

A Systematic Review of Factors Influencing Medication Adherence to Hypertension Treatment in Developing Countries

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How to cite this paper: Dhar, L., Dantas, J. and Ali, M. (2017) A Systematic Review of Factors Influencing Medication Adherence to Hypertension Treatment in Developing Countries. *Open Journal of Epidemiology*, 7, 211-250.

<https://doi.org/10.4236/ojepi.2017.73018>

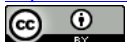
Received: May 18, 2017

Accepted: August 6, 2017

Published: August 9, 2017

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Abstract

Background: Coronary heart disease (CHD), a complication of hypertension, is one of the most important and common causes of morbidity, hospitalisation, and mortality among hypertensive population. In recent decades, increased urbanisation and changes to lifestyle, diet and physical activity in developing countries have led to a major increase in the population incidence of chronic diseases including CHD. Poor medication adherence is one of the leading causes of failure to achieve hypertension control. The objective of this systematic review is to describe the prevalence of non-adherence to anti-hypertensive medications among hypertensive population in developing countries and identify factors associated with it. **Methods:** A literature search was conducted using the following scholarly electronic databases: Proquest, PubMed, JSTOR and Science Direct. The online search engine, Google Scholar was also used to search for and identify relevant papers. Peer-reviewed full-text articles published in English on hypertensive adults in developing countries that measured adherence to antihypertensive medications and their associations with different factors were eligible for inclusion. The review followed the PRISMA reporting and analytical guidelines for systematic reviews. **Results:** In all, 42 studies conducted across 19 developing countries were selected for the review. The mean prevalence of medication non-adherence (MNA) among the select hypertensive population was 47.34%. Very few studies were conducted in community settings and except for one, no study examined gender differences in MNA factors. The analysis revealed a range of factors that can influence MNA including low household income and socioeconomic status; knowledge and beliefs of hypertension and its management; avoiding side effects of medications; cost of medication; use of herbal preparations; absence of symptoms; irregular follow-up; and dissatisfaction with the treatment and health services provided. There was a general lack of consideration of role of health system in health care delivery, self-efficacy, cultural barriers, per-

ceived individual risk of hypertension complications. There was also a lack of gender-specific research which is necessary at community settings given the social and economic vulnerabilities faced by women in developing countries that may affect adherence to antihypertensive medications. **Conclusions:** Future research in developing countries should consider individual risk perceptions, cultural barriers, gender and the role of local health system in health care delivery when assessing MNA among hypertensive population at community settings.

Keywords

Medication Adherence, Compliance, Hypertension, Antihypertensive Treatment, Developing Countries

1. Introduction

High blood pressure or hypertension is one of the most important risk factors for cardiovascular disease and a leading cause of premature adult deaths worldwide [1]. Uncontrolled hypertension causes 50% of the total coronary heart disease (CHD) deaths globally [1]. An analysis of global data reveals that of the deaths from CHD approximately 80% will occur in low and middle-income countries, [2] and this is particularly common among people of low socioeconomic status [3] [4]. Regardless of race or ethnicity, the disease also accounts for the death of one in three women globally [5] with an estimated 3.4 million women dying from CHD every year worldwide [6].

Among all the WHO regions, the prevalence of hypertension is highest in the African Region (46%) and lowest in the region of the Americas (35%) [7]. One in three adults in the South East Asia region has hypertension [7]. Findings from recent studies also indicate a higher prevalence of hypertension in middle-aged and older women compared to men in developing countries [8] [9] [10] and CHD causes significant morbidity and mortality in women during childbearing years [11].

In developed countries, strong public health policies, multi-sectored preventive action and widely available diagnosis and treatment have led to an appreciable reduction in the prevalence of high blood pressure (BP) [7]. As little as 2 mmHg population-wide decrease in BP can prevent 151,000 strokes and 153,000 CHD deaths globally [12]. Despite the availability of over a hundred different effective drugs for hypertension treatment, the reported rates of blood pressure control are very disappointing [13]. Between 2000 and 2013, the number of deaths attributable to hypertension rose from 7.6 to 9.4 million [14]. A systematic review of the studies published from 2001 to 2007 revealed that BP was poorly controlled in developing countries, the mean proportion of control of hypertension among all hypertensive patients being only 13% [15]. Poor medication adherence is one of the leading causes of failure to achieve BP control

[16]. In developing countries, the degree of non-adherence is assumed to be higher particularly due to the shortage of health resources and difficulties in access to healthcare [4].

The WHO defines adherence to long term therapy as “the extent to which a person’s behaviour—taking medication, following a diet, and, or executing life-style changes corresponds with agreed recommendations from a healthcare provider” [4]. The term compliance to medicine is defined as “the extent to which a patient acts in accordance with the prescribed interval and dose of the dosing regimen” reported as a percentage of prescribed doses taken at the prescribed time interval [17] [18]. Despite these variations, these terminologies have been used interchangeably in most studies [19]. Most of the studies on adherence have been undertaken in developed countries. However, healthcare access, cultural beliefs, education about chronic illnesses and the functions of medication, the nature of patient-physician interactions and social support, among many other factors, are very different in developing countries compared to developed countries and may profoundly affect rates of medication adherence [20] [21].

Over the past decade, though some studies have been conducted in developing countries to explore the factors influencing medication adherence among hypertensive patients, little has been documented about MNA and its determinants of hypertensive patients. This systematic review was conducted to address this gap and examine the prevalence of MNA among hypertensive patients as well as investigate factors affecting MNA in this population.

2. Methods

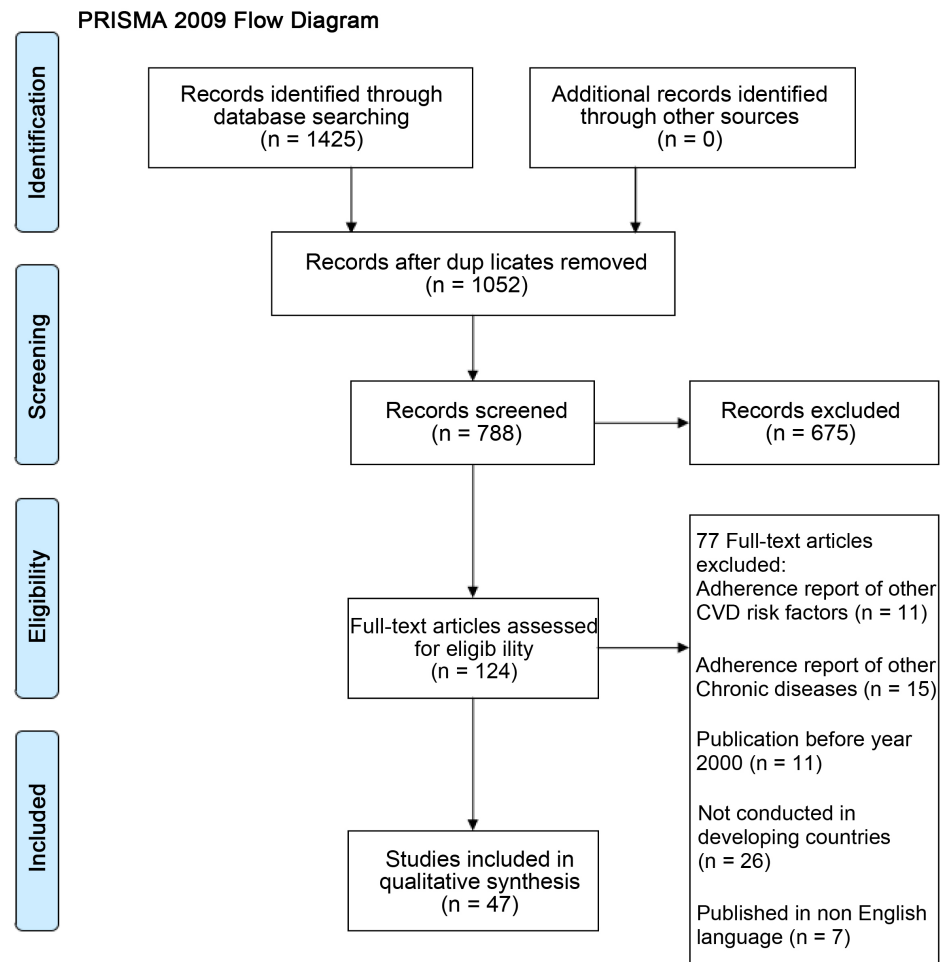
Literature search was conducted using the electronic databases: Proquest, PubMed, JSTOR and Science Direct for articles published during 2000-15. The online search engine, Google Scholar was also used to search for and identify likely papers. The search strategy included the following terms:

- adherence, non-adherence, compliance, persistence (related to medication adherence).
- hypertension, high blood pressure (Blood pressure $\geq 140/\geq 90$ mm of Hg).
- belief, perception of hypertension and
- developing countries (the World Bank classifies all low- and middle-income countries as developing countries-however, this term is not intended to imply that all economies in the group are experiencing similar development or that other economies have reached a preferred or final stage of development).

2.1. Study Selection

From the initial search, 1425 titles and abstracts were identified. Duplicates were removed. Abstracts and titles were screened for relevance, and an initial list of 124 relevant articles was made (**Figure 1**). The full-texts of these articles were then examined to determine eligibility for inclusion in the systematic review using the following selection criteria:

The inclusion criteria for the review were clinical research:



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 6(6): e1000097. doi: 10.1371/journal.pmed1000097
For more information, visit www.prisma-statement.org.

Figure 1. Results of screening process.

- 1) Measured adherence to antihypertensive medications in developing countries.
- 2) Identify factors related to medication adherence with the antihypertensive treatment.
- 3) Enrolled hypertensive adults (18 years and older).
- 4) Published in English as a peer-reviewed full-text article.

We excluded studies that measured adherence of other chronic diseases or were conducted in developed countries and published in a non-English language.

2.2. Data Extraction and Analysis

The total number of relevant articles meeting the above criteria was 47, consisting of 45 peer-reviewed journal articles and two thesis papers: 40 were on quantitative studies, five on qualitative studies and two were mixed methods stu-

dies. To check the quality of quantitative studies the National Collaborating Centre for Methods and Tools' quality assessment tool for quantitative studies was used [22]. Qualitative studies were checked based on NICE guidelines [23].

A standardised data extraction form was used to record the citation details, methodology and objectives, and main findings of each paper. The following information was extracted and tabulated by the first reviewer and verified by the second and third reviewers: author name, date of publication, the country in which research was conducted, sample size, sampling method, study design, sex (% female), the adherence measure used, key findings and any statistical information (odd ratios, 95% CI p-value, correlation coefficients). A summary of the studies reviewed was provided in **Table 1**. A meta-analysis of the findings was not possible due to the heterogeneity in important aspects of methodology of the

Table 1. Summary of variables under the domain of demographic factors investigated by the studies.

Variables being investigated	Study	Measurement of medication adherence	Setting and sample size
Age	Boima <i>et al.</i> [26]	MMAS 8	Ghana and Nigeria; N = 357
	Nagarkar <i>et al.</i> [27]	MMAS 8	India; N = 174
	Bilal <i>et al.</i> [60]	Questionnaire	Pakistan; N = 113
	Lalic <i>et al.</i> [28]	MMAS 8	Serbia; N = 170
	Khanam <i>et al.</i> [29]	Questionnaire	Bangladesh; N = 29,960
Sex	Praveen <i>et al.</i> [30]	Questionnaire	India; N = 804
	Ismael <i>et al.</i> [31]	Questionnaire	Iraq; N = 200
	Bilal <i>et al.</i> [60]	Questionnaire	Pakistan; N = 113
	Joho <i>et al.</i> [32]	Questionnaire	Tanzania; N = 135
Level of education	Khanam <i>et al.</i> [29]	Questionnaire	Bangladesh; N = 29,960
	Bhandari <i>et al.</i> [33]	MMAS 4	Nepal; N = 154
Household income and employment	Boima <i>et al.</i> [26]	MMAS 8	Ghana and Nigeria; N = 357
	Hussain <i>et al.</i> [34]	Questionnaire	Bangladesh; N = 120
	Gelaw <i>et al.</i> [35]	Questionnaire	Ethiopia; N = 91
Type of family	Bilal <i>et al.</i> [40]	Questionnaire	Pakistan; N = 113
	Nagarkar <i>et al.</i> [27]	MMAS 8	India; N = 174
	Hareri <i>et al.</i> [36].	Questionnaire	Ethiopia; N = 365
Comorbidities	Khanam <i>et al.</i> [29]	Questionnaire	Bangladesh; N = 29,960
	Ambaw <i>et al.</i> [37]	MMAS 4	Ethiopia; N = 384
	Al-Ramahi <i>et al.</i> [38].	MMAS 8	Palestine ; N = 450
	Boima <i>et al.</i> [26].	MMAS 8	Ghana and Nigeria; N = 357
Use of herbal preparation	Saleem <i>et al.</i> [39]	Qualitative	Pakistan
	Oduola <i>et al.</i> [40]	Qualitative	Nigeria

selected studies including sampling procedure (random/purposive) population ages, study settings (hospital/clinic/community), study design (cross-sectional/longitudinal/qualitative) and measurement procedure of medication adherence. Descriptive analysis of studies examining similar variables and any association observed were considered to offer a simple indication of the level of evidence. Summary ranges of quantitative proportions and measures relating to prevalence and factors associated with MNA were compiled and presented. The evidence from the studies was synthesised and presented in a narrative review. The review followed the PRISMA reporting guidelines [24].

3. Result

3.1. Description of the Studies

The selected studies were conducted in developing countries in Asia (22) Africa (17), the Middle East (4), South America (2), and Europe (1). Among the 42 quantitative studies, the majority (33 studies [78.57%]) were conducted in urban hospital or clinic settings, with only nine studies were carried out in community settings (five in India and one each from Bangladesh, Nepal and Nigeria). Most of the studies (34 studies) were cross-sectional quantitative in type. A study from Nigeria was mixed methods in type, comprising both quantitative and qualitative methods for data collection [25]. A summary of the characteristics and the aim of each study are shown in **Table A1**.

The five qualitative studies were from India (1), Pakistan (1), Congo (1), Malaysia (1) and Nigeria (1). Three studies used one-to-one qualitative interviews, one study used focus group discussion, and one used a combination of these methods. Further details of the study designs and results are presented in **Table A1**. In all of the studies, the study population included both males and females. Overall women comprised 55.98% of study participants.

3.2. Reported Adherence to Antihypertensive Treatment

To measure medication adherence, 21 (50%) of the quantitative studies used the 'Morisky Medication Adherence Scale'. Other scales used in the four different studies were: Medicines Team Questionnaire-Qualiaids (QAM-Q) (1); Beliefs about Medicine Questionnaire (BMQ) (1); Hill-Bone Adherence to Blood Pressure Therapy Scale (1); Drug Attitude Inventory (DAI-10) (1); One study used Medication Event Monitoring System (MEMS) and one used pill count to measure adherence. The remaining studies used questionnaires. Among them, eleven studies used structured questionnaires with established reliability and or validity, while eight studies (33%) did not cite information on their reliability or validity. The rate of MNA among hypertensive population ranged from 23% - 6.76% with the mean being 47.34%.

3.3. Factors Impacting on Adherence

The identified factors related to MNA in the reviewed studies could be catego-

rised into seven domains: demographic; psychosocial; perceptions regarding hypertension and its severity; perceptions regarding antihypertensive treatment; perceived barriers to treatment adherence; treatment and disease related factors; and health care services.

3.3.1. Demographic Factors

Sixteen studies reported significant associations between demographic variables (such as age, sex, level of education, types of family, household income, employment, type of family, co-morbidities and use of herbal preparations) and MNA to hypertensive therapy (**Table 1**).

The effect of age on medication adherence showed conflicting results. Younger age was found to be significantly associated with MNA to hypertensive medications in India (≤ 57 years) [OR (odd ratio) 3.348; 95% Confidence Interval (CI): 1.665 - 6.732] [27], Palestine (< 45 years) (OR = 0.40; 95% CI: 0.157 - 0.99) [38] and Pakistan (≤ 51 years) (OR = 1.0; 95% CI: 1.00 - 1.04). The mean age of hypertensive patients who were not adherent to medications was 54.5 ± 13.2 years while those who were adherent had a mean age of 60.9 ± 12.1 years ($P < 0.001$) in Ghana and Nigeria [26]. On the other hand, a significantly lower level of adherence was identified in a study with elderly patients in Serbia. In this study patients less than 65 years were found to be more likely to adhere to their prescribed treatment, compared to older patients (AOR = 6.0; 95% CI: 2.76 - 13.04) [28].

Being female was independently and significantly associated with poor adherence in a study in India (AOR = 2.95; 95% CI: 1.39 - 6.24) with hypertensive women 2.95 times more likely to be non-adherent to their medications than men [30]. A study in Iraq also revealed that female hypertensive patients (61.7%) were more non-adherent than male (30.3%) patients [31]. On the other hand, MNA was significantly associated with male gender in Pakistan ($P = 0.008$) [60], Tanzania ($P = 0.044$), [32] and Bangladesh (AOR = 1.67; 95% CI: 1.42 - 1.97) [29]. However, several studies [26] [33] [34] [41] [42] found no significant association between gender and MNA among hypertensive patients. Thus, the effect of gender on MNA showed conflicting results across countries.

Hypertensive patients in Nepal who were illiterate almost five times less likely to be adherent to medications than those who were literate (AOR = 5.34, 95% CI: 1.23 - 23) [33]. Similarly, lower level of education was significantly associated with MNA among hypertensive patients in Bangladesh (OR = 6.34; 95% CI: 1.65 - 24.41) [34]. On the other hand, formal education was associated with MNA ($P = 0.001$) in Ghana and Nigeria [26]. A study in India found that educational level was not a significant contributing factor to non-adherence [43]. From these results, it seems that educational level may not always be a good predictor of MNA.

Hypertensive patients with low monthly income (AOR = 11.60; 95% CI: 3.77 - 35.65) in Bangladesh [34] and Ethiopia ($P = 0.04$) [35] were more non-adherent

to their medications. In Pakistan, [44] the likelihood of MNA was also found to be higher among unemployed persons ($P = 0.002$) and people with low socioeconomic status ($P = 0.046$). Hypertensive patients who had private businesses were 72% less likely to adhere to medication compared to government employees (AOR = 0.28, 95% CI: 0.130 - 0.606) in Ethiopia [45]. Hypertensive patients living in a nuclear family setup in India were more likely to have lower adherence to medication as compared to staying in the extended family (OR = 2.67; 95% CI: 1.378 - 5.175) [27].

Hypertensive patients with co-morbidities were 50% less likely to be adherent to their medications compared to patients with no co-morbidity (AOR = 0.50; 95% CI: 0.290 - 0.893) in Ethiopia [36]. In Bangladesh, hypertensive patients with cardiovascular co-morbidity were significantly associated with MNA (AOR = 0.79; 95% CI: 0.64 - 0.97) [29]. A study in north-west Ethiopia [37] also found that patients with no and one co-morbidity were more likely to adhere to their treatment than those with two (AOR = 2.50, 95% CI: 1.01 - 6.21) or more than two co-morbidities (AOR = 2.68, 95% CI: 1.07 - 6.71). However, having no other chronic disease ($P = 0.009$) was a significant factor influencing MNA among hypertensive patients in Palestine [38].

In Ghana and Nigeria, patients who used herbal preparations for the treatment of hypertension were more likely to show MNA ($P = 0.014$) [26]. In a qualitative study in Pakistan, [39] almost all the hypertensive patients surveyed firmly supported the utilisation of traditional or herbal remedies for the control of their high BP and confirmed that usually only in the case of failure of these therapies would they seek help from modern or biomedical health care providers. A qualitative study in Nigeria found some patients with low medication adherence substituted or complemented prescribed pills with herbal remedies on their own without informing their doctor [40].

3.3.2. Psychosocial Factors

Seven studies reported significant associations between psychosocial variables (such as family support, depression and use of social drugs) and MNA to hypertensive treatment (Table 2).

An absence of household support had a strong negative effect on adherence among hypertensive patients in Ethiopia (AOR = 0.170, 95% CI: 0.030 - 0.905) [46] and Nigeria ($p < 0.05$) [47]. Likewise, studies [41] [49] in Congo reported that patients who received no support from family members regarding reminders about taking their medications were likely to be more non-compliant than the others. A qualitative study in Congo [49] found that there was a perception among some family members that the hypertensive patient had brought the condition upon him-/herself by being a bad person: “*They say I developed hypertension because I killed her sister*’ (through witchcraft).” Though family cohesion is very high in Bangladesh, lack of an accompanying person to go to the physician/hospital was a significant factor in determining non-adherence to antihypertensive treatment (OR = 3.54; 95% CI: 1.04 - 11.99) [34]. This lack of

Table 2. Summary of variables under the domain of psychosocial factors investigated by the studies.

Variables being investigated	Study	Study design	Study setting and sample size
Family support	Hussain <i>et al.</i> [34]	Questionnaire	Bangladesh; N = 120
	Nsitou <i>et al.</i>	Questionnaire	Congo; N = 212
	Lubaki <i>et al.</i> [48]	Qualitative	Congo
	Ali <i>et al.</i> [46]	MMAS 8	Ethiopia; N = 121
Depression	Oloookere [47]	Questionnaire	Nigeria; N = 420
Use of social drugs	Boima <i>et al.</i> [26]	MMAS 8	Ghana and Nigeria; N = 357
	Khanam [29]	Questionnaire	Bangladesh; N = 29,960
	Ahmed <i>et al.</i> [48]	MMAS 8	India; N = 334
	Kamran <i>et al.</i> [50]	MMAS 4	Iran; N = 671
	Bhandari <i>et al.</i> [33].	MMAS 4	Nepal; N = 154

support may be due to lack of knowledge of the family members about the disease process. When patients are depressed, they are less likely to follow health care providers' treatment plan for hypertension. In Ghana and Nigeria [26] MNA occurred in patients who had varying degrees of depression ($r = -0.208$, $P < 0.001$) ($r =$ Pearson's correlation coefficient).

A World Health Organization report observed that alcohol abuse and tobacco smoking were important modifiers of compliance behaviour. Patients' habit of alcohol consumption, [29] [48] tobacco chewing, [48] and smoking [29] [48] [50] were strongly associated with poor adherence to anti-hypertensive treatment in studies in India, Iran and Ethiopia. In contrast, a study in Nepal did not find any significant association between tobacco use and alcoholism with MNA among hypertensive study participants [33].

3.3.3. Perceptions Regarding Hypertension and Its Severity

Four studies reported significant associations between variables related to perceptions of hypertension and MNA to hypertensive medications. These factors included: awareness, knowledge and belief of hypertension and knowledge of the severity of hypertension.

Researchers found that poor understanding and belief in high blood pressure were significant factors associated with MNA in Bangladesh (AOR = 12.90; 95% CI: 1.65 - 100.63) [34] and in Ethiopia ($P < 0.01$) [35]. A qualitative study in Pakistan [39] revealed that once patients achieved control of their high BP, they tended to discontinue their medications. Those patients with an inadequate knowledge of hypertension related complication were also more likely to be non-adherent with the treatment regimen, as found in a study in Bangladesh (OR = 23.71; 95% CI: 3.38 - 166.46) [34] and Congo (OR = 2.9; 95% CI: 1.61 - 5.29) [41]. Diagnosed hypertensive patients who lacked knowledge regarding the severity of hypertension were also more likely to be non-adherent to medica-

tions in Congo (AOR = 0.34; 95% CI: 0.13 - 0.94) [41] and Bangladesh (AOR = 23.71; 95% CI: 3.38 - 166.46) [34].

3.3.4. Perceptions Regarding Antihypertensive Treatment

Eight studies found significant associations between variables related to antihypertensive treatment and MNA (Table 3).

Studies in Congo (AOR = 0.36; 95% CI: (0.15 - 0.83), [41] Bangladesh (AOR = 24.50; 95% CI: 6.28 - 95.58), [34] and Ethiopia [35] ($P < 0.01$) reported that patients' lack of knowledge about hypertension management was significantly associated with non-adherence to therapy. A significant correlation between beliefs about medication and MNA was found among hypertensive patients in Ghana and Nigeria [26] with patients who were worried about the adverse effects of antihypertensive drugs less likely to be adherent to their medications ($r = -0.0347$, $P = 0.002$). Qualitative studies in Pakistan [39] and Malaysia [51] also found patients hesitated to take medications continuously due to their lack of belief in medications. As one hypertensive patient in Pakistan commented: "Medications are hot (warm) in nature. They enter the stomach and increase temperature which interferes with digestion." A study in Palestine found that patients with hypertension were not adhering to their medication due to the fear of dependent on medicines (AOR = 8.00; 95% CI: (2.44 - 26.19) [38]. Similarly avoiding side effects of drugs (AOR = 3.0; 95% CI: 1.4 - 6.7) was an important reason for non-adherence to their treatment regimen among hypertensive patients in Nigeria [42].

Hypertensive patients who did not understand their drug regimen well were poorly adherent to their prescribed medications (AOR = 4.06, 95% CI: 1.01 - 16.32) in India [30] and Ethiopia (AOR = 0.12, 95% CI = 0.258 - 0.583) [36].

Table 3. Variables summarised under the domain of perceived barriers to antihypertensive treatment and MNA investigated by studies.

Variables being investigated	Study	Measurement of medication adherence	Study setting and sample size
Knowledge about hypertension management	Hussain et al. [34]	Questionnaire	Bangladesh; N = 120
	Nsitou et al. [41]	Questionnaire	Congo; N = 212
	Gelaw et al. [35]	Questionnaire	Ethiopia; N = 91
Belief about medication	Boima et al. [26]	MMAS 8	Ghana and Nigeria; N = 357
	Saleem et al. [39]	Qualitative	Pakistan
	Shima et al. [51]	Qualitative	Malaysia
	Al-Ramahi et al. [38]	MMAS 8	Palestine; N = 450
	Campbell et al. [42]	MMAS 4	Nigeria; N = 262
Avoiding side effect of medications	Hareri et al. [36]	Questionnaire	Ethiopia; N = 365
	Praveen et al. [30]	Questionnaire	India; N = 804
Do not understand drug regimen well	Gelaw et al. [35]	Qualitative	Ethiopia
	Oduola et al. [40]	Qualitative	Nigeria

Gelaw *et al.* [35] found that insufficient information about the consequence of non-adherence to hypertension treatment contributed to the non-adherence of the hypertensive patients in Ethiopia. In Nigeria, a qualitative study also found ignorance about regular use of medication was an important contributor to medication non-adherence [40].

3.3.5. Perceived Barriers to Adherence

Sixteen studies found significant associations between aspects related to perceived barriers and MNA. These perceived barriers were: the cost of medications, the number of pills that needed to be taken on a daily basis, forgetfulness, side effects of medications, duration of therapy, satisfaction with the treatment and health services provided, and distance from health care centre (Table 4).

Table 4. Variables investigated under the domain of perceived barriers and MNA.

Variables being investigated	Study	Measurement of adherence	Study setting and sample size
Cost of medications	Bhandari <i>et al.</i> [33]	MMAS 4	Nepal; N = 154
	Nsitou [41].	Questionnaire	Congo; N = 212
	Eizubier [52]	Pill count	Sudan ; N = 198
	Praveen [30]	Questionnaire	India; N = 804
	Bhandari <i>et al.</i> [33]	MMAS 4	Nepal; N = 154
	Srikanth <i>et al.</i> [53]	MMAS 8	India; N = 304
	Olowookere [47]	Questionnaire	Nigeria; N = 420
Number of pills	Ramli [54]	The hill bone adherence to BP scale and MMAS 8	Malaysia; N = 653
	Bilal <i>et al.</i> [44]	Questionnaire	Pakistan; N = 113
Forgetfulness	Srivastava <i>et al.</i> [55]	Self-report and MMAS 4	India; N = 440
	Campbell <i>et al.</i> [42]	Morisky Green	Nigeria; N = 262
	Al-Ramahi [38]	MMAS 8	Palestine; N = 450
Side effect of medicine	Lalic <i>et al.</i> [28]	MMAS 8	Serbia ; N = 170
	Shima [51]	Qualitative	Malaysia
	Oduola [40]	Qualitative	Nigeria
Duration of therapy	Bhandari <i>et al.</i> [33]	MMAS 4	Nepal; N = 154
	Hareri <i>et al.</i> [45]	Questionnaire	Ethiopia; N = 286
	Lalic <i>et al.</i> [28]	MMAS 8	Serbia; N = 170
	Bilal <i>et al.</i> [44]	Questionnaire	Pakistan; N = 113
	Hu <i>et al.</i> [56]	Questionnaire	China; N = 318
Distance from health care facilities	Gelaw <i>et al.</i> [35]	Questionnaire	Ethiopia; N = 91
	Al Ramahi [38]	MMAS 8	Palestine; N = 450
	Ambaw <i>et al.</i> [37].	MMAS 4	Ethiopia; N = 384

In non-adherent patients surveyed in Nepal, a significantly greater proportion of patients considered the price of medications to be too high (AOR = 5.14; 95% CI: 1.1 - 23.9) [33] and for which they missed taking their medications (AOR = 0.143; 95% CI: 0.02 - 0.78). The cost of medicine was also a significant factor associated with MNA among patients in Congo (OR = 1.84; 95% CI: 0.93 - 3.64) [41]. Similarly, the inability to buy medications ($P < 0.001$) was positively and significantly related to MNA in Sudan [52]. Even being able to afford only some of the prescribed antihypertensive drugs (AOR = 3.70, 95% CI: 1.81 - 7.59) was also significantly related with MNA in India [30].

In Nepal, non-adherence was significantly associated with therapy requiring more than one pill per day (AOR = 5.33; 95% CI: 1.19 - 23.7) compared to patients prescribed only one pill per day [33]. MNA was also greater among patients with higher pill burden in India, [53] Nigeria, [47] and Malaysia [54] ($P < 0.05$). On the other hand, a couple of studies [44] [55] found that when patients had to take multiple medications, perhaps, they were less likely to fail to remember to take them, compared to having only one pill. A study in Pakistan [44] found non-adherence was higher among those patients who were on monotherapy and di-therapy compared to patients using 3 or >3 drugs ($P = 0.02$).

Patients also often forget to take even once daily medications. Studies in Nigeria (OR = 14.8; 95% CI: 3.9 - 54.8) [42] and Palestine (AOR = 5.12; 95% CI: 3.12 - 8.41) [38] found significant correlation between forgetfulness and non-adherence among hypertensive patients.

Hypertensive patients who experienced side effects of their medications were less adherent to their medication than those who did not experience side effects in Palestine (AOR = 4.58; 95% CI: 1.87 - 11.25) and Serbia (OR = 7.95; 95% CI: 1.48 - 42.6) [28] [38]. Qualitative studies in Malaysia [51] and Nigeria [40] also found perceived side effects were inhibitors of antihypertensive medication adherence. However, Praveen *et al.* [30] in India did not find a correlation between adverse drug events and non-adherence.

Patients who had had a diagnosis of hypertension of five or more years were less likely to adhere to treatment than those who had been diagnosed for less than five years in Nepal [33] (OR = 2.98; 95% CI: 1.73 - 5.14) and Ethiopia (AOR = 0.11, 95% CI: 0.013 - 0.955) [45]. Lower levels of adherence in elderly patients with longer duration of antihypertensive therapy were also found in Serbia [28]. On the other hand, patients with shorter duration of hypertension were less likely to be adherent to treatment in Pakistan (<5 years) (AOR = 0.11, 95% CI: 0.013 - 0.955) [44] and China (<3 years) (AOR = 3.31; 95% CI: 1.91 - 5.72; $P < 0.001$) [56].

Distance from health care facilities was a significant barrier for adherence to treatment. Longer distance from medical centres contributed to MNA of hypertensive patients in Ethiopia [35]. In the same way, those living in rural areas had poorer adherence to hypertensive medications in Palestine than those living in urban areas (AOR = 1.79; 95% CI: 1.10 - 2.92) [38]. As the remoteness from the hospital decreased, adherence to hypertension treatment improved (AOR = 2.02;

95% CI: 1.19 - 3.43) in Ethiopia [37].

3.3.6. Treatment and/or Disease Related Factors

Eleven studies found a number of treatment or disease related factors associated with MNA. These included absence of disease symptoms, complication, irregular follow-up, family history of hypertension and poor BP control (Table 5).

The absence of symptoms significantly contributed to poor compliance to hypertensive therapy in Nigeria (AOR = 3.3; 95% CI: (1.3 - 8.0) [42] and India (OR = 0.414; 95% CI: 0.192 - 0.892) [27]. Qualitative studies in Congo [49] and India [58] also found hypertensive medications were more likely to be taken when the patient experienced symptoms of hypertension.

The presence of hypertension-related complications such as heart diseases (AOR = 21.73, 95% CI: 1.568 - 418.42 $P = 0.000$) was found to be associated with decreased medication adherence among patients in Ethiopia [46]. In contrast, a study in Pakistan found that cases suffering from hypertension-related complications were more likely to be adherent to medications [57].

In Nepal, those with no family history of hypertension were less adherent to their medications compared to those with a family history of high BP (OR =

Table 5. Variables summarised under the domain of treatment and/or disease related factors investigated by the studies.

Variables being investigated	Study	Measurement of medication adherence	Study setting and sample size
Absence of disease symptoms	Campbell <i>et al.</i> [42]	Morisky Green	Nigeria ; N = 262
	Nagarkar <i>et al.</i> [27]	MMAS 8	India; N = 174
	Lubaki <i>et al.</i> [49]	Qualitative	Congo
	Kusuma <i>et al.</i>	Qualitative	India
Presence of hypertension related complications	Oduola [40]	Qualitative	Nigeria
	Ali <i>et al.</i> [46]	MMAS 8 and patient medication chart	Ethiopia; N = 121
Family history of hypertension	Hashmi <i>et al.</i> [57]	History of pill taken and MMAS 4	Pakistan
	Bhandari <i>et al.</i> [33]	MMAS 4	Nepal; N = 154
Irregular follow up	Bhandari <i>et al.</i> [33]	MMAS 4	Nepal; N = 154
	Praveen <i>et al.</i> [30].	Questionnaire	India; N = 804
Blood pressure control	Boima <i>et al.</i> [26]	MMAS 8	Ghana and Nigeria N = 357
	Lalic <i>et al.</i> [28]	MMAS 8	Serbia; N = 170
	Ramli [54]	The hill bone adherence to BP and MAASA 8	Malaysia; N = 653
	Ali <i>et al.</i> [46]	MMAS 8	Ethiopia; N = 121

4.46; 95% CI: 1.21 - 16.4, $P = 0.024$) [33]. Frequent meetings/appointments provide better monitoring of blood pressure levels, as well as the opportunity to have more access to information and can serve as the basis for adherence to antihypertensive medication management [59]. Irregular follow-up (AOR = 6.39; 95% CI: 1.22 - 33.3), [33] was significantly associated with MNA in Nepal. Similarly, an Indian study reported that a longer time since the last visit to a doctor for advice (AOR = 7.26, 95% CI: 2.65 - 19.86) was significantly related with non-adherence to hypertensive medications [30].

Poor BP control was significantly associated with MNA in Ghana and Nigeria ($P = 0.006$) [26]. BP values over 140/90 mmHg were also reported in 59.1% of non-adherent patients and 21.4% of adherent patients, [Chi Square (χ^2) = 19.84; $P < 0.01$; OR = 5.30 95%, CI: 2.39 - 11.85] in Serbia [28]. Similarly, the average systolic and diastolic blood pressure for non-adherents was significantly higher ($P = 0.05$) than that in adherents in Malaysia [54]. In contrast, a study in Northern Ethiopia [46] found that patients at the pre-hypertension level (BP values below 140/90 mmHg) (AOR = 0.026; 95% CI: 0.003 - 0.242) were less adherent to their medications.

3.3.7. Health Care Services

Four studies found dissatisfaction with the health services and treatment provided' influenced MNA significantly among hypertensive patients (Table 6). A study conducted in Brazil confirmed the high correlation between MNA and dissatisfaction with health services [60]. Hypertensive individuals who were dissatisfied with the care received in primary public health services (such as reception service, scheduling appointment and care received from the health team) were more likely to not adhere to the proposed medication treatment. Inconve-

Table 6. Variables summarised under the domain of health care services investigated by studies.

Variables being investigated	Study	Measurement of medication adherence	Study setting and sample size
Dissatisfaction with the health care services received	Barreto <i>et al.</i> [60]	Morisky-Green test	Brazil; N = 68
	Lubaki <i>et al.</i> [49]	Qualitative	Congo
	Kusuma [58]	Qualitative	Delhi
	Odusola <i>et al.</i> [40]	Qualitative	Nigeria
Inadequate information from health care Centre	Hussain <i>et al.</i> [34].	Questionnaire	Bangladesh; N = 120
Dissatisfaction with treatment	Al-Ramahi <i>et al.</i> [38].	MMAS 8	Palestine; N = 450
Fewer Interaction with physicians	Hussain <i>et al.</i> [34]	Questionnaire	Bangladesh; N = 120

nient clinic operating hours, long waiting time and under-dispensing of medications were found to be inhibitors of adherence in a qualitative study in Nigeria. Studies in Congo [49] and Delhi [58] found that antihypertensive medication were sometimes not readily available at health care centers. Patients waited for long periods to receive medications once they had been prescribed. Rude or unsympathetic behavior and attitudes by staff members at the health clinics was the other reason found for the dissatisfaction of the patients in Congo [49].

In Bangladesh, inadequate information from health care professionals about hypertension and its treatment (AOR = 5.16; 95% CI: 1.13 - 23.66) were significantly associated with MNA [34]. Also in Palestine, patients dissatisfied with treatment were less likely to adhere to prescribed hypertensive medications than those satisfied with their treatments (AOR = 2.93; 95% CI: 1.22 - 7.02) [38]. Due to fewer interactions with the physicians, those receiving treatment at government hospitals had a 30 times greater chance of being non-adherent than those treated at private hospitals or clinics (AOR = 35.29; 95% CI 9.76 - 127.63) in Bangladesh [34].

3.4. Summary of the Result

The results of the review provide insight into factors influencing MNA of hypertensive patients. Factors related to demography, barriers for adherence and treatment and disease related factors were the most commonly examined among the studies reviewed while factors related to perceptions regarding hypertension and its severity were the least examined. Associations of MNA with demographic and psychosocial factors such as age, gender, ethnicity, level of education, co-morbidities, duration of therapy, the number of medicines, use of social drugs, were often varied and not consistent. Factors affecting MNA consistently were: low socioeconomic status and low monthly income; family support; the use of traditional herbal preparations; knowledge and belief regarding hypertension and its management; cost of medications, avoiding side effect of medications; forgetfulness; absence of symptoms; distance from health facilities; irregular follow-up; and dissatisfaction with the treatment and health services provided.

4. Discussion

Though non-adherence to antihypertensive treatment is a significant problem in CHD management few studies on medication adherence have been conducted in developing countries [61]. Moreover, the majority of these studies were conducted in hospital and clinical settings. Studies carried out in low-income community settings are extremely limited.

Our review found that although there was substantial heterogeneity in methods and populations across studies, approximately half of the participated hypertensive population both male and female 18 years and older did not adhere properly to the treatment for hypertension as prescribed by their doctors. De-

spite the higher prevalence of hypertension and its poor control among women in developing countries, we did not find any studies that focused specifically on this vulnerable population. Women in developing countries living with chronic non-communicable diseases such as hypertension experience particular challenges in accessing cost-effective prevention, early detection, diagnosis, treatment and care. The lack of knowledge and information regarding health, poor access to healthcare, family responsibilities, and poor economic, legal and political status further worsen their situation [62].

From 25 studies, we identified significant factors associated with MNA. A limitation of the selected studies was the fact that factors associated with MNA were not examined for gender differences. However, a study in Brazil reported reasons for non-adherence to medication and non-medication regimen in patients' opinion according to gender [63]. Considering the magnitude of inadequately treated or controlled hypertension among women in developing countries, studies that explore factors affecting MNA in this vulnerable population are urgently needed.

4.1. Implications for Hypertension Management and Research

The present review reveals that gender may not be a good predictor of non-adherence because of inconsistent conclusions. However, it is conceivable that women with low socioeconomic status and lower level of education are more vulnerable. Their lack of adherence might be due to their inability to buy medicines, and lack of access to free health facilities as governments in developing countries spend comparatively less of their budgets on health than developed countries. The importance of cost-related factors should be considered against the background of the relatively high out-of-pocket payments for most treatments in developing countries especially in South Asia and Africa.

The review also found that fear of side effects make some hypertensive patients stop their medications or reduce their daily doses without consulting their health care providers. Therefore, information tailored to patient's literacy level about the side effects of prescribed medications and how to manage these should be provided to all patients. From the review, it appears that educational level may not be a good predictor of MNA. However, sceptical attitudes towards anti-hypertensive treatment even among educated participants necessitate the health education on hypertension and its treatment to all hypertensive patients irrespective of the patients' educational status. Understanding potential complications of hypertension could be a motivating factor for adherence to treatment. For this to happen, patients need to be aware of the seriousness of their condition and all risks involved without being worried unnecessarily [64]. To better deal with these problems, educational interventions are required that recognise patients' apprehension and perceptions. In particular, patients should be provided an explanation of the benefits and adverse effects of treatment. The safety of long-term use of drugs needs to be discussed, including the information that treatment

does not cause physical dependence irrespective of the length of treatment.

The review indicated that adherence to antihypertensive medication treatment would be improved if patients experience positive encounters with their doctors or health care providers regarding adequate and accurate advice on achieving control of their high blood pressure [65]. Among the selected studies, there was a general lack of assessment of individual risk perceptions of hypertension complications such as CHD. This is an unfortunate omission given the importance of such risk perceptions in medication adherence. Earlier studies in developed countries have shown that patients who accurately perceive their risk of cardiovascular disease are more likely to be adherent to medications and guidelines compared to those who do not perceive themselves to be at risk [66] [67] [68] [69]. Women's perceptions of their risk for heart disease can significantly influence their decision-making process concerning healthcare choice [70].

The studies in the review did not examine in depth cultural and psychological issues, in particular those relating to self-efficacy (*i.e.* the belief that one can perform a particular behavior under differing conditions which can greatly impact on medication adherence. Cultural restrictions make it difficult for women to seek medical care from male health care providers, [71] but there is, at the same time, a shortage of female health professionals [71]. These issues are compounded by health systems that often fail to respond to the particular needs of women with NCDs such as hypertension [72]. Weak health systems have been identified as a major obstacle in effectively responding to the rising burden of chronic conditions such as hypertension in developing countries. Studies are required that recognise and analyse the intricate associations between health systems and their effects on hypertension management in developing countries [73]. In spite of the need for research on health systems, little attention has also been given to the role of local health systems in the delivery of care for the control of hypertension. Moreover, belief-laden factors including confidence in the physician's knowledge or ability, belief of control over one's health and illness perception were all found to be significantly related to medication adherence in developed countries [74]. Studies in developing countries especially at community settings on these factors influencing adherence would be helpful to address the knowledge gap and contribute to global strategies for addressing non-compliance among hypertensive patients.

4.2. Strengths and Weaknesses of the Review

We have included studies from 20 developing countries (27.40% of all developing countries). Having the study population from less than one third of the developing countries incorporated in the analysis, the conclusions of this review might not be extrapolated to the whole population of the developing countries.

Most of the studies in our review that met inclusion criteria were quantitative in type. Only half of the quantitative studies (20) chose study participants using simple or systematic random sampling techniques. Eight studies used purposive sampling method, thus their results may not be necessarily generalisable to the

wider population. The remaining studies selected all eligible hypertensive patients from clinics/hospitals or communities as their study participants.

The review followed the PRISMA reporting guidelines for identifying, reporting, and synthesising research. The results of the review are robust. Most of studies selected for the review were judged to be of moderate to strong quality in terms of research rigour, reliability and validity. A large number of MNA related factors were consistently identified across different countries. However, this review was subject to a few limitations. This study included only English peer-reviewed journal articles. The majority of the studies relied solely on self-reported adherence, which may be subject to self-presentation and recall bias. Moreover, heterogeneity in important aspects of methodology of the selected studies limits the results that can be drawn from the synthesis of the data. MNA may also be influenced by the time in which the study was performed. Among the selected quantitative studies, only two prospective cross-sectional studies were found. Longitudinal assessment is desirable to differentiate between chronic and occasional non-adherence and related barriers that may contribute to non-adherence.

4.3. Conclusion

This systematic review examined the prevalence of MNA among hypertensive population as well as investigated factors affecting MNA. Approximately half of hypertensive men and women were found to be non-adherent to their medications. Among the selected studies, very few studies were conducted in low-income community settings. MNA was influenced by a range of factors including socio-economic status, knowledge of hypertension and its management, medication side effects, costs of medication, and dissatisfaction with the treatment and health services provided. There was a general lack of consideration of cultural barriers, role of health system in health care delivery, self-efficacy, and perceived individual risk of hypertension complications. Policymakers and health service providers should take these factors into account to tailor culturally appropriate intervention strategies to enhance adherence among hypertensive patients. There is also a lack of gender-specific research which is necessary given the social and economic vulnerabilities faced by women in developing countries that may affect adherence to antihypertensive medications.

Acknowledgements

LD would like to acknowledge the Australian Postgraduate Award and Curtin University Research Scholarship for supporting her research that formed part of her PhD study.

Author Contributions

LD, JD, MA designed the study. LD Carried out the search, selected papers and extracted data. LD, JD, MA participated in data analysis and drafted the manuscript. All authors approved of the final version of the manuscript.

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Appendix

Table A1. Overview and statistics details of the included studies.

Author and year	Country	Study aim	Sampling method and patient population*	% women	Design	Prevalence of MNA (%) and % of female not adhering	Factors associated with medication adherence/MNA
1. Khanam <i>et al.</i> 2014 [29]	Bangladesh	To describe hypertension and factors affecting adherence to treatment among hypertensive person	N = 29,960 Stratified two stage sampling from the population of three rural sites	52.6	Cross-sectional	26/-	Factors associated with MNA: male sex (AOR = 1.67; 95% CI: 1.42 - 1.97), hypertension diagnosed by unqualified providers (AOR = 1.52; 95% CI: 1.31 - 1.77), and patients with cardiovascular comorbidity (OR = 0.79; 95% CI: 0.64 - 0.97).
2. Hussain <i>et al.</i> 2011 [34]	Bangladesh	To identify factors that influence non-adherence to antihypertensive therapy	N=120 Simple random sampling from eligible hypertensive patients of inpatient departments of a medical college and a private clinic	30.8	Cross-section	85/-	Factors determining MNA: lower level of education (OR = 6.34; 95% CI: 1.65 - 24.41), low family income (OR = 11.60; 95% CI: 3.77 - 35.65), poor Knowledge levels regarding management and consequence of untreated hypertension (OR = 24.50; 95% CI: 6.28 - 95.58), believes and understanding of disease (OR = 12.90; 95% CI: 1.65 - 100.63), lack of accompanying person to go to the physician/hospital (OR = 3.54; 95% CI: 1.04 - 11.99), deficiencies in information from service provider (OR = 5.16; 95% CI: 1.13 - 23.66) and government hospital (OR = 35.29; 95% CI: 9.76 - 127.63).

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3. Barreto <i>et al.</i> 2015 [59]	Brazil	To investigate the association between dissatisfaction with the public health service and MNA to antihypertensive therapy.	N = 392 Hypertensive patients were selected randomly and stratified way from eligible patients in outpatients of primary health care	60	Cross-sectional	42.1/-	Factors associated with MNA: dissatisfaction with the health services: reception service (OR = 1.6; 95%CI:1.08 - 2.46; p = 0.01), scheduling appointment (OR = 2.1; 95% CI:1.31 - 3.29; p = 0.000), care received from the health team (OR = 3.8; 95% CI: 2.24 - 6.45; p = 0.000), solvability of health problems (OR = 5.4; 95% CI: 3.08 - 9.56; p = 0.00), group activities (OR = 4.7; 95% CI: 2.77 - 7.81; p = 0.00) and physician professional (OR = 6.5; 95% CI: 3.47 - 12.3; p = 0.00)
4. Dosse <i>et al.</i> 2009 [63]	Brazil	To determine attendance of patients to medical appointments; the % of adherence to medication and non-medication regimens, and also identify the main reasons of hypertensive patients report for MNA	N = 68 Hypertensive patients registered in the outpatient clinic of a teaching hospital	64.71	Cross-sectional	86.76/-	Main reasons reported for MNA: emotional factor (69.1%), could not tell the reason (10.3%) and eating habits (8.8%). Statistically significant relation between men and women-reasons reported: could not tell the reason (p = 0.006), alcohol consumption (p = 0.013), and associated disease (p = 0.049)
5. Hu <i>et al.</i> 2013 [56]	China	To explore how and why patients adopt home blood pressure monitoring (HBPM) and examine the association between HBPM and medication adherence.	N = 318 Eligible hypertensive patients from a community health centre.	71.7	Cross-sectional	38.67/38.59	Risk factors of MNA: shorter duration of hypertension (AOR = 3.31; 95% CI: 1.91 - 5.72; p < 0.001) and less frequency in performing BP measurements (AOR = 2.33; 95% CI: 1.42 - 3.83; p < 0.001)

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6. Nsitou <i>et al.</i> 2013 [41]	Congo	To assess the level of compliance in hypertensive patients and identify patients-related predictors of MNA	N = 212 Eligible hypertensive patients of outpatient departments of three urban hospital	57.5	Prospective cross-sectional	32.5/27.86	Patient related predictors that could predict poor adherence by bivariate analysis: no Knowledge of the treatment (OR = 4.16; 95% CI; 2.25 - 7.68; $p \leq 10^{-5}$) no knowledge of high BP related complications (OR = 2.9; 95% CI: 1.61 - 5.29; $p = 0.000$), other pays for the medicine (OR = 2.17; 95% CI:1.20 - 3.92; $p = 0.009$), no Knowledge of the severity of hypertension (OR = 3.25; 95% CI: 1.5 - 7.02; $p = 0.001$), costly medication (OR = 0.42; 95% CI: 0.23 - 0.76; $p = 0.004$), no tensinometer for self-monitoring (OR = 3.16; 95% CI: 1.44 - 6.92; $p = 0.002$) and not existence of family member to remind to take medication (OR = 0.52 ; 95% CI: 0.29 - 0.93) $p = 0.03$. After adjustment by logistic regression, statistically significant association with poor compliance: knowledge of the treatment ($p = 0.0170$) and perception of the severity of complication ($p = 0.0373$)
7. Fina Lubaki <i>et al.</i> 2009 [49]	Congo	To explore reasons for MNA among patients with hypertension	N = 3 focus groups. Purposive sampling from hypertensive patients of a cardiovascular clinic	-	Qualitative study/Focus group interviews	Major causes of MNA: side effects of the medications, lack of information and support, difficulty in obtaining the medication and fact that the disease is mainly silent.	

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8. Hareri <i>et al.</i> 2014 [36]	Ethiopia	To assess the prevalence of poor adherence and factors associated to anti-hypertensive treatment	N = 365 Systematic random sampling technique to select hypertensive patients from a specialized hospital	51.2	Cross-sectional	40.5	Factors hinder adherence: age group (46 - 55) (AOR = 0.30; 95% CI: 0.142 - 0.640), lack of medication information (AOR = 0.12; 95% CI: 0.258 - 0.583) and presence of co-morbidities (AOR = 0.50; 95% CI: 0.290 - 0.893). Muslim followers were 3 times more likely to be adherent to their treatment (AOR = 3.20; 95% CI: 1.69 - 6.08)
9. Ali <i>et al.</i> 2014 [46]	Ethiopia	To investigate antihypertensive medication non-adherence and its determinants among patients	N = 121 All eligible hypertensive patients from outpatients of two referral hospitals	62	Prospective cross-sectional	26.4	Factors significantly associated with MNA: family support (AOR = 0.170; 95% CI: 0.030 - 0.905); spot blood pressure (AOR = 0.052, 95% CI: 0.003 - 0.242), place of patient residence (AOR = 0.184; 5% CI: 0.024 - 0.597) and hypertension related complications (AOR = 21.73; 95% CI: 1.568 - 418.42)
10. Gelaw <i>et al.</i> 2013 [35]	Ethiopia	To assess the adherence of the patients to anti-hypertensive medication and main risk factors contributing to MNA	N = 91 Purposive sampling was conducted among eligible hypertensive patients who attended a referral Hospital during the study period	56.06	Cross-sectional	68.13	Factors contributed to MNA significantly: economic problems (p = 0.04), less awareness about hypertension and its treatment (p < 0.01), social drug use (p < 0.01). Other factors were distance, forgetfulness, insufficient information about the effect of MNA and adverse effect understanding

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11. Hareri <i>et al.</i> 2013 [45]	Ethiopia	To assess medication adherence and factors associated with it among hypertensive patients	N = 286 Systematic random technique was used to selected eligible hypertensive patient from a specialised hospital	57.7	Cross-sectional	30.8/59.1	<p>Respondents less likely to adhere to medication who had: private business (AOR = 0.28, 95% CI: 0.130 - 0.606; p = 0.001) and duration of diagnosis of five or more years (AOR = 0.11; 95% CI: 0.01 - 0.95; p = 0.045).</p> <p>Respondents more likely to adhere to anti-hypertensive medication: who were married (AOR = 2.00; 95% CI: 1.33 - 6.74), attended most of the time private clinic to receive health care (AOR = 6.34; 95% CI: 1.17 - 33.96), treatment duration two to four years (AOR = 3.81; 95% CI: 1.26 - 11.51) and who were motivated (AOR = 2.84; 95% CI: 1.47 - 5.43)</p> <p>Variables, significantly associated with treatment adherence: female sex (AOR = 0.48; 95% CI: 0.28 - 0.82), knowledgeable about hypertension and its treatment (AOR = 6.21; 95% CI: 3.22 - 11.97), decreased distance from the hospital (AOR = 2.02; 95% CI: 1.19 - 3.43), having no or one co morbidity (AOR = 2.5; 95% CI: 1.01 - 6.21) and who have controlled hypertension (AOR = 2.93; 95% CI: 1.73 - 4.96)</p> <p>Adherence showed association with concern about medications ($r = -0.0347$, p = 0.002) and knowledge of hypertension ($r = 0.14$, p = 0.006). MNA was related with: depression ($r = -0.208$, p < 0.001), formal education (p = 0.001), younger age (p = 0.000), use of herbal preparation (p = 0.014), insured participants (p = 0.032) and poor BP control (p = 0.006).</p>
12. Ambaw <i>et al.</i> 2012 [37]	Ethiopia	To assess adherence to antihypertensive therapy and associated factors among hypertensive patients on follow up	N = 384 Systematic random sampling technique to select patients from an university teaching hospital	63	Cross-sectional	35.4/33.5	<p>Adherence showed association with concern about medications ($r = -0.0347$, p = 0.002) and knowledge of hypertension ($r = 0.14$, p = 0.006). MNA was related with: depression ($r = -0.208$, p < 0.001), formal education (p = 0.001), younger age (p = 0.000), use of herbal preparation (p = 0.014), insured participants (p = 0.032) and poor BP control (p = 0.006).</p>
13. Boima <i>et al.</i> 2015 [26]	Ghana and Nigeria	To determine factors associated with MNA among hypertensive patients	N = 357 All eligible patients were recruited from four hospitals from Ghana and Nigeria	57.5	Cross sectional	66.7/65.4	<p>Adherence showed association with concern about medications ($r = -0.0347$, p = 0.002) and knowledge of hypertension ($r = 0.14$, p = 0.006). MNA was related with: depression ($r = -0.208$, p < 0.001), formal education (p = 0.001), younger age (p = 0.000), use of herbal preparation (p = 0.014), insured participants (p = 0.032) and poor BP control (p = 0.006).</p>

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14. Srivastava <i>et al.</i> 2015 [55]	India	Measuring the medication adherence using validated tools and investigating the patient, disease, medication and health care system related factors affecting adherence to antihypertensive therapy.	N = 440 Multistage sampling method to select eligible hypertensive patient from the community	54.7	Cross sectional	27/30.8	Older people was found to be significantly and independently associated with better adherence. Patients on mono therapy were less adherent compared to those on two or three drugs. Patients who were aware of the association between certain risk factors for hypertension had better adherence.
15. Srikanth <i>et al.</i> 2015 [53]	India	To provide screening for hypertension to all the elderly and assess their compliance to medication	N = 304 All elderly individuals > 60 years residing in an urban slum.	66.7	Cross-sectional	38.6/-	Pearson's Chi square test showed significant association ($p < 0.005$) between compliance to medication and number of drugs consumed. With increase in number of drugs to be consumed, the adherence to medication decreased ($p = 0.039$)
16. Venkatachalam <i>et al.</i> 2015 [75]	India	To study the factors determining adherence to antihypertensive medication	N = 473 All eligible hypertensive individual willing to participate from a community.	52.2	Cross-sectional	75.89/74.5	The participants exhibited poor adherence with lifestyle factors like unrestricted meal habits (OR = 4.8), alcohol consumption (OR = 3.1), smoking (OR = 12.9), and salt intake > 5 gm (OR = 3.6). Adherence was significantly higher among respondents taking only one medication and once daily compared with individuals taking four types of medication and as frequent as three or more times a day.
17. Kumar <i>et al.</i> 2014 [76]	India	To assess the level of adherence and the factors influencing adherence among hypertensive patients	N = 120 All eligible consenting hypertensive patients attending medicine outpatient department and peripheral outreach clinic of a medical college	36.7	Cross-sectional	45.8/50	Factors significantly associated with good adherence: absence of side-effects (OR = 0.1; 95% CI: 0.03 - 0.52; $p = 0.003$) availability of free medication (OR = 0.4; 95% CI: 0.2 - 0.9; $p = 0.030$) and regular checkup of BP (OR = 0.5; 95% CI: 0.2 - 0.9; $p = 0.034$)

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18. Rao <i>et al.</i> 2014 [77]	India	To assess adherence to antihypertensive therapy and to assess associated factors for adherence among hypertensive patients	N = 220 Eligible hypertensive patient residing in an urban slum settlement	59.1	Cross-sectional	39.4/35.8	Factors contributed to treatment adherence significantly ($p < 0.05$): patient > 60 years of age (67.2%) (OR = 1.91; 95% CI: 3.40 - 1.08), married people (84.7%) (OR = 3.45; 95% CI: 8.43 - 1.37); nonsmokers (74.8%) (OR = 3.83; 95% CI: 7.01 - 2.12), non-tobacco users (68.9%) (OR = 6.36; 95% CI: 14.63 - 2.93) and people consuming 1 tablet a day (67.7%) (OR = 2.26; 95% CI: 4.11 - 1.26)
19. Nagarkar <i>et al.</i> 2013 [27]	India	To translate and validate MMAS-8 and to determine association between patient characteristics and medicine adherence in hypertension	N = 174 Randomly selected hypertensive patients attending medicine outpatients of a district hospital	44.87	Cross-sectional	76.5/70.7	MNA was significantly associated with patients ($p < 0.05$): age less than 57 year (OR = 3.348; 95% CI: 1.665 - 6.732), living in nuclear family setup (OR = 2.670; 95% CI: 1.378 - 5.175) and not experience of symptoms of hypertension (OR = 0.414; 95% CI: 0.192 - 0.892)
20. Ahmad, S. 2013 [48]	India	To assess the level of adherence and associated factors to antihypertensive treatment	N = 334 Purposive sampling of hypertensive patients reporting to a urban health and training centre	41.6	Cross-sectional	42.8/53.95	Good adherence to treatment was present more among males (OR = 1.25) and in those patients who were either receiving one medicine per day (OR = 4.27), or taking medicine once a day (OR = 1.96). Poor adherence to anti-hypertensive treatment was seen in patients with the habit of alcohol consumption (OR = 0.52), tobacco chewing (OR = 0.73) and smoking (OR = 0.40)

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21. Bhandari, S. 2011 [78]	India	To determine the prevalence and predictors of adherence to modern antihypertensive pharmacotherapy	N = 348 All the eligible hypertensive patients living in a selected urban slum	68	Cross-sectional	27/28.7	<p>Factors significantly associated with adherence ($p < 0.05$): duration of hypertension for ≥ 5 years (AOR = 2.98; 95% CI: 1.73 - 5.14), hypertension was detected during checkups for conditions related to hypertension (AOR = 2.35; 95% CI: 1.25 - 4.39), living with ≤ 4 family members (AOR = 2.01; 95% CI: 1.52 - 3.50), family income of ≥ 3000 rupees (AOR = 2.56; 95% CI: 1.47 - 4.45), getting free drugs (AOR = 4.16; 95% CI: 1.36 - 12.69), perceived BP under control (AOR = 2.23; 95% CI: 1.17 - 4.26) and satisfied with current treatment (AOR = 3.77; 95% CI: 1.32 - 10.76)</p> <p>Belief barrier was reported in 39.14% patients. Access barrier and recall barrier were reported by 82.57% and 62.17%, respectively. 78.62% of patients reported that it is difficult to pay for the medication and 54.93% indicated that it is difficult to get a refill timely. Logistic regression analysis showed that the education level was not contributing to non-adherence (OR = 0.75, 95% CI: 0.64 - 0.87). However, duration of hypertension, ($p = 0.031$) showed a significant contributory effect to MNA ($p = 0.031$). Chi square analysis showed no relation between the adherence pattern and the number of antihypertensive medications being prescribed.</p>
22. Dennis <i>et al.</i> 2010 [43]	India	To assess medication adherence in hypertensive patients and to identify the main barriers associated with medication adherence.	N = 608 Randomly selected hypertensive patients from the outpatient of internal medicine department of a teaching hospital	48.68	Cross-sectional	49.67/-	

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23. Praveen <i>et al.</i> 2010 [30]	India	To determine factors that are associated with non-adherence to antihypertensive treatment	N = 804 All eligible hypertensive patient from the outpatients of General Medicine department of a tertiary care hospital	70%	Cross-sectional	29/34.5	Factors independently associated with MNA ($p < 0.05$): female sex (OR = 2.95, 95% CI: 1.39 - 6.24), not understand drug regimen well (OR = 4.06, 95% CI: 1.01 - 16.32), affordability to only some/none of prescribed drugs (OR = 3.70, 95% CI: 1.8 - 7.59) and longer time since last visit to a health care facility (OR = 7.26; 95% CI: 2.65 - 19.86)
24. Kusuma, Y. S. 2010 [58]	India	To gain insights into the perceptions of socio-economically disadvantaged migrants in Delhi regarding treatment seeking behaviour for hypertension	N = 14 key informants and 3 focus groups. Purposive sampling from a community	-	Qualitative	-	Treatment seeking for hypertension was not adequate. Several patient- and provider-related issues have emerged as barriers in treatment seeking and adherence.
25. Kamran <i>et al.</i> 2014 [50]	Iran	To determine the factors of adherence to hypertension medication based on HBM	N = 671 Two stage random sampling methods to select eligible hypertensive patients from rural health care centres	74.81	Cross-sectional	76/75.3	MNA was significantly associated with: unrestricted meal habits (OR = 4.8; 95% CI: 37.5), smoking (OR = 1.9; 95% CI: 1.3 - 2.9) and salt intake > 5 g (OR = 19.7; 95% CI: 12.2 - 31.7). Respondents with regular physical activity and non-smokers were more adherent to medication when compared to respondents with sedentary lifestyle and smoking ($p < 0.01$).

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26. Ismael <i>et al.</i> 2015 [31]	Iraq	To assess the level of compliance to treatment and identified factors contributing to poor compliance	N = 200 Purposive sampling was used to select participants among all eligible hypertensive patients in a general teaching hospital	34	Cross-sectional	55/61.7	Major factor for MNA was forgetfulness. There was a significant association between high level of adherence and age group of > 65 years (p = 0.000), male gender (p = 0.003), no formal education (p = 0.000), and duration of hypertension less than 10 years (p = 0.003). Also there was significant relation between adherence and benefit of treatment, barrier of treatment, severity of disease, susceptibility to complication and reminder by advice from nurses (strongest predictor)
27. Shima <i>et al.</i> 2013 [51]	Malaysia	To explore patients' experiences with their illnesses and the reasons which influenced them in not following hypertensive care recommendations	N = 2 Purposive sampling from patients attending follow-up at primary health clinics	56	Qualitative	-	Most of the reasons given for not taking antihypertensive medication were side effects or fear of the side effects of antihypertensive medication, patients' attitudes, lack of information from health care professionals and insufficient social support
28. Ramli <i>et al.</i> 2012 [54]	Malaysia	To assess adherence to medications by adult patients undergoing hypertensive treatment	N = 653 Random sampling method to select hypertensive patients from 7 primary health care clinics	62.8	Cross-sectional multicentre study	46.6/43.7	Female patients were found to be more likely to be adherent than male patients (OR = 1.38; 95% CI: 1.00 - 1.90; p = 0.05)]. Patients from the Malay (OR = 1.68; 95% CI: 1.03 - 2.73) and Chinese ethnic group (OR = 2.64; 95% CI: 1.52 - 4.58) were also more likely to adhere, compared to patients from the Indian subgroups. The mean number of drugs that patients were taking was higher in non-adherers (3.67) than in adherers (3.17 [t = 3.81, df = 651; p = 0.001])

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29. Turki. <i>et al.</i> 2009 [79]	Malaysia	To identify patients with poor adherence to antihypertensive therapy and compare the levels of adherence with daily dose frequency of antihypertensive therapy	N = 518 Convenience sampling to select hypertensive patients from a clinic of a general hospital	42.6	Cross-sectional	51.3	Study found a significant relationship between daily dose frequency groups and adherence at level $p < 0.001$. It shows that that who have more daily dose frequency, will show higher level of adherence towards antihypertensive medications
30. Bhandari <i>et al.</i> 2015 [33]	Nepal	To explore the extent of adherence towards prescribed antihypertensive treatment and to elucidate the factors of MNA	N = 154 Participants were selected from all the diagnosed hypertensive patients of a selected community by simple random sampling method		Cross-sectional	43.5/54.2	Predictors of MNA by logistic regression analysis ($p < 0.05$): Illiteracy (OR = 5.34; 95% CI: 1.23 - 23), price of medicine (OR = 5.14; 95% CI: 1.1 - 23.9), missed medicine due to cost (OR = 0.143; 95% CI: 0.02 - 0.78), no family history of hypertension (OR = 4.46, 95% CI: 1.21 - 16.4), irregular follow up (OR = 6.39; 95% CI: 1.22 - 33.3) and more than one pills per day (OR = 5.33; 95% CI: 1.19 - 23.7).
31. Olowookere <i>et al.</i> 2015 [47]	Nigeria	To assess perceived family support and other factors that determine medication adherence among hypertensive patients	N = 420 Adult patients on antihypertensive medications attending a medical outpatient clinic	51	Cross-sectional	39	Common reasons for MNA include belief of cure (43%), high cost of treatment (33%), and the experiencing of side effects (27%). Patients with good family support had better adherence compared to those with poor family support ($p < 0.05$). MNA was higher among newly diagnosed hypertensive patients, those with higher pill burden, and those without family support ($p < 0.05$).

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32. Campbell <i>et al.</i> 2014 [42]	Nigeria	To assess compliance and knowledge of antihypertensive therapy amongst outpatients attending a hypertensive clinic	N = 262 Multistage sampling technique was used to select the eligible hypertensive outpatients of a hypertension clinic	52.6	Cross-sectional	74.81/78.83	The significant reasons for MNA (p < 0.05): forgetfulness (OR = 14.8; 95% CI: 3.9 - 54.8); ran out of prescribed drugs (OR = 1.3; 95% CI: 0.1 - 0.4); avoiding side effects (OR = 3.0; 95% CI: 1.4 - 6.7) and absence of symptoms (OR = 3.3; 95% CI: 1.3 - 8.0). Factors significantly associated with adherence to antihypertensive treatment: religion (X ² = 5.0068, df = 1, p = 0.025) and knowledge (X ² = 6.6848; df = 1, p = 0.0097; F-exact test = 0.0184) Facilitators of medication adherence included affordability of care (through health insurance), trust in orthodox "western" medicines, trust in doctor, dreaded dangers of hypertension, and use of prayer to support efficacy of pills. Inhibitors of medication adherence included inconvenient clinic operating hours, long waiting times, under-dispensing of prescriptions, side-effects of pills, faith motivated changes of medication regimen, herbal supplementation/ substitution of pills, and ignorance that regular use is needed. Local practices and norms were identified as important inhibitors to the uptake of healthier behaviours.
33. Odusola <i>et al.</i> 2014 [40]	Nigeria	To explore patients views on hypertension management.	N = 40 Purposive sampling from a rural primary health care	60	Qualitative	-	

Continued

34. Osamor <i>et al.</i> 2011 [25]	Nigeria	To investigate the factors associate with self-reported compliance among hypertensive subjects in a poor urban community	N = 440 and 8 focus groups. Consecutive sampling method was used to recruit participants from a list of hypertensive patients of a poor urban community. A purposive sampling technique was used for FGD from hypertensive patients.	65.2	Survey and qualitative interviews	41.5	Factors associated with adherence: regular clinic attendance ($p < 0.0001$); not using non-western prescription medication ($p < 0.001$); support from family members ($p = 0.038$); friends who were concerned about the respondent's hypertension ($p < 0.0001$) and helpful in reminding the respondent about taking medication ($p < 0.0001$). Beliefs about cause of hypertension were not associated with compliance ($p = -0.090$). Reasons given for MNA in focus group discussion: feeling better, forget to take medication and cost.
35. Atulomah <i>et al.</i> 2010 [80]	Nigeria	To collect information about perceived severity and threat to life from poor treatment response and medication adherence in hypertensive people	N = 130 Systematic random technique was used to select hypertensive patients from a teaching hospital	45.6	Cross-sectional	30.7	Bivariate analysis revealed that perception of severity of hypertension complications from poor treatment and threat to life positively correlated with medication adherence ($r = 0.46$; $p < 0.0001$).
36. Bilal <i>et al.</i> 2015 [44]	Pakistan	To determine the frequency and factors associated with non-compliance to anti-hypertensive medications	N = 113 Purposive sampling was conducted among all the eligible hypertensive patients of inpatients department of a specialized Hospital	64	Cross-sectional	68.14/58.33	MNA was found to be associated with: male gender $p = 0.008$; less monthly income $p = 0.046$; unemployed persons ($p = 0.002$); duration of hypertension < 5 years ($p = 0.03$); mono therapy and di-therapy ($p = 0.02$) and who paid themselves for their drugs ($p = 0.06$)
37. Saleem <i>et al.</i> 2012 [39]	Pakistan	To explore the perceptions and experiences of hypertensive patients toward medication use and adherence.	N = 16 Purposive sampling among hypertensive patients of a government hospital	25	Qualitative	-	The majority of the patients carried specific unrealistic beliefs regarding the long-term use of medication; yet these beliefs were heavily accepted and practiced by the society. Physician's attitude, patient's past experiences, and knowledge related to hypertension were noted as major contributing factors thus resulting in non-adherence to prescribed therapy.

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38. Saleem <i>et al.</i> 2011 [81]	Pakistan	To evaluate the association between patient's knowledge of hypertension management and medication adherence	N = 385 Eligible hypertensive patients from two tertiary care hospitals	31.2	Cross-sectional observational	64.7	Study shows an inverse association between knowledge scores of hypertension and adherence level. Correlation coefficient between total score of knowledge of hypertension and total adherence was -0.170 ($p < 0.001$) Factors significantly improved adherence (univariate analyses) were increasing age, better awareness, increasing number of pills prescribed (by multivariate analyses): number of drugs that a patient was taking ($p = 0.02$) and whether he/she was taking medication regularly or only for symptomatic relief ($p = 0.00001$) Factors significantly associated with MNA: younger age (<45 years) (AOR = 1), living in a village (AOR = 1), forgetfulness (AOR = 5.12; 95% CI: 3.12 - 8.41), dissatisfaction with treatment (AOR = 2.93; 95% CI: 1.22 - 7.02), side effects (AOR = 4.58; 95% CI: 1.87 - 11.25), fear of getting used to medication (AOR = 8.00; 95% CI: 2.44 - 26.19) and evaluating health status as very good, good or poor (AOR = 1). Other factors (by univariate analysis): having lower income ($p = 0.035$); receiving a higher number of antihypertensive tablets ($p = 0.001$); a higher dosing frequency ($p \leq 0.0001$) and having no other chronic disease ($p = 0.009$).
39. Hashmi <i>et al.</i> 2007 [57]	Pakistan	To measure adherence to antihypertensive therapy and to investigate the factors associated with adherence in the studied population	N = 460 Randomly selected participants from eligible hypertensive patients of two tertiary care hospitals	54.6	Cross-sectional	23/23.8	
40. Al-Ramahi <i>et al.</i> 2015 [38]	Palestine	To assess adherence to antihypertensive therapy and to investigate the effect of a range of demographic and psychosocial variables on medication adherence.	N = 450 Simple random sample from patients visiting outpatient clinics of governmental primary healthcare centers in addition to a group of private clinics and pharmacies	56.2	Cross-sectional	54.2/54.2	

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41. Zyoud <i>et al.</i> 2013 [82]	Palestine	To investigate factors associated with adherence to therapy among hypertensive patients and assess the relationship between medication adherence and treatment satisfaction	N = 410 Convenient sampling of hypertensive patients from outpatients of a clinic and a hospital	52%		36.8	After adjusting the covariates using multiple regression, global treatment satisfaction was statistically significantly ($p = 0.001$) associated with medication adherence ($R = 0.373$; adjusted $R^2 = 0.122$; $F = 8.107$; $df = 8$; $p < 0.001$)
42. Lalic <i>et al.</i> 2013 [28]	Serbia	To evaluate the degree of adherence in hypertensive patients and to study risk factors affecting adherence and the effects of non-adherence on BP	N = 170 All eligible hypertensive patients treated in a primary health care outpatients	65.9	Cross-sectional	25.88	MNA was associated with elderly patients, longer duration of therapy and side effects of drugs. ($p < 0.01$). Patients < 65 years were found to be more likely to adhere to their medication regimen, compared to elderly patients ($\chi^2 = 21.3$; $p < 0.01$; OR = 6.0; 95% CI: 2.76 - 13.04). BP values over 140/90 mmHg were reported in 59.1% of MNA patients and in 21.4% of adherent patients ($\chi^2 = 19.84$; $p < 0.01$; OR = 5.30; 95% CI: 2.39 - 11.85)
43. Edo, TA. 2009 [83]	Seychelles	To describe factors that affected compliance with hypertension medications and lifestyle modification strategies in hypertensive people	N = 102 Systematic random sampling from all eligible hypertensive patients registered at two public health centres	56.86	Quantitative, descriptive-co relational study	29.41	Significant determinants of compliance behaviour: individual perception of the benefits of hypertension treatment ($p = 0.0004$); individual perception of risks of hypertension treatment ($p = 0.0120$) and cues to action ($p = 0.0025$)
44. Bovet <i>et al.</i> 2002 [84]	Seychelles	To examine the compliance to medication among newly diagnosed hypertensive patients screened from the general population of the Seychelles	N = 50 Eligible hypertensive patients form a subset of participants in a population-based cross sectional survey	34	Population based survey and follow up	Initially 26%-after 12 months 32%	12-month adherence was higher with: skilled workers ($p = 0.034$); who knew their BP before diagnosis ($p = 0.028$) and who thought current lifestyle was important for future health ($p = 0.050$)

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45. Elzubier <i>et al.</i> 2000 [52]	Sudan	To estimate adherence with drug use, associated factors, and the effect of adherence on BP control	N = 198 Registered eligible hypertensive patient attended medicine department of a teaching hospital	76.3	Cross sectional	40.4	Using multiple logistic regression analysis only variable that is positively and significantly associated with MNA is being unable to buy drugs ($p < 0.001$)
46. Joho <i>et al.</i> 2012 [32]	Tanzania	To investigate factors affecting treatment adherence with antihypertensive therapy among hypertensive patients with the guide of the HBM conceptual framework	N = 135 Randomly selected patient from three hypertensive clinics	56.3	Cross sectional	44/35.44	With the use of bivariate analysis treatment compliance showed significant positive association with perceived benefit ($r = 0.27$; $p = 0.001$) cues to action ($r = 0.19$; $p = 0.022$). Treatment adherence showed significant negative association with: perceived barrier to treatment ($r = -0.53$; $p = 0.000$)
47. Mukora-Mutseyekwa <i>et al.</i> 2013 [85]	Zimbabwe	Measurement of BP control achievement, estimating prevalence of drug adherence behaviour and establishing the association between drug adherence behaviour and achievement of BP control	N = 102 Convenience sampling from outpatients of a tertiary hospital	69.6	Cross-sectional	59.8/66.19	Participants with normal BP measurements were more than three times as likely to report maximal adherence to prescribed drug schedule (AOR = 3.37; 95% CI: 1.38 - 8.24)

Note: MNA = medication non-adherence; BP = Blood pressure; OR = odds ratio; AOR = adjusted odd ratio; r = Pearson's correlation coefficient. ^aPatient population comprised of both male and female.

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