (HAM-D)	Eight-item Morisky Medication Adherence Scale (MMAS)
Chen S [18]	Patient Health Questionnaire-9 [PHQ-9] Hamilton Depression Rating Scale (HDRS)	Not done
Shi W [19]	Zung Self-Rating Depression Scale (SDS) Zung Self-Rating Anxiety Scale	Not reported
Qin W [20]	Patient Health Questionnaire-9 (PHQ-9)	Self-report
Bogner HR [21]	Patient Health Questionnaire	Not done
Schoenthaler AM [22]	Patient Health Questionnaire (PHQ-9)	four-item Morisky Medication Adherence Scale
Williams LG [23]	20-item Center for Epidemiologic Studies Depression Scale	Pharmacy refill adherence (proportion of days covered)
Xue J [24]	Patient Health Questionnaire-9 (PHQ-9) 17- item Hamilton Depression Rating Scale Patient Health Questionnaire-9 (PHQ-9)	Self-report
Khadoura KJ [25]	Beck's Depression Inventory (BDI-II)	Morisky, Green, and Levine Adherence Scale (MGL)

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