

Original article

Evaluation of antihypertensive prescriptions for rationality and adherence to treatment guidelines: An experience from United Arab Emirates

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ABSTRACT

Objectives: Prescription pattern focused drug utilization is an effective technique which provides an unbiased assessment of the prescribing habits and aids in identifying suboptimal prescribing. The aim of the present study was to evaluate rationality in antihypertensive prescribing and adherence to international treatment guidelines. **Methods:** It was an observational, prospective, cross sectional study carried out in 588 adult patients with hypertension presenting to medicine department of a secondary care hospital in United Arab Emirates. Electronic medical records of the patients were reviewed and demographic, clinical and antihypertensive prescription data were obtained. The antihypertensive prescriptions were assessed for rationality and adherence to the latest Joint National Committee (JNC) and National Institute for Health and Care Excellence (NICE) guidelines for hypertension. Statistical analysis of the data was performed using statistical package for social sciences (SPSS) version 24.0.

Results: Out of the total 588 patients included in the study, majority (57.1%) of the patients were females. The mean age of the patients was 63.2 ± 14.3 years, with majority of them aged 68 years and above (37.9%). Majority of the patients (67.9%) were on combination therapy receiving multiple drugs for the management of their hypertension. Overall, 69% of our antihypertensive prescriptions were adherent to the JNC 7 recommendations and 80.9% were as per JNC 8 recommendations. Also, 55% of the antihypertensive prescriptions were adherent to the 2011 and 2019 NICE guidelines.

Conclusion: In conclusion, the antihypertensive prescriptions at the study site mostly adhere to the latest international guidelines for the management hypertension.

1. Introduction

More than one billion people in the world are suffering from hypertension and it is the major cause of premature deaths worldwide.¹ The estimated prevalence of hypertension in the Arab countries is higher than the US and sub-Saharan Africa.² Keeping in view the high burden of hypertension and its associated morbidity and mortality, Ministry of Health and Prevention, United Arab Emirates (UAE) has aligned the national strategy with World Health Organization's global target to reduce hypertension by 25% by 2025.³

Appropriate management of hypertension can lead to reduction in cardiovascular morbidity and mortality.⁴ In spite of the advances in hypertension management, studies show that majority of the patients remain sub optimally controlled.^{5,6} Non-adherence to lifestyle modifications and non-compliance to antihypertensives are the major

contributory factors to this suboptimal blood pressure control.⁷

Prescription pattern focused drug utilization is an effective technique which provides an unbiased assessment of the prescribing habits and aids in identifying suboptimal prescribing.⁸ Scientific organizations like National Heart, Lung, and Blood Institute (NHLBI),^{9,10} National Institute for Health and Care Excellence (NICE),^{11,12} European Society of Hypertension (ESH)¹³ and others periodically publish reports or guidance for the prevention, diagnosis, evaluation, and management of high blood pressure. These guidelines assist healthcare providers in clinical decision making, minimize variations in practice and serve as measures of healthcare quality. However, implementation of these clinical guidelines in practice is affected by a number of factors and barriers.¹⁴

Evaluating the antihypertensive drug utilization in UAE population is vital as the region is witnessing an increasing prevalence of

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Table 1
Socio-demographic and clinical characteristics of hypertensive patients: Overall and by antihypertensive therapy.

Variable	Overall (n = 588)	Antihypertensive Therapy		P-value
		Monotherapy (n = 189)	Combination Therapy (n = 399)	
Age, year (%)				0.003
18–27	1.4	1.6	1.3	
28–37	3.4	4.2	3.0	
38–47	8.3	13.8	5.8	
48–57	18.0	22.2	16.0	
58–67	31.0	26.5	33.1	
68 and above	37.9	31.7	40.9	
Gender (%)				0.246
Female	57.1	60.8	55.4	
Male	42.9	39.2	44.6	
Nationality (%)				0.247
Emirati	79.6	81.5	78.7	
Omani	16.8	13.8	18.3	
Others	3.6	4.8	3.0	
Number of comorbidities (%)				0.001
No comorbidity	23.6	33.3	19.0	
One comorbidity	37.5	31.7	40.1	
Two comorbidity	38.9	34.9	40.9	
Type of Comorbidities (%)				< 0.001
Diabetes Mellitus	8.2	10.1	7.3	
Hyperlipidemia	23.2	17.5	25.8	
Ischemic Heart Disease	6.0	4.2	7.0	
Diabetes Mellitus + Hyperlipidemia	32.7	31.7	33.1	
Diabetes Mellitus + Ischemic Heart Disease	6.3	3.2	7.8	

Statistically significant values are in bold.

hypertension,¹⁵ leading cause of mortality in the region is cardiovascular diseases¹⁶ and lack of data on rationality and adherence of antihypertensive prescriptions to international treatment guidelines. Keeping these observations in view, the present study was conducted to evaluate rationality in antihypertensive prescribing and adherence to international treatment guidelines like the Eighth¹⁰ and Seventh⁹ Reports of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 8 and JNC 7) and NICE Hypertension in adults: diagnosis and management 2019¹² and 2011¹¹ guidelines.

2. Methods

2.1. Study design and sample size

It was a prospective-observational study conducted in hypertensive patients presenting to the internal medicine department of Dibba Hospital, Fujairah, UAE. The study site is a multi-specialty hospital with Internal Medicine, Orthopedics, Obstetrics and Gynecology, Ophthalmology, Dermatology, Otorhinolaryngology, Pediatrics, Radiology, Accident and Emergency Medicine, Physical Medicine and Rehabilitation departments. The study sample was selected using convenience sampling technique and was calculated on the basis of number of patients visiting the internal medicine department (124 patients/month approximately) of the hospital during the six month study period considering 20% drop-out rate. A total of 588 patients were enrolled in the study. Out of these 588 patients, 88 patients were from the inpatient department whereas 500 patients were from the outpatient department.

2.2. Study criteria

2.2.1. Inclusion criteria

Patients aged more than 18 years, of either gender with a confirmed diagnosis of hypertension and on antihypertensive medications attending the internal medicine department of the study site were included in the study.

2.2.2. Exclusion criteria

Patients with significant renal and hepatic diseases, malignant hypertension and pregnancy were excluded from the study.

2.3. Data collection procedure

Electronic patient case records were reviewed by the study investigators and demographic and clinical data were documented in the study specific data collection form. Patient data including age, gender, nationality, marital status, number of comorbidities, comorbidity types, concomitant medications, antihypertensive drugs with dose, frequency and duration were documented. Data completeness was ensured by the study investigators. Rationality of antihypertensive prescriptions was assessed as per NICE and JNC guidelines. Adherence to the guidelines was calculated as percentage of the total number of prescriptions in line with the recommendations of guidelines.

2.4. Data analysis

Statistical Package for the Social Sciences (SPSS) version 24.0 was used for analyzing the study data. The socio-demographic and clinical characteristics of the patients were examined by carrying out descriptive analyses. Pearson χ^2 test was used for establishing relationship between different variables. $P \leq 0.05$ were considered statistically significant.

2.5. Ethical considerations

The ethical approval of the study was obtained by Ras Al Khaimah (RAK) Medical and Health Sciences University Research and Ethics Committee (Number: RAKMHSU REC 3-2017-PG-P) and RAK Research and Ethics Committee (RAK REC 34-2017-PG-P), UAE.

3. Results

3.1. Socio-demographic and clinical characteristics

Out of the total 588 patients included in the study, majority (57.1%) of the patients were females. The hypertensive patients had a mean age of 63.2 ± 14.33 years, with majority of them aged 68 years and above (37.9%). Since the study site was a government hospital, majority of the patients were Emirati (79.6%) followed by Omani (16.8%) and other nationalities (3.6%). Table 1 represents the socio-demographic and clinical characteristics of the study population stratified by type of antihypertensive therapy. Five major classes of antihypertensive drugs namely angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), calcium channel blockers (CCB), beta blocker (BB) and diuretic were prescribed to the hypertensive patients at the study site. Majority of the patients (67.9%) were on combination therapy receiving multiple drugs for the management of their hypertension. Calcium channel blocker was the most frequently prescribed antihypertensive drug class (300 prescriptions) followed by ARB (274 prescriptions), diuretics (220 prescriptions), ACEI (210 prescriptions), BB (198 prescriptions) and other antihypertensive class (8 prescriptions).

3.2. Rationality of prescriptions as per international guidelines

3.2.1. Rationality of prescriptions as per JNC guidelines

According to JNC 7 guidelines for the management of stage 1 hypertension thiazide type diuretics should be considered for most patients and ACEI, ARB, BB or CCB may also be considered either alone or in combination. In the present study 98% of antihypertensive prescriptions were adherent to this JNC 7 recommendation for the management of stage 1 hypertension. Out of the 188 stage 1 hypertensive patients, 10 patients were prescribed thiazide diuretics, 67 patients were prescribed ARBs, 39 patients were on CCBs, 38 patients with ACEIs and 30 patients were prescribed BBs. Two patients were on non-thiazide diuretics and one each on moxonidine and terazosin respectively. These four prescriptions were not as per the JNC 7 recommendations for stage 1 hypertension (Table 2). However, as per JNC 8 for the initial antihypertensive therapy only four classes; thiazide diuretic, ACEI, ARB or CCB alone or in combination are recommended. Hundred and fifty-six (82.9%) of our antihypertensive prescriptions

were adherent to this JNC 8 recommendation. Thirty-two prescriptions (17.1%) for initial antihypertensive therapy did not have the recommended four classes of antihypertensive drugs.

For the management of stage 2 hypertension, JNC 7 recommends use of two drug combination for most patients usually a combination of thiazide diuretic and ACEI/ARB or thiazide diuretic and CCB or thiazide diuretic and BB. In our study only 22.9% of antihypertensive prescriptions were adherent to this two drug combination recommendation of JNC 7. Out of the 210 prescriptions of two drug combination, only 48 prescriptions were having two drug combination as per JNC 7 while the remaining 162 prescriptions were not as per the guidelines. Of these 48 prescriptions, 39 prescriptions were of thiazide diuretic and ACEI/ARB, 8 patients were on thiazide diuretic and CCB, while only 1 prescription had a combination of thiazide diuretic and BB. Whereas, majority (75.2%) of two drug combination prescriptions were in line with the JNC 8 recommendation for two drug combination.

According to JNC 7 recommendation for three drug combination therapy, thiazide diuretic should be one of the three classes and it can be combined with ACEI, ARB, BB, or CCB. Fifty-three percent of the prescriptions were adherent to this recommendation with 51 patients on combinations of thiazide diuretic, ACEI/ARB and CCBs, 21 patients were on combinations of thiazide diuretic, ACEI/ARB and BB. Sixty-four prescriptions contained other three drug combinations which were not as per JNC 7 recommendations. Regarding JNC 8 recommendation for adding a third antihypertensive drug, 126 three drug prescriptions (92.6%) of the study adhered to this recommendation. For four drug antihypertensive therapy, 72.9% of our prescriptions were as per the JNC 8 recommendation. Overall, 69% of the antihypertensive prescriptions were adherent to the JNC 7 recommendations and 80.9% were as per JNC 8 recommendations (Fig. 1).

3.3. Rationality of prescriptions as per NICE guidelines

NICE guidelines recommend four steps for the management of hypertension. In the present study, 42.8% of the prescriptions were adherent to the step 1 treatment recommendation of NICE 2011 and 2019 guidelines. Out of 189 patients falling under the step 1 antihypertensive treatment, only 81 patients were treated as per the step 1 recommendation. For patients aged less than 55 years, ACEI or ARB were prescribed to 39 patients, 32 patients aged more than 55 years were prescribed CCB, 9 patients were treated as per the third point of step 1

Table 2
Rationality of prescriptions as per JNC guidelines.

JNC 7 Hypertension Classification	Recommendations	No. of Prescriptions	Non-adherence (%)	Adherence (%)
Stage 1 Hypertension (n = 188)	Thiazide Diuretic	10	-	5.4
	ARB	67	-	35.7
	CCB	39	-	20.8
	ACEI	38	-	20.2
	BB	30	-	15.9
	Diuretic but not thiazide	2	1	-
	Centrally acting	2	1	-
Total		188	2%	98%
Stage 2 Hypertension (n = 210)	Two drug combination			
	ACEI/ARB + Thiazide	39	-	18.6
	CCB + Thiazide	8	-	3.8
	BB + Thiazide	1	-	0.5
	Other two drug combination	162	77.1	-
Total		210	77.1%	22.9%
Three drug combination	Three drug combination			
	Thiazide diuretic + CCB+ ACE/ARB	51	-	37.5
	Thiazide diuretic + BB + ACE/ARB	21	-	15.5
	Other three drug combination	64	47	-
Total		136	47%	53%
Four, five and six combinations	Not Recommended	54	100%	-
Overall Adherence to JNC		407	-	69%
Overall Non-Adherence to JNC		181	31%	-

ACEI: Angiotensin-converting-enzyme inhibitors, ARB: Angiotensin receptor blockers, BB: Beta blockers, CCB: Calcium channel blockers, JNC: Joint National Committee.

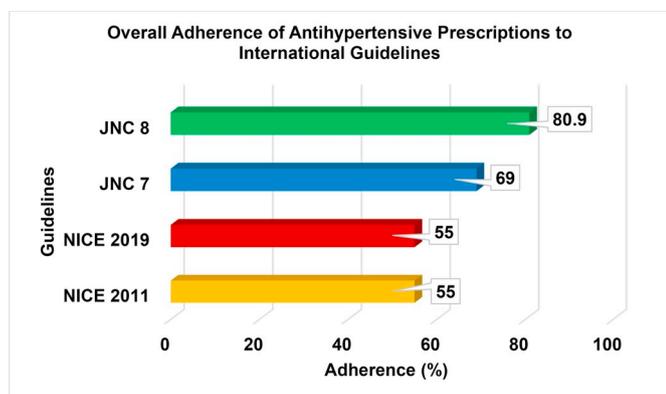


Fig. 1. Overall adherence of antihypertensive prescriptions to international Guidelines.

JNC: Joint national committee, NICE: National institute for health and care excellence.

recommendation while one patient was on a combination of thiazide diuretic and BB.

A high proportion of prescriptions (71.3%) were adherent to the step 2 treatment recommendation of NICE 2011 and 2019 guidelines as elaborated in Table 3. Out of the 208 patients needing drugs as per Step 2 antihypertensive treatment, 110 patients were prescribed CCB with either ACEI or ARB, 39 patients were on thiazide diuretic with ARB or ACEI. Sixty patients were receiving drug combinations which were not as per recommendations of NICE guidelines.

Step 3 treatment recommendation of NICE guidelines states that if treatment with three drugs is required, the combination of ACEI/ARB, CCBs and thiazide like diuretic should be used. In the present study 38.3% prescriptions were adherent to this step 3 treatment recommendation with 51 prescriptions with a three drug combination of thiazide diuretic, ARB and CCB.

Step 4 treatment is recommended in cases of resistant hypertension. NICE guidelines recommend three options for the management of resistant hypertension. First option is adding a low dose diuretic with spironolactone dose to the three drug combination in step 3 recommendation. In the present study only one patient is treated as per this recommendation. Second option is to consider high dose thiazide

Table 3
Rationality of prescriptions as per NICE 2011 and 2019 guidelines.

NICE Guideline	Recommendations	No of Prescriptions	Non-adherence (%)	Adherence (%)
Step 1	ACEI or ARB for less than 55 years	39	-	20.7
	CCB for above 55 years	32	-	16.8
	Thiazide diuretic if CCB intolerant for above 55 years	9	-	4.7
	BB + Thiazide	1	-	0.6
	Prescriptions with other monotherapy	18	57.2	-
Total		189	57.2%	42.8%
Step 2	CCB with ARB/ACEI	110	-	52.6
	Thiazide diuretic with ARB/ACE (CCB intolerant)	39	-	18.7
	Prescriptions other two drug combination	60	28.7	-
Total		209	28.7%	71.3%
Step 3	Thiazide diuretic + ARB/ACEI + CCB	51	-	38.3
	Prescriptions with other three drug combination	82	61.7	-
Total		133	61.7%	38.3%
Step 4	Thiazide diuretic + ARB/ACEI + CCB + another diuretic (spironolactone)	1	-	2
	Higher dose thiazide diuretic + ARB/ACEI + CCB	3	-	5.9
	Thiazide diuretic + ARB/ACEI + CCB + α blocker/BB	34	-	66.6
	Prescriptions with other four drug combination	13	25.5	-
Total		51	25.5%	74.5%
Five & Six Drug Combination	Not Recommended	6	100%	-
Overall Adherence to NICE		323	-	55%
Overall Non- Adherence to NICE		265	45%	-

ACEI: Angiotensin-converting-enzyme inhibitors, ARB: Angiotensin receptor blockers, BB: Beta blockers, CCB: Calcium channel blockers, NICE: National Institute for Health and Care Excellence.

diuretic treatment in the three combination therapy; 3 of our prescriptions were as per this recommendation. Final option is to consider addition of an alpha blocker or BB to the three drug combination. In the study 34 patients were on this type of prescription. For step 4 treatment recommendation, 55% of prescriptions were in the line with the NICE guidelines. Overall, 55% of the antihypertensive prescriptions were adherent to the NICE 2011 and 2019 guidelines (Fig. 1).

4. Discussion

This is the first study in Dibba hospital, Fujairah, UAE which assessed the antihypertensive prescriptions for rationality and adherence to international treatment guidelines. We have previously reported that majority of the antihypertensive prescriptions at the study site were of combination type.¹⁷ Combination antihypertensive therapy has shown to be more effective in controlling hypertension in patients with comorbidities than the monotherapy.¹⁸ Combining two drugs with different mechanisms can give an antihypertensive effect which is two to five times greater than obtained by monotherapy.¹⁹ Selection of antihypertensive treatment is governed by a number of factors like patient's comorbidities and concomitant medications, physician's choice depending on patient characteristics, availability of drugs at the hospital site and guidelines followed by the hospital. Overall, 69% of the antihypertensive prescriptions were adherent to the JNC guidelines, 80.9% were as per JNC 8 and 55% of the study prescriptions were adherent to 2011 and 2019 NICE guidelines.

For the management of stage 1 hypertension, JNC 7 recommend thiazide diuretics as initial therapy for most patients and ACEI, ARB, BB or CCB may also be considered. For initial antihypertensive therapy JNC 8 also recommend thiazide, ACEI, ARB or CCB alone or in combination but does not recommend BB. The JNC 8 panel did not recommend BB for the initial antihypertensive therapy based on a clinical trial which showed a higher rate of cardiovascular events with use of BB compared with use of an ARB.²⁰ Majority of our study prescriptions (98% to JNC 7 and 82.9% to JNC 8) were adherent to the JNC recommendations for initial antihypertensive therapy. These findings are in line with the results of a study conducted in a tertiary hospital in India.²¹ However contrasting findings were reported by many studies where thiazide diuretics were not the preference of the physicians for initial management of hypertension.^{22–24}

Studies have shown that in stage 2 hypertension combination

therapies afford better blood pressure control and effect of combining drugs is greater than doubling the dose of a single antihypertensive.²⁵ For the management of stage 2 hypertension JNC 7 also recommends use of two drug combination for most patients usually a combination of thiazide diuretic with ACEI/ARB or thiazide diuretic with CCB or thiazide diuretic with BB. Our results revealed that only 22.9% of antihypertensive prescriptions were adherent to this two drug combination recommendation of JNC 7. A study conducted by Tandon et al. reported a higher proportion (43.2%) of antihypertensive prescriptions in line with the JNC 7 recommendation for stage 2 hypertension.²¹ JNC 8 states that if after initial antihypertensive therapy blood pressure goal is not achieved titrate drugs to the maximum doses or add second drug from ACEI, ARB, CCB or thiazide class. Majority (75.2%) of our two drug study prescriptions were in line with this JNC 8 recommendation. Majority of the two drug combination prescriptions (52.8%) were of ARB/ACEI with CCB. Studies have shown that ARB/ACEI and CCB combinations are more effective in decreasing blood pressure with greater clinical benefits in cardiovascular outcomes.^{26,27}

According to JNC 8, if blood pressure goal cannot be reached with two drugs, a third drug can be added and titrated from the recommended classes of drugs. Nearly one-fourth of our total antihypertensive prescriptions were of three drug combination. This finding can be attributed to the fact that majority of our study participants had more than two comorbidities. Majority (92.6%) of these three drug combination prescriptions were in line with the JNC 8 recommendations. JNC 8 recommend that if blood pressure goal is not achieved by using three drugs from ACEI, ARB, BB, or CCB then a fourth antihypertensive drug can be added from other classes. Only a fraction (8.2%) of our antihypertensive prescriptions contained four drugs, out of these majority of them were as per the recommendation of JNC 8.

NICE 2011 and 2019 guidelines for diagnosis and management of hypertension in adults state that “offer step 1 antihypertensive treatment with a CCB to people aged over 55 years. If a CCB is not suitable, offer a thiazide-like diuretic”. Our results revealed that 42.8% of our prescriptions were adherent to this recommendation. Several studies have shown that in elderly population CCB are effective and safe providing good blood pressure control.^{28,29} According to Step 2 of NICE guidance 2011 and 2019, if hypertension is not controlled in adults taking CCB in step 1 then combine CCB with ARB/ACEI or thiazide diuretic. Majority of our antihypertensive prescriptions (71.3%) were in accordance with this recommendation of NICE guidelines.

NICE guidance recommend that before considering the step 3 treatment for hypertension a review of patients’ medications should be done ensuring that they are being taken at the optimal tolerated doses and adherence should also be discussed with the patients.¹² For step 3 hypertension treatment, both the 2011 and 2019 NICE guidelines recommend that “if treatment with three drugs is required, the combination of ACEI/ARB, CCBs and thiazide like diuretic should be used”. In our study, 38.3% of the prescriptions were adherent to this step 3 treatment recommendation.

If hypertension is not controlled by the three drug combination as per step 3 recommendation then it should be regarded as resistant hypertension. For the management of resistant hypertension addition of a fourth antihypertensive should be considered as step 4 treatment. More than half (55%) of our study prescriptions were in line with this recommendation of NICE 2011 and 2019 guidance for diagnosis and management of hypertension.

The present study reports that the antihypertensive prescriptions at the study site largely adhere to the latest JNC and NICE guidelines for the management of hypertension. There are a number of barriers which affect the implementation of clinical practice guidelines.¹⁴ This adherence pattern in the study can be attributed to number of factors like specific patients’ characteristics, presence of different comorbidities, adverse reactions and contraindication to drugs, availability of drugs at the study site, lack of awareness towards guideline recommendations, time constraints and physicians’ disagreement with the guidelines.

Antihypertensive prescriptions at the study site are mostly as per the international guidelines for the management of hypertension. For appropriate management of hypertension there is a significant use of different antihypertensive drug combinations at the study site. Overall, evaluation of antihypertensive prescriptions for rationality remains largely understudied in UAE and the present study gave a picture of antihypertensive drug utilization at a secondary care hospital in the region. This study can be the foundation for further research in the region and can assist the clinicians in achieving rational drug utilization leading to better therapeutic outcomes.

There are some limitations to our study. Firstly, since it a single center study the sample may not be a complete depiction of region’s patient population. Secondly, physicians’ prescriptions were considered as sole measure of adherence to the guidelines. Achievement of blood pressure goals, follow up and monitoring should also have been evaluated for determining the adherence to treatment guidelines. Thirdly due observational nature of our study, factors like physicians’ educational background, influence of pharmaceutical companies and hospital administration, and availability of drugs at the study site were not evaluated.

5. Conclusion

In conclusion, antihypertensive prescribing at the study site is largely rational and adheres to the latest international guidelines but still there is a scope for improvement in terms of achieving rational drug utilization. This study can serve as the stepping stone for large scale multicenter prescription focused drug utilization studies.

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Declaration of competing interest

None declared.

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