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Original Research

Patterns of Antihypertensive Pharmacotherapy Prescription and Blood Pressure Control in Hypertensive People in Middle Eastern Countries: A Systematic Review

Zain-ul-Abadeen (1), Hamza Farooq (2), Muhammad Anas Aamir (2), Hafiz Muhammad Maaz (2), Seerat Fatima (2), Muskan Irfan (2), Rabia Mahmood (2), Amina Qumar (2)

(1) Department of Pharmacy, National Institute of Blood diseases and Bone marrow Transplantation, Lahore, PAKISTAN

(2) Department of Basic Medical Sciences, Faculty of Pharmaceutical Sciences, Lahore University of Biological and Applied Sciences, Lahore, PAKISTAN.

Correspondence:

Zain-ul-Abadeen, Department of Pharmacy, National Institute of Blood Diseases and Bone Marrow Transplantation, Lahore, PAKISTAN. Email: babazain 34@gmail.com

Conflict of Interest

All the authors have no conflict of interest

Reference

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ABSTRACT

Background

The prevalence of vascular disorders like hypertension is high, especially among adults around the globe. One-half of this population does not use medication for the management of hypertension, which most of the time leads to cardiovascular risk, fatal outcomes, and a high mortality rate. If the prescription patterns of anti-hypertensive drugs are known, we can better evaluate and optimize patient compliance and adherence to antihypertensive therapy.

Objective

This review is focused on the patterns of prescribing the antihypertensive drugs across the Middle East and adherence to prescription guidelines.

Methodology

We conducted this systematic review according to PRISMA guidelines. In this regard, we conducted a literature search in different databases, such as PubMed, Springer Link, Elsevier Science Direct, NIH, Wiley Online Library, ResearchGate, and Google scholar. Twenty-two studies met the inclusion criteria out of 28,168 search result. Data extraction included study characteristics, prescription patterns, and blood pressure control outcomes.

Reculto

This review processed 22 articles published from 2003 to 2023. A cumulative total of 378,101 prescriptions were analyzed across the included studies. The evidence which was given in the literature was that "Angiotensin-converting enzyme inhibitors (ACEIs)" were the most frequently prescribed agent, "Beta-blockers (BBs)", Calcium blockers (CCBs) and angiotensin receptor blockers (ARBs) were the next in descending order. The paper also revealed that combination therapy is widely used in the Middle East with ACEI/ARBs and ACEI/CCBs being the most used in combination regimens. The prescriptive use of antihypertensive medication in the Middle East conformed overall to global guidelines. Nevertheless, there was the necessity of optimization in relation to the compliance with prescribing guidelines.

Conclusion

This systematic review presented a holistic insight of the patterns of antihypertensive prescribing across the Middle Eastern countries and the compliance with guidelines. This review concluded that the refinement of patterns of prescribing in accordance with the updated guidelines is needed. For better patient care in hypertension, policies must be designed and implemented to calibrate the patterns of prescription and compliance to guidelines.



1. INTRODUCTION

Hypertension (HTN) is a prevalent health problem in the world that draws high morbidity and mortality. More than one billion people have HTN, causing approximately 40 million deaths annually (41). Data on the prevalence of HTN in the Middle East is scarce; only 13 studies across 10 Arab countries were present. The estimated HTN prevalence in Arab countries is 29.5%, higher than in the U.S. (28%) and Sub-Saharan Africa (27.6%). Awareness rates stand at 46%, with prevalence rising with age and being more common in Arab women. Alarmingly, nearly half of individuals with HTN do not use medication, increasing their risk of fatal outcomes. The American College of Cardiology and the American Heart Association define blood pressure (BP) categories as follows: Normal BP: Systolic / Diastolic: <120 mmHg / <80 mmHg; Elevated BP: 120-129 mmHg / <80 mmHg; Hypertension Stage 1: Systolic 130-139 mmHg / 80-89 mmHg; Stage 2: Systolic ≥140 mmHg / ≥90 mmHg [1]

Definition and Classification

Hypertension is a condition of persistently raised blood pressure (BP) that increases cardiovascular event risk. According to the 2017 American guidelines, hypertension is defined by a daytime mean BP of ≥130/≥80 mmHg, a nighttime mean of ≥110/≥65 mmHg, or a 24-hour mean of ≥125/≥75 mmHg. Types of hypertension include: White Coat HTN: BP elevation due to clinical settings. Masked HTN: Elevated BP outside the office but normal in clinical settings [2]. HTN is closely linked to diabetes and cardiovascular diseases, including atherosclerosis, heart failure, and myocardial infarction. It is one of the leading cause of mortality globally, although it can be controlled with lifestyle modifications and medication.

Antihypertensive Medications

Antihypertensive drugs help regulate BP and include Beta Blockers (β -blockers), Angiotension Converting Enzyme Inhibitors (ACE inhibitors), Angiotensin Receptor Blockers (ARBs), Diuretics, Calcium Channel Blockers (CCBs), and Statins (sometimes used for hyperlipidemia)[1, 3].

Prescription Patterns in the Middle East

A Saudi study found amlodipine (CCB) to be the most prescribed for pregnant women with

uncomplicated hypertension, while an Indian study reported centrally acting drugs as the most common. Arshad et al. 2021 [4] reviewed prescribing trend of antihypertensives in low- and middle-income countries (2000-2018), identifying ACEIs/ARBs as the most prescribed monotherapy, followed by CCBs and β-blockers. Common dual-therapy combinations included β-blockers with CCBs, CCBs with ACEIs/ARBs, and thiazides with ACEIs/ARBs. Despite strong evidence, diuretics were the primary monotherapy in only three studies. The frequent use of β-blockers as first-line therapy is concerning due to lower stroke and mortality protection, especially in older patients. CCBs and ARBS were the frequently prescribed agents in Chronic Kidney Disease patients in accordance with guidelines recommending ACEIs/ARBs which were capable of slowing down the disease progression [5].

Hypertension Management in Middle Eastern Populations

The Middle East and North Africa (MENA) region is affected by poor antihypertensive prescribing practices and low BP control rates aggravated by rising obesity and metabolic syndrome. Despite the increasing burden of cardiovascular disease, the healthcare spending in low. (6). Non-communicable diseases are the cause of global morbidity and are in need of effective medication and lifestyle interventions. Studies point out to inconsistent adherence to treatment guidelines especially in the Palestinian refugee and primary care settings in Qatar. (7).

This review analyzes antihypertensive prescription practices and BP control in Middle Eastern countries in terms of common drug; classes used for treatment; the effectiveness of monotherapy and combination therapy; and adherence to international guidelines. Highlighting gaps in hypertension management, it offers insights to improve treatment strategies and healthcare policies in the region.

2. METHODOLOGY

Review protocol and registration

This systematic review study was conducted and reported in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) flow statement guidelines 2020.

Keywords

The keywords we used for finding the research studies include "Prescription pattern of



antihypertensives", "Blood pressure control", "Prescription pattern of antihypertensive drugs", "Antihypertensive medications", "Blood pressure control in hypertensive patients", "Prescription pattern of antihypertensives in middle eastern countries", "Blood pressure control among hypertensive patients in middle eastern countries" and with specific country names of middle east.

Data sources and search strategy

To ensure thorough coverage, the present systematic review incorporated searches from SpringerLink, Elsevier ScienceDirect, ResearchGate, PubMed, NIH, Wiley Online Library, as well as a manual search on Google Scholar. The studies were included regardless of study design and were restricted to the English language. Out of 28,168 studies, 22 studies that met the inclusion criteria were included in this study. The count of the studies included and excluded at each stage of the review process is presented in the PRISMA flow diagram in Figure#1 below

Eligibility criteria Inclusion criteria

The studies examining the prescribing patterns of antihypertensive agents, regardless of the study design and specific study population, were included in this review article. Articles were included in this systematic review if they fulfilled the following inclusion criteria:

- 1. The studies from countries of Middle East.
- 2. The studies with prescription pattern of

antihypertensive drugs.

- 3. The studies on Blood pressure (BP) control in hypertensive patients.
- 4. The studies published in the English language
- 5. The studies were published in peer-reviewed journals.

Exclusion criteria

- 1. Reviews
- 2. Letters
- 3. Editorials
- 4. Commentaries
- 5. Non-English studies
- 6. Studies outside of Middle Eastern countries

Data Extraction

The extracted data from the studies included comprised author details, country of the study, study design, duration of study, sample size, study population, and mean age of study population, prescription pattern of antihypertensives in the Middle Eastern countries, and the control of BP in the patients of Middle Eastern countries.

Data Synthesis and Analysis

The control of BP in patients of Hypertension was assessed across all of the included studies. Moreover, the prescription pattern of the antihypertensive medications was also investigated in all all of the included studies.

Characteristics of the studies included

| Sr. | Reference | Study | Study Design | _ | • | Prescription Pattern | B.P. Control |
|-----|--|---------|------------------------|--------|---|---|--|
| No | | Country | | e Size | population/me | | |
| • | | | | | an age | | |
| 1. | (K. A. Al Khaja et al., 2019)[6] | Bahrain | Observational Study | 8746 | Adults / mean age of older and young adults was 72.1 ± 6.6 and 51.9 ± 7.7y, respectively. | Renin–angiotensin– aldosterone system (RAAS) inhibitors [either (ACE) inhibitors or (ARBs)] β-blockers CCBs Diuretics. | The updated guidelines for hypertension treatment in older adults have had a limited impact on primary care practice [6] |



| 2. | (K. A. Al Khaja, Ahmed Isa, Veeramuthu , Sequeira, & Practice, 2018)[7] | Bahrain | Observational Study | 2090 | Older adults/ mean age = 72.1 ± 6.6 years | Long-term digoxin >125 μg/day. Furosemide monotherapy. β-blocker in combination with verapamil. β-blocker in patients with COPD. Vasodilators | 712 out of 2,090 outpatient prescriptions were potentially inappropriate, and there was inappropriate polypharmacy with Antihypertensives [7] |
|----|---|---------|---|--------|---|---|---|
| 3. | (K. A. J. Al Khaja, P. Sequeira, & Damanhori, 2005)[8] | Bahrain | Retrospective Analysis | 220 | Females and males. / Mean age =54.9 ± 10.7 years. | ACEIs (captopril, lisinopril, enalapril, perindopril). BBs (atenolol, propranolol). CCBs (nifedipine, diltiazem, verapamil). Diuretics (hydrochlorothiazide/tri amterene, chlorthalidone, indapamide). Methyldopa, hydralazine, and fixeddose reserpine/dihydroergoc ristine/clopamide. Lipid-lowering and antiplatelet drugs were rarely prescribed. | B.P was inadequately controlled.[8] |
| 4. | (Jassim Al Khaja, Sequeira, Damanhori, & research, 2004)[9] | Bahrain | Multicentric Therapeutic Audit of Medical Records | 547 | Mean age=67.1 (range 60-89 years) | β-blockers 7. Angiotensin- converting enzyme (ACE) inhibitors | BP targets were achieved in 11.1% Patients [9] |
| 5. | (Khaled, Mohammed , & Faiza, 2018)[10] | Yemen | Cross sectional Study | 277 | Adult hypertensive patients/ mean age = 57.5 ± 12.3. | Combined therapy include: ACEI + Diuretic Monotherapy include: ACEI Beta blockers | BP controlled was achieved in 34 patients [10] |
| 6. | (Abaci et al., 2007) [11] | Turkey | Cross sectional Screening study | 16,270 | 12,897 patients were studied with the mean age of 60±11 years (60.2% female). | ACEIs BBs CCBs Diuretics ARBs | In this study, the BP in most patients were treated with a single agent ACEI. [11] The ACEI /ARB therapy of diabetic patients was employed more frequently as compared to less frequently employed BBs and CCBs. ACEIs and BBs |



| | | | | | | | were more common in the treatment of patients with CVD. |
|----|--|-----------------|--|---|--|--|---|
| 7. | (Sepehri, Talebizadeh , Mirzazadeh, Mohsenbeig i, & safety, 2008) [12] | Iran | Random sampling method. | 1102 | The average ages of the study population were 57.3+ -13 years. It was not significantly different between the groups | BBs CCBs ACEIs Diuretics ARBs (JNC 7 guidelines) age of males (57.3± 12.6) and females (57.2± 13.3). | The study did not show an enormous level of difference in the type of antihypertensive drug class in men and women. In simple words, the most used antihypertensive drugs were BBs (46.2%), ACEIs, ARBs (22.9%) and CCBs (19.2) in that order.[12] |
| 8. | (S. Alavudeen, Mohammed Alakhali, Mohammad Asif Ansari, & Abdulla Khan, 2015)[13] | Saudi Arabia | Retrospective descriptive cross-sectional study. | 149 | It studied 149 female prescriptions (81 participants or 54.4 per cent) and 68 (45.6 per cent) male prescriptions. The average age of the male was 55.2+ -8.5 years and the average age of the female was determined to be 1+-12.9 years. | ACEIs CCBs BBs ARBs Diuretics (JNC 7 guidelines). | In this study, ACEIs, ARBs and CCBs were mostly used in controlling BP, then diuretics and BBs no matter on mono or poly therapy. In this study, majority of patients were taking polytherapy. The Hypertensive patients were also diabetic and therefore more use of ACEIs was seen which was compliant with JNC-7 Guidelines [13] |
| 9. | (Syed et al., 2021)[14] | Qatar | Retrospective cross-sectional study. | 359,079 prescript io ns belongin g to 81,569 patients were analyzed | 145,546 (40.5) prescriptions belonging to hypertensive patients were studied with the mean age 30 years and | ACEIs ARBs BBs Diuretics CCBs (NICE guidelines). | In this study, the most frequently prescribed drugs for hypertension were ACEIs and ARBs, followed by the BBs, diuretics and CCBs. The hypertensive class of drugs were prescribed in accordance with NICE guidelines[14] |



| 10. | (Omran, 2016)[15] | Iraq | Retrospective descriptive cross-sectional study. | 750 diabetic patients were enrolled in the study | hypertensive patients out of 750 were studied. The mean age of the patients was 54.93± 9.88 years and the mean age for males were 53.05± 10.06 years and females 58.36± 8.58 years. | ACEIs ARBs CCBs BBs Diuretics (JNC 7 and JNC 8 guidelines). | Monotherapy in which antihypertensive agents are used is the most common form of prescription in this research. The individual medications applied to diabetic hypertensive patients were ACEI, ARB, BB with CCBs and diuretics. This research showed the fact that no significant differences in mono or polytherapy patterns were found in the management of hypertension of patients with diabetes [15] |
|-----|---|--------|--|--|---|---|--|
| 11. | (Weitzman, Chodick, Shalev, Grossman, & Grossman, 2014)[16] | Israel | Retrospective Study | 172432 | Patient with >140mm Hg systolic BP and diastolic BP > 90 mmHg. Mean age > 18 | Diuretics ACE Inhibitors CCB's B-blocker | Patients along with diabetes and CKD have 3 time more prevalence than those without these comorbidities of uncontrolled hypertension. [16] |
| 12. | (Badawy, Labeeb, Alsamdan, Alazemi, & Practice, 2020)[17] | Kuwait | Data were collected by questionnaire with the help of nursing staff. | 500 | Geriatric Patients/ mean age = 65-87 | CCBs Angiotensin II antagonist ACE inhibitors RAAS antagonists β-blocking agents | There was nothing mentioned regarding BP control in patients. [17] |
| 13. | (Arshad et al., 2021) [4] | Egypt | Systematic study (meta- analysis) | Range =100- 4139 | Geriatric patients/ mean age≥65years | CCBs RAAS antagonists Diuretics B-blocker Sublingual captopril, along with sedatives | Nothing was mentioned regarding BP control with several prescription patterns. [4] |
| 14. | (Al-Azayzih, Al-Azzam, Alzoubi, Shawaqfeh, & Masadeh, 2017) [18] | Jordan | Cross- sectional study | 24089 | males: 11,819 females: 2,270, the average age of patients was 49.76 years | General use of antihypertensive medications in patients was described and no specific sequence of medication was mentioned. | Nothing was mentioned regarding blood pressure control in the patients mentioned. [18] |
| 15. | (Bulatova, Yousef, AbuRuz, & Farha, 2013) [19] | Jordan | Cross- sectional study | 408 | males: 193 females: 215, average age was 58.60±10.85 (20-89) | ACEIS ARBS BRBS CCBS Thiazides Loop-diuretics K sparing Others | BP was controlled using the antihypertensive medications that include monotherapy with beta-blockers (48 %), followed by angiotensin-converting enzyme inhibitors (ACEIs) with 28 % and angiotensin II receptor blockers (ARBs) with 23 %. Beta blockers |

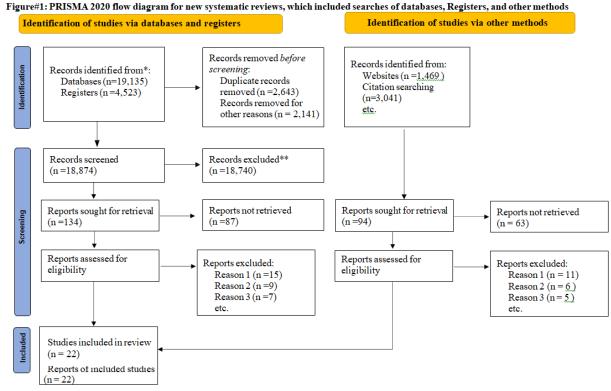


| | | | | | | | were most commonly prescribed. [19] |
|-----|------------------------------|---------|------------------------------|------|--|---|--|
| 16. | (Kamel & Barhoom, 2013)[20] | Jordan | Cross- sectional study | 273 | males: 84 females:189 all patients were above 60 years of age | No anti-hypertensive medication-specific sequence was mentioned/found | BP was controlled using the anti-hypertensive medications by giving the patients knowledge about their medication. The elder patients' compliance level and knowledge were assessed using different tools that helped in the control of hypertensive incidence [20] |
| 17. | (Abbas et al., 2020) [21] | Lebanon | Cross-sectional Study | 1497 | Males: 48.3% Females: (51.7%) By age group, 200 (13.4%) were between 18 and 44, 392 (26.2%) were between 45 and 64, and 905 (60.4%) were above 65 years of age | Diuretics followed by beta-blockers 3-ACE inhibitors, then Angiotensin II receptor blocker, Calcium channel blockers, alpha blockers, alpha-2 receptor agonists followed. | The patients who have shown compliance with antihypertensive drugs were 1253 (83.7). Following the multivariate analysis, patients who attempted to manage their level of stress (OR= 0.77, 95% CI [0.38-0.95]; patients who had a normal reading of BP (OR= 0.49, 95% CI [0.18-0.97]) and the patients who believed that their treatment was effective (OR= 0.31, 95% CI [0.14-0.76]) had a much better chance of non-adhering to the Non-adherence was however very likely to be noticed among older patients, divorced/separated patients, married and widowed patients, patients who smoked hookah and cigarettes, and obese patients [21] |



| 18. | (A.Salmi, Al-Raisi, Al-Harbi, Al-Rawahi, & Al- Naamani, 2009) [22] | Oman | Retrospective study | 120 | Male/mean age =55.8 years± 14.2 | 50% of the patients were placed on an ACE inhibitor and changed to Valsartan. Valsartan was initiated as the other half of the patients. a primary option that lacks clinical grounds | It was reported that there were only three (6) patients where ineffectiveness occurred. Out of the 48 patients who were taking ACEi before, the only reasonable explanation of switching the medication of 35 patients (73) to Valsartan was not specified. Among 109 patients, 49 (45) patients were initiated on Valsartan and no reason had been given on why they were not making attempts to use an ACEi during the first-line intervention. [22] |
|-----|---|-----------|---|-----|--|--|--|
| 19. | (Hanbali, Hashmi, Za'abi, & Al- Zakwani, 2021) [23] | Oman | Retrospective study | 249 | 151 Males/mean age =63±15 years | (carvedilol 25 mg BD, bisoprolol 10 mg OD); ACEIs (lisinopril 20-40 mg OD, captopril 50mg TID); ARBs (irbesartan 300 mg OD, valsartan 160 mg BD); MRA that (spironolactone 25-50 mg OD); [3–5] | Achievement of at least target doses of spironolactone by all patients, but about half of patients all by targeted doses of b-blockers and less than half of patients by targeted doses of b-blockers.[23] |
| 20. | (Castelino, Al Hashmi, Al Za'abi, & Abdelrahma n, 2023) [24] | Oman | Retrospective Observational Study | 400 | 221 Male/ mean age = 62.5 ± 16.6 years | Procainamide, lidocaine, flecainide, atenolol, bisoprolol, carvedilol, esmolol, propranol, amiodarone, sotalol, diltiazem, verapamil, adenosine, digoxin and magnesium sulfate. | Beta blockers were the most frequent agents, with bisoprolol following the trend. Intervention was mainly related to the selection and dose optimization of antiarrhythmic agents [24] |
| 21. | (Alkaabi, Rabbani, Rao, & Ali, 2019) [25] | UAE | Prospective Observational | 588 | 252 Males 336 Females/ mean age = 63.2± 14.33 years | CCBs ARBs Diuretics ACEIs B-blockers | The trend in prescribing antihypertensive drugs in a secondary care hospital in the UAE. To a great extent, the use of the antihypertensive drugs is adherent to the international Guidelines. [25] |
| 22. | (Sweileh, 2003) [26] | Palestine | Pharmaco- economic study | 574 | The monotherapy prescriptions rate was 48.25, the Combinational therapy rate was 51.75 | Monotherapy BB, ACE-I CCB Diuretics AT1-RA Direct vasodilators Central sympatholytic Two-drug Combinational therapy BB | There has been a shift towards prescription of antihypertensive drugs as a form of combinational therapy and the use of new types of antihypertensive drugs has had an overall high influence in the use of the drugs in prescription.[26] |





Source: Page MJ, et al. BMJ 2021;372;n71. dgj. 10.1136/bmj.n71. This work is licensed under CC BY 4.0. To view a copy of this license, visit https://creativecommons.org/licenses/by/4.0/

3. RESULTS

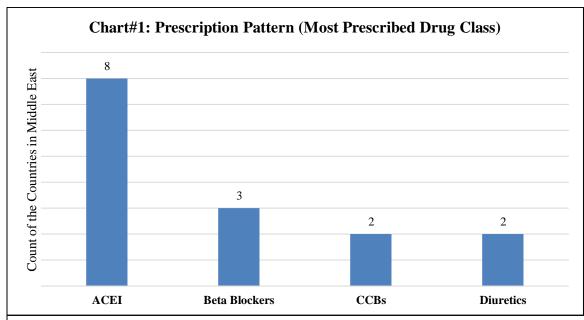
A cumulative total of 596,679 prescriptions were analyzed during the study period. However, prescriptions belonging to the non-hypertensive patients were excluded from the study analysis. A total of 378,101 prescriptions were then successfully evaluated. For the systematic review of prescription patterns of antihypertensive agents in the Middle Eastern countries, the number of reports that were sought for retrieval was n=134 via databases and registers, while the reports that were sought for retrieval via other methods were n=94. After screening and eligibility criteria, n=78 reports were selected, and then, following the exclusion criteria, the n=22 studies were included to be studied, belonging to the different Middle Eastern countries in this systematic review of prescription patterns of antihypertensive agents.

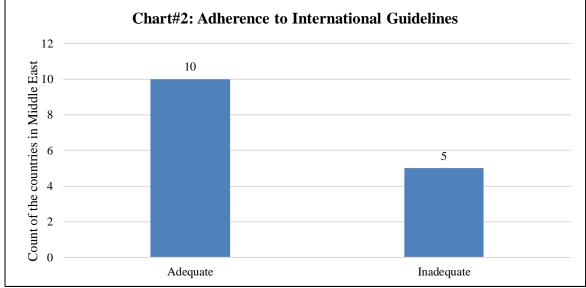
The most common comorbidities among our hypertensive group include diabetes mellitus, glaucoma and hyperlipidemia. Antidiabetic, antiplatelet, and antihyperlipidemic were the most common concomitant medications. Some of the participants who had other conditions; however, were not included in the systematic review since

most of the studies included in the review were the retrospective descriptive cross-sectional prescription studies.

The mean age of cohort was 57.5 +14.33 -years; most of the subjects were 54-67 -year-old. Prescription of ACEIs/ARBs and BBs as first initial therapy in patients below the age of 55 years were the most common therapies showing a high degree of adherence to NICE guidelines in the Middle East as can be seen in Chart 2. Most of them were under monotherapy, then dual and triple combination therapy. ACEIs were the most common prescription in both monotherapy and combined therapy, then in order, there were BBs, CCBs, diuretics, and ARBs as indicated in Chart 1. In the concept of monotherapy, Angiotensin converting enzyme inhibitors (ACEIs) and Beta-blockers (BBs) were the most frequently used agents that were used on hypertensive patients; ACEIs/ARBs ACEIs/CCBs were used on most patients in combination therapy.









Table#1: AXIS TOOL: FOR ASSESSMENT OF THE QUALITY OF THE STUDY USED IN THE REVIEW

| Table#1: AXIS TOOL: FOR ASSESSMENT OF THE QUALITY OF | | | | | | | | | | | | T THE STUDY USED IN THE REVIEW | | | | | | | | | | |
|--|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|--------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| | Study 1 | Study 2 | Study 3 | Study 4 | S ybuds | Study 6 | 2 kpms | Study 8 | Study 9 | Study 10 | Study 11 | Study 12 | Study 13 | Study 14 | Study 15 | Study 16 | Study 17 | Study 18 | Study 19 | Study 20 | Study 21 | Study 22 |
| | | | | | | | Intr | oduct | ion | | | | | | | | | | | | | |
| Were the aims/objectives of the | √ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | √ | ✓ | ✓ | ✓ | × | × | ✓ | V |
| study clear? | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | M | ethod | ls | | | | | | | | | | | | | |
| Was the study design | ✓ | ✓ | ~ | ✓ | ✓ | ✓ | √ | ✓ | √ | √ | ✓ | ✓ | ✓ | √ | ✓ | √ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| appropriate for the stated aim(s)? | | | | | | | | | | | | | | | | | | | | | | |
| Was the sample size | √ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | √ | √ | √ | × | × | ✓ | ✓ | √ | ✓ | ✓ | × | ✓ | ✓ | ✓ |
| justified? | | | | | | | | | | | | | | | | | | | | | | |
| Was the target/reference population | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | √ | ✓ | ✓ | ✓ | ✓ | √ | ✓ |
| clearly | | | | | | | | | | | | | | | | | | | | | | |
| defined? | | | | | | | | | | | | | | | | | | | | | | |
| Was the sample frame taken from an | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | √ | ✓ |
| appropriate population base so | | | | | | | | | | | | | | | | | | | | | | |
| that it closely represented the | | | | | | | | | | | | | | | | | | | | | | |
| target/reference population under | | | | | | | | | | | | | | | | | | | | | | |
| investigation? | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | |
| Was the selection process likely to select | ~ | ~ | ~ | ~ | _ | ~ | Y | ~ | V | ~ | _ | ~ | V | ~ | × | ~ | ~ | ~ | × | × | ~ | ~ |
| subjects/participants that were | | | | | | | | | | | | | | | | | | | | | | |
| representative of the target/reference | | | | | | | | | | | | | | | | | | | | | | |
| population under | | | | | | | | | | | | | | | | | | | | | | |
| investigation? | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | |
| Were measures undertaken to address and | _ | эc | × | × | / | × | × | × | × | × | × | ✓ | × | × | ✓ | ✓ | × | × | × | × | × | × |
| categorize | | | | | | | | | | | | | | | | | | | | | | |
| non-responders? | | | | | | | | | | | | | | | | | | | | | | |
| - | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | |
| Were the risk factor and outcome variables | | ✓ | V | ✓ | V | ✓ | V | ✓ | V | ✓ | × | se | ~ | × | ✓ | × | × | ✓ | ✓ | ✓ | ✓ | ✓ |
| measured appropriately to the aims of the | | | | | | | | | | | | | | | | | | | | | | |
| study? | | | | | | | | | | | | | | | | | | | | | | |
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| | | | | | | | | | | | | | | | | | | | | | | |
| Were the risk factor and outcome variables | ✓ | ✓ | V | ✓ | · | ✓ | · | ✓ | V | ✓ | ✓ | ✓ | V | × | ✓ | × | ✓ | ✓ | × | ✓ | √ | ✓ |
| measured correctly using | | | | | | | | | | | | | | | | | | | | | | |
| instruments/measurements that had been | | | | | | | | | | | | | | | | | | | | | | |
| trialed, piloted, or | | | | | | | | | | | | | | | | | | | | | | |
| published previously? | | | | | | | | | | | | | | | | | | | | | | |
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| Is it clear what was used to determine | ~ | ~ | _ | ~ | ' | ~ | ~ | ~ | Y | ~ | ~ | ~ | Y | ~ | ' | se | ' | ~ | _ | ~ | ' | ~ |
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| adequately described? | | | | | | | | | | | | | | | | | | | | | | |
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Several tools assess the quality of analytical crosssectional studies, including the Newcastle-Ottawa Scale (NOS), NIH Quality Assessment Tool, Johanna Briggs Institute (JBI) Checklist, and the Appraisal Tool for Cross-Sectional Studies (AXIS). In this systematic review, we utilized the AXIS tool (Appraisal tool for Cross-Sectional Studies) to assess the methodological quality and potential risk of bias in the included studies. It consists of a 20-point questionnaire covering a structured, quantitative evaluation of study quality across domains such as study design, sample selection, measurement validity, reporting clarity, and ethical considerations. Its systematic approach allowed us to ensure transparency and rigor in evaluating cross-sectional evidence related to prescription patterns of antihypertensive medications and blood pressure control in Middle Eastern countries. By applying this tool, we were able to identify key areas of risk, including potential selection bias, measurement bias, and reporting bias, which influence study findings and their interpretation. The use of the AXIS tool in our review strengthened the validity of our synthesis, offering both a numerical appraisal of study quality and a narrative understanding of methodological strengths and limitations across the included studies. The AXIS tool appraisal is presented in Table#1 above.

4. DISCUSSION

This review is the pioneer to analyze prescription patterns of antihypertensive medications across Middle Eastern countries, encompassing a total of 378,101 evaluated prescriptions. It includes 22 summarizing commonly studies prescribed antihypertensive drugs. Our results offer information about the actual Hypertension treatment approaches and underscores both regional specific prescription behaviors and compliance with international guidelines. The average age of patients (57.5+-14.3 consistent with the years) is worldwide epidemiological profile of hypertension where prevalence is much higher in older age (29). The finding of increased concentration of patients with 54 to 67 years support previous reports that hypertension is more common in middle-aged and older populations (30). Additionally, the presence of comorbidities such as diabetes mellitus, glaucoma and hyperlipidemia are consistent with the fact that these patients are known to cluster cardiovascular risk factors.20.31 The high prevalence of antidiabetic, antiplatelet and antihyperlipidemic drugs use with antihypertensive therapy demonstrates a clinical need for a comprehensive approach to cardiovascular risk reduction, which is similar to studies performed in south Asia and Europe (32, 33).

As far as the therapeutic approaches are concerned, in our review we have shown that monotherapy is still the most commonly prescribed regimen, followed by combinations of dual and triple drugs. According to a 2019 review by Khalid A. J. Al Khaja et al., RAAS inhibitors (ACEIs/ARBs), betablockers, calcium channel blockers and diuretics medications were given the most. This study had analysis the prescribing patterns in Bahrain and a sample of 8746 patients. Prescription patterns had an effect on BP control, but there was a low effect from updated guidelines in primary care.8 An observational study conducted by Khalid A.J. Al Khaja et al. in Bahrain in 2018 found that high-dose digoxin, furosemide monotherapy, BB-verapamil combinations, The prescribing pattern of 2090 patients was above the BBs among patients with chronic obstructive lung disease and vasodilators. Out of 2090 prescriptions, 712 prescriptions were potentially inappropriate, wherein inadequate adherence with international guidelines (9).

Among the single agents, the most commonly prescribed were ACE inhibitors (ACEIs), followed by "beta-blockers (BBs), calcium channel blockers (CCBs) and diuretics, and angiotensin receptor blockers (ARBs)", according to a study in Bahrain in 2005 (10). These findings are consistent with patterns of prescribing reported from global studies in the literature as part of previous systematic reviews (34, 35). It is possible that the preference for ACEIs is based on the proven efficacy of ACEIs in BP lowering, cardiovascular morbidity and mortality, especially for patients with diabetes and other comorbidities (36). Another study in Bahrain demonstrated 11.1% of patients had their blood pressure targets met with BB's and ACE I's being the most common antihypertensive prescribed (11). The reason behind such a small percentage of patients achieving their target of blood pressure control might be that of non-adherence to the international guidelines or patient-specific non-compliance with the treatment.

Interestingly, an ACEI/ARB and ACEI/CCB were the predominant most common combinations Middle Eastern practice. This is in accordance with groups of people, including the NICE, recommending ACEIs/ARBs in patients younger than 55 years and combination therapy in patients demanding better blood pressure control (37). The frequent



prescription of BBs as a first-line therapy in younger hypertensive patients also reflects adherence to guideline-based practices (38). However, the relatively high use of BBs compared to diuretics and CCBs in some cohorts suggests that prescriber preference and regional clinical practices may influence prescribing behavior beyond international standards (39).

A study in Yemen by Al-Aghbari Khaled et al. reported that ACEIs or BB are the most common monotherapy, while combination therapy included ACEIs + Diuretics. Blood pressure was controlled in 34 patients [10]. These findings support ACEIs as the most frequently prescribed monotherapy agents, achieving the desired blood pressure target. The control in patients using ACEIs is appreciable, which suggests adequate adherence with the international guidelines of hypertension treatment. Another study in Turkey by Adnan Abaci et al., Saudi Arabia by Sirajudeen Shaik Alavudeen et al. [13], In Qatar, by Mohamed Ahmed Syed et al. [14], in Iraq by Amir Omran et al. [15], In Israel by Dahlia Weitzman et al. [16], in Jordan by Nailya R. Bulatova et al. [19], in Oman by Zaheer Al-Salmi et al. [22] [23], reported the same preference in the prescription pattern of antihypertensive agents.

Contrary to the use of ACEIs as the first choice for monotherapy, BBs are also used as first-line agents, as shown in a 2008 review in Iran by Gholamreza Sepehri, PhD et al., in Lebanon by Hanine Abbas et al. [21], in Oman by Rohan D. Castelino et al. [24], in Palestine by Waleed Sweileh et al. [26] followed by ACEIs/ARBs, and CCBs, aligning with JNC 7 guidelines. More specifically, Bisoprolol was the most frequently prescribed BB (26). No significant gender differences were observed in drug class usage [12]. This may be attributed to the economic factors influencing prescribing practices in low and middle-income countries. Due to historical prescribing habits and delayed adoption of updated guidelines, BBs might be prescribed as first-line agents because older guidelines emphasize it [17]. Some of the studies also reported CCBs and Diuretics being used as the first-line agent for controlling hypertension, as in Egypt, a study by Verda Arshad et al [4], in Lebanon by Hanine Abbas et al. [21], in the UAE by Maryam Salem Alkaabi et al. (27). This might be because these drug classes work better in low-renin hypertension (common in Black, Asian, and older patients) and are cost-effective. Others use ACEIs/ARBs first-line as they are more effective in high-renin hypertension (younger, Caucasian patients) and offer renal/cardiac protection. Thus, population response, comorbidities, and resource factors guide

the choice between them (40). In some countries, a few studies reported that there was no specific sequence of antihypertensive drugs being followed [20]. This may be because all major classes (thiazides, CCBs, ACEIs, ARBs) exhibit similar efficacy in reduction of BP and prevention of cardiovascular events (40).

The comparative analysis of prescribing patterns between countries reveals excellent variation in the management of hypertension in different countries. Prescription patterns for antihypertensive therapy differ greatly from region to region because of a combination of existing clinical evidence and local habits of practice. In Bahrain, a series of studies have revealed the preference for ACE inhibitors, beta-blockers and combinations for both, even though inappropriate prescribing and low adherence to guidelines are of concern. Yemen also showed ACEIs and beta-blockers as the most common monotherapy while combinations such as ACEIs and diuretics were found to have a moderate degree of blood pressure control. In Turkey, Saudi Arabia, Qatar, Iraq, Israel, Jordan, and Oman, ACEIs were common choices, in most cases with the combination of CCBs or ARBs, being consistent with international recommendations, like NICE. By contrast, in Iran, Lebanon, Oman, and Palestine, beta-blockers were found as first-line agents, which may reflect the past reliance on older guidelines, i.e. JNC 7, as well as the economic considerations. Studies from Egypt, Lebanon, and UAE emphasized CCBs and diuretics as common first choice drugs. This diversity suggests that demographics of the patient, drug cost and regional health priorities are strong drivers of prescribing behavior. Importantly, ACEIs and ARBs are more commonly favored in younger or diabetic patients because of the renal and cardiovascular protective effects of these agents and CCBs and diuretics are highlighted in older or Black/Asian individuals. Despite these trends, results of some studies pointed out that in some countries none of the strict sequence of antihypertensives were followed, and physicians prescribed of all classes. The kinds practiced correspond to evidence of equality of major classes in reducing blood pressure and decreasing cardiovascular events. Overall, although the worldwide guidelines emphasize individualized therapy, there is regional variation underscoring areas of lack of adherence and the factors of socioeconomic and clinical contexts.

5. CONCLUSION

This systematic review investigated antihypertensive prescribing pattern in the Middle



East and those that are according to clinical guidelines and areas of gap and improvement. While numerous studies were descriptive of prescribing trends only four studies quantitatively assessed guideline adherence and few studies provided data on comorbidities, ethnicities and sociodemographic factors. Prescribing data was limited in several countries underlining the need for further research to be carried out in the Middle East. the Americas, Australia, and European countires to measure the alignment with updated guidelines. The study quality was of moderate to high standard overall, but there were limitations, including small sample sizes, single-center focus, and short study durations, that impacted on study generalizability. Hypertension prescribing practices suboptimal and misaligned with guidelines. Addressing this gap requires targeted interventions, continuous professional development, evidencebased treatment protocols, and quality improvement strategies to enhance prescribing standards.

6. LIMITATIONS

There were some limitations in our systematic review. It proved to be quite difficult to compare the study results of various countries because of the diversity of the study results as different studies had different study designs and data representation was varied in different studies. We had conducted our systematic review on the Middle Eastern nations, and therefore, we might have missed reviews that were written in Arabic or any other other language since we had restricted our search mechanisms to Englishwritten studies. Specifically, this systematic review failed to evaluate the variables that influence the prescribing of antihypertensive medications by physicians and their objectives (therapeutic outcomes) in the prescribing of a particular antihypertensive drug instead of another. Further researches, systematic reviews in the field are necessary to assess hypertension blood pressure treatment prescription patterns by clinicians to develop future strategic policies, and comprehensive plans and guidelines to enhance the condition of hypertension patients.

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