MEDICATION ADHERENCE IN HYPERTENSIVE PATIENTS IN LUMBINI PROVINCE OF NEPAL

Gautam Prasad Chaudhary [*], Bijay Gautam, Shristi Bauddhacharya, Bipana Bhusal, Saraswati Khatri, Mukesh Kumar Chaudhary and Ram Bahadur Khadka

Department of Pharmacy, Crimson College of Technology, Pokhara University, Pokhara - 37003, Nepal.

ABSTRACT: Medication Adherence is defined as "the extent to which a person's behavior in taking medication, lifestyle management, diet, corresponding with an agreed recommendation from a healthcare provider". Hypertension also called high blood pressure is defined as persistency with an elevation in systolic blood pressure ≥140 mmHg and /or diastolic pressure ≥ 90 mmHg. A cross-sectional study was carried out in order to measure medication adherence, Morisky Green Levine-Medication Adherence Questionnaire developed by Donald Morisky was used to assess medication adherence assessment, which consists of 4 questions (items) whose wording questions are formulated to avoid answering 'yes' or 'no' and three levels of medication adherence: high, medium, and low were measured based on the scores 0, 1-2,3-4 respectively. The study carried out an evaluation of medication adherence among hypertensive patients. Among 245 respondents, 5.7% were found to be highly adherent, 37.6% were found to be medium adherent and 56.7% were found to be low adherent. A significant association between a family history of hypertension, diabetes, and smoking behavior was observed. A high proportion of patients had low adherence to their medications, very low proportion of patients were found to have high adherence to their medications. Regular follow up, patient education, and improved social habits of smoking, and alcoholism can be contributing factors to improving medication adherence.

INTRODUCTION: Hypertension, commonly known as high blood pressure, is characterized by a persistent increase in systolic blood pressure of at least 140 mm Hg and /or diastolic blood pressure of at least 90 mm Hg [1]. Over a billion people in the world- 1 in 4 men and in 5 women are having this condition [2]. Various increasing trends show prevalence variations according to a different population [3].

In Nepal, hypertension prevalence ranges from 23-48% which is found to increase three times within 25 years due to salt intake [4].

Medication adherence is defined as "the degree to which a person's conduct is taking medications, lifestyle management, and nutrition, corresponds with agreed upon recommendation from a healthcare professional" and the avoidance of patients in the instructions given by the healthcare professionals and disagreement with their physician's recommendation due to various reasons such as lack of knowledge, disbelief, etc is medication non-adherence. About half of hypertension patients stop taking their medicine within a year of being diagnosed, which ultimately

results in non-adherence [5]. Multiple medical conditions have also been considered to be a hindrance to effective drug adherence and to cause non-adherence. Intentional and unintentional non-adherence is the two main causes of non-adherence. When a patient consciously chooses not to take their prescribed medications, this is considered intentional non-adherence. It is typically based on perceptual elements that affect the desire to start and continue with therapy, such as false beliefs and preferences. Non-intentional non-adherence occurs when a patient intends to follow a recommendation but is unable to do so due to inadequate knowledge or information, difficulties, comprehending the instructions, or unintentionally forgetting to remember the prescribed course of action [6].

Outcomes such as therapeutics failure, escalating diagnostics and therapeutic measures, increased risk of adverse effects, hospitalization, increased health care cost, prescription cascade, disease progression, low quality of life, and waste of medication resources [7]. There are generally two methods of adherence assessment: Direct and Indirect Assessment. Direct methods include Biological Markers, Plasma Concentrations of medications or their metabolites, and observation of the treatment process whereas indirect assessment includes the use of electronic devices measuring medication intake, questionnaire-based surveys, pharmacy register analysis, clinical-based observational and progress or termination of illness assessment [8].

MATERIALS AND METHODS: A cross-sectional study was conducted on hypertensive patients from march to august 2022 at the outpatient department of Gautam Buddha community heart hospital which is located in Rupandehi. This hospital has got various clinical departments like the cardiac department, general department, intensive care unit (ICU), pathology, pharmacy, outpatient department, and many other departments. Daniel's Formula was used for (i.e., N = z^2 * P (1-P) / d^2) was used for the determination of Sample Size consideringa margin of sampling error of 5% and a confidence level of 95%, and a random sampling technique was used for the calculation of sample size [9]. The minimum sample size of our study was found to be 245 Where N= Minimum sample size required

according to estimating proportion, Z= Standard normal value for 95%, Cl= 1.96, P= Proportion of population possessing characteristics of Interest = 0.199, 1-P= Proportion of population possessing characteristics of interest = 0.801, d- margin of sampling error (5%) = 0.05. In this study, Various variables were taken such as Age, Gender, Sex, Education, Smoking behavior, alcoholic behavior, Family history of Hypertension, follow-up, *etc*. The inclusion criteria were Patient with either sex of age≥18 years and diagnosed with hypertension at least 6 months before the study and consuming antihypertensive medications. The Patient Profile Form was developed manually by the researchers.

The duly filled form contains patient demographic details like name, address, age, gender, occupation, education, and family history of hypertension. Morisky Green Levine-Medication Adherence Questionnaire was used to assess medication adherence in patients and was developed by Donald Morisky. It was applied in interviews with patients in a study of Hypertension control which consists of 4 questions (items) whose wording of the questions are formulated to avoid answering 'yes' to questions regardless of content. Items 1 to 4 have response choices 'Yes or 'No'. The total score on the MGL scale ranges from 0 to 4. Three levels of medication adherence based on this score: High, Medium, and low adherence with 0,1-2 and 3-4 points respectively and is also commonly used with 0 points indicating perfect adherence and 1+ points indicating some level of non-adherence.

Self-report including the potential reason for non-adherence including 4 questions asking about medication adherence. The sensitivity of MGL_MAQ is 81% and the specificity is 44%[10].

Ethical Consideration and Statistical Analysis: The purpose of the research was clearly explained to the patients and assured them to protect their privacy and confidentiality as well written consent or thumb impression (if unable to write) was obtained using a consent form in Nepali language (annex-2). The record of patient medications was collected from the outpatient Pharmacy department paying attention to inclusion criteria. All of the above information on the record were noted and captured into the personal computer (MS Excel). Data were coded and checked for completeness and

consistency with the help of IBM SPSS Statistics for Windows, version 20. Descriptive statistics for all studied variables and a chi-square test were used. A p-value< 0.05 was considered significant throughout the study and frequency, percentage, mean and standard deviation were used to carry out to describe the general characteristics of the participants [11]. Simple percentage distribution was used to assess Medication Adherence in Hypertensive Patients.

RESULTS AND DISCUSSION:

Assessment of Medication Adherence: Among 245 respondents, 14 (5.7%) were highly adherent to their medication, 139(56.7%) were found to be low adherent and 92 (37.6%) were found to be medium adherent as seen in **Table 1.**

TABLE 1: ASSESSMENT OF MEDICATION ADHERENCE

Medication adherence (n=245)		
Medication adherence	Respondents (n)	Respondents %
High adherent	14	5.7
Medium adherent	92	37.6
Low adherent	139	56.7

Age Group Distribution: A total of 245 patients were enrolled in the study and it found that the maximum of the respondents 26.9% were in the age group of 50-60 years, followed by 21.2% 60-70 years, 40-50 years 18.8%, 17.1% were 70-80 years, 8.6% were 30-40 years 4.9% were 80-90 years, 2% were 20-30 years and above 90 years 0.4%. The mean age was found to be 58.56 years and the standard deviation was found to be 13.914 as seen in **Table 2.**

TABLE 2: AGE GROUP DISTRIBUTION OF THE PATIENTS

Age group	Respondents (n)	Respondents %
20-30	5	2
30-40	21	8.6
40-50	46	18.8
50-60	66	26.9
60-70	52	21.2
70-80	42	17.1
80-90	12	4.9
>90	1	0.4

Gender-wise age Distribution: Among the total patients enrolled in the study, it was found that the maximum number of respondents were females which were 139(56.7%) and males 106(43.3%) **Table 3.**

TABLE 3: GENDER-WISE DISTRIBUTION OF PATIENTS

Gender	Respondents (n)	Respondents %
Male	106	43.3
Female	139	56.7

Education-wise Distribution of Patients: In our study, we noticed that the Maximum number of respondents were illiterate, among 245 respondents, 96(39.2%) were found to be illiterate and 149 (60.8%) were found to be literate as seen in **Table 4.**

TABLE 4: EDUCATION-WISE DISTRIBUTION OF PATIENTS

Education	Respondents (n)	Respondents %
Literate	96	39.2
Illiterate	149	60.8

Profession-wise Distribution of Patients: Among the total respondents, more than half of the respondents were housewives which was 53.9% (132), and about one-fourth of respondents were found to be engaged in agriculture which was 23.7%. Our study shows that 11.0% (27) were involved in business and only 6.9% (17) were found to be unemployed as seen in **Table 5.**

TABLE 5: PROFESSION-WISE DISTRIBUTION OF PATIENTS

Profession	Respondents (n)	Respondents %
Agriculture	58	23.7
Business	27	11
Housewife	132	53.9
Employed	11	4.5
Unemployed	17	6.9

Distribution of Patient Based on Social Habits: Distribution of Patients Based on Smoking Habits: Among 245 respondents, 66.53% (163) were nonsmokers, 19.18% (47) were past smokers and 14.29% (35) were smokers as seen in **Table 6.**

TABLE 6: DISTRIBUTION OF PATIENTS BASED ON SMOKING HABITS

Smoking behavior	Respondents (n)	Respondent %
Smoker	35	14.29
Nonsmoker	163	66.53
Past smoker	47	19.18

Distribution of Patients Based on Alcoholic Behavior: Based on alcoholic behavior our study shows that 16.3% (40) were alcoholic, 64.9% (159) were non-alcoholic and 18.8% (46) were past alcoholic as seen in **Table 7.**

TABLE 7: DISTRIBUTION OF PATIENTS BASED ON ALCOHOLIC BEHAVIOR

Alcoholic behavior	Respondents (n)	Respondents %
Alcoholic	40	16.3
Nonalcoholic	159	64.9
Past alcoholic	46	18.8

Distribution of Patients Based on Family History of Hypertension: While studying for a family history of hypertension, it was found that 47.3% (116) had a family history of hypertension, and 52.7% (129) did not have a family history of hypertension **Table 8.**

TABLE 8: DISTRIBUTION OF PATIENTS BASED ON FAMILY HISTORY OF HYPERTENSION

Family history of Hypertension	Respondents (n)	Respondent %
Yes	116	47.3
No	129	52.7

Distribution of Patients Based on Follow-up: Based on follow-up visits, it was found the majority of respondents 223(91%) do follow-up visits, and 22(9%) did not do follow-up visits as seen in **Table 9.**

TABLE 9: DISTRIBUTION OF PATIENTS BASED ON FOLLOW UP

Follow up	Respondents (n)	Respondents %
Yes	223	91
No	22	9

Association of Variables with Medication Adherence:

TABLE 10: ASSOCIATION OF VARIABLES WITH MEDICATION ADHERENCE FOR P<0.05, CHI-SQUARE TEST

Variables	Medication Adherence			P value
	Low adherent	Medium adherent	High adherent	
The age range of patients in years				
20-30	3 (60.0%)	1(20.0%)	1(20.0%)	0.309
30-40	15 (71.4%)	6(28.6%)	0(0%)	
40-50	28 (60.9%)	16(34.8%)	2(4.3%)	
50-60	40 (60.6%)	20(30.3)	6(9.1%)	
60-70	22 (42.3%)	28(53.8%)	2(4.8%)	
70-80	23 (54.8%)	17(40.5%)	2(4.8%)	
80-90	8 (66.7%)	3(25.0%)	1(8.3%)	
90-100	0 (0)	1(100.0%)	0(0%)	
Gender of patients				
Male	55(51.9%)	43(40.6%)	8(7.5%)	0.313
Female	84(60.4%)	49(35.3%)	6(4.3%)	
Education of patients				
Illiterate	55(57.3%)	34(35.5%)	7(7.3%)	0.642
Literate	84(56.4%)	58(38.9%)	7(4.7%)	
Profession of patients				
Agriculture	44(75.9%)	12(20.7%)	2(3.4%)	6.04
Business	21(77.8%)	5(18.5%)	1(3.7%)	
Housewife	62(47.0%)	63(47.7%)	7(5.3%)	
Employed	9(81.8%)	2(18.2%)	0(0%)	
Unemployed	3(17.6%)	10(58.8%)	4(23.5%)	
Smoking behaviors of patients				
Nonsmoker	98(60.1%)	53(32.5%)	12(7.4%)	0.029*
Past smoker	19(40.4%)	26(55.3%)	2(4.3%)	
Smoker	22(62.5%)	13(37.1%)	0(0%)	
Alcoholic behaviors of patients				
Alcoholic	26(65.0%)	11(27.5%)	3(7.5%)	0.367
Non-alcoholic	92(57.9)	59(37.1%)	8(5.0%)	
Past alcoholic	21(45.7%)	22(47.8%)	3(6.5%)	
Family history of hypertension				
Yes	78(67.2%)	35(30.2)	3(2.6%)	0.004*
No	61(47.3%)	57(44.2)	11(8.5%)	
Follow-up done by patients				

Yes	123(55.2)	86(38.6%)	14(6.3%	0.207
No	10(72.71)	6(27.3)	0(0%)	
Diabetes mellitus				
No	110(61.8%)	57(32%)	11(6.2%)	0.014*
Yes	29(43.3%)	25(52.2%)	3(4.5%)	
Thyroid				
No	58.30%	37.00%	4.60%	0.095
Yes	44.80%	41.40%	13.80%	
Uric Acid/Rheumatoid Arthritis				
No	56.40%	38.00%	5.60%	0.722
Yes	63.60%	27.30%	9.10%	
Cholesterol				
No	62.40%	32.90%	7(4.7%)	0.08
Yes	47.90%	44.80%	7(7.3%)	
Others				
No	56.50%	37.90%	5.60%	0.985
Yes	57.10%	36.90%	6.00%	

*Significant association for p<0.05, Chi-square test.

Table 10 shows no significant association between age group and medication adherence. No significant association was observed with Gender. Among them, 51.9% (55) males were low adherent and 40.6% (43) were medium adherent and 7.5% (8) were highly adherent. Similarly, among the studied female population it was found that 60.4% (84) were low adherent and 35.3% (49) were medium adherent and 4.3% (6) were highly adherent. In our study, no significant association was observed between education and medication adherence Among the illiterate 57.3.7% (55) were found to be low adherent, 35.4%(34) were found to be medium adherent, and 7.3% (7) were found to be highly adherent Similarly, among literate 56.4% (84) were found to be low adherent, 38.9% (58%) were found to be medium adherent and 4.7% (7%) were found to be highly adherent.

Similarly, no significant association between professions too with medication adherence. There was a significant association observed between smoking behavior and medication adherence among on-smokers, 60.1% (98), 32.5% (53), and 7.4% (12) were found to be low adherent, medium adherent, and high adherent respectively. Among past smokers, 40.4% (19), 55.3% (26), and 4.3% (2) were found to be low adherent, medium adherent, and high adherent respectively. Among smokers, 62.9% (22), 37.1% (13), and 00% (0) were found to be low adherent, medium adherent, and high adherent respectively. There was no significant association observed with drinking alcohol behavior. Among alcoholics, 65.0% (26),

27.5% (11) and 7.5% (3) were found to be low adherent, medium adherent, and high adherent respectively. Among nonalcoholic, 57.9% (92), 37.1% (59), and 5.0% (8) were found to be low adherent, medium adherent, and high adherent respectively. Among past alcoholics, 45.7% (21), 47.8% (22), and 6.5% (3) were found to be low adherent, medium adherent, and high adherent respectively. There was a significant association observed for a family history of hypertension. Among people who had a family history of hypertension, it was found that among them 67.2% (78), 30.2 %(35), and 2.6 %(3) were found to be low adherent, medium adherent, and high adherent to their medication respectively. Similarly, those who did not have a family history of hypertension were found to be 47.3% (61), 44.2% (57), and 8.5% (11) low adherent, medium adherent, and high adherent to their medication respectively. No significant association was observed with follow-up for medication adherence in our study. Among people who had follow-up visits, it was found that among them 55.2% (123), 38.6% (86), and 6.3% (14) were found to be low adherent, medium adherent, and high adherent to their medication respectively. Similarly, those who did not do follow-up were found to be 72.7% (16), 27.3% (6), 0% (0) low adherent, medium adherent, and high adherent to their medication respectively.

Distribution of Different Types of Antihypertensive Drugs Prescribed to Hypertensivepatients: Our study showed that among 245 respondents, Metoprolol was prescribed

to 75 people followed by amlodipine to 58 people, followed by losartan potassium to 50 people and only one individual has prescribed combination of frusemide and amlodipine.

TABLE 11: DISTRIBUTION OF DIFFERENT TYPES OF ANTIHYPERTENSIVE DRUGS TO HYPERTENSIVE PATIENTS

Name of Medicine	Respondents	Respondents %
Amlodipine	58	18.89%
Losartan potassium + Hydrochlorothiazide	10	3.25%
Amlodipine + Atenolol	6	1.95%
Amlodipine + Hydrochlorothiazide	28	9.12%
Atenolol	5	1.62%
Metoprolol	75	24.42
Telmisartan	20	6.51%
Telmisartan + Amlodipine	4	1.30%
Amlodipine + Losartan	18	5.86%
Frusemide + Amlodipine	1	0.32
Propranolol	10	3.25%
Losartan Potassium	50	16.28%
Enalapril	22	7.16%

Distributions of Patients Based on Comorbid Conditions: Among 245 respondents, while studying for co-morbid conditions it was found that 67 (27.35%) had Diabetes Mellitus, 123(50.21%) had heart disease, 29(11.89) had thyroid disease, 11(4.49%) had uric acid, 96(31.18%) had cholesterol and 84(34.29%) had others which included Chronic obstructive pulmonary disease (COPD), asthma, gastritis, prostrate, allergy, kidney disease, depression, urinary tract infection (UTI).

TABLE 12: DISTRIBUTION OF PATIENTS BASED ON COMORBID CONDITIONS

Comorbid conditions	Respondents (n)	Respondents %
Diabetes mellitus	67	27.35%
Heart disease	123	50.21%
Thyroid	29	11.895
Uric acid	11	4.49%
Cholesterol	96	31.18 %
Others	84	34.29 %

Distribution of Patients Based on Number of Drugs Consumed: Among 245 respondents, about 24.5% (60) consume three medicines. 0.4% (1) was found to be consuming ten numbers of medicines, 1.6% (4) was found to be consuming eight numbers of medicines, 6.1% (15) was found to be consuming seven numbers of medicines, 8.2% (20) was found to be consuming six numbers of medicines, 12.7% (31) was found to be consuming five numbers of medicines, 20.8% (51) was found to be consuming four numbers of medicines, 10.2% (25) was found to be consuming one number of medicines, 15.5% (38) was found to be consuming two number of medicines.

TABLE 13: DISTRIBUTION OF PATIENTS BASED ON THE OF DRUGS CONSUMED

Number of medicines	Respondents (n)	Respondents %
1	25	10.2
2	38	15.5
3	60	24.5
4	51	20.8
5	31	12.7
6	20	8.2
7	15	6.1
8	4	1.6
9	0	0
10	1	0.4

Racial Distribution of Patients: Among the races enrolled in Study 65(26.53%) were Bhramins, 29(11.84%) were Chettri, 35(14.29%) were Madhesi, 69(28.16%) were Janajati which included

Gurung, Magar, Tharu, Newar), 24(9.75%) were Dalit, 15(6.12%) were Muslims and 8(3.26%) were others which included Rajput, shah, Sen, Malla. The detail of the racial distribution study patients is given in **Fig. 1.**
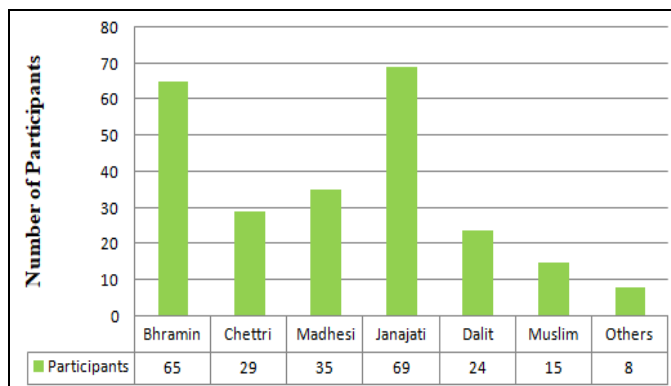

FIG. 1: RACIAL DISTRIBUTION OF PATIENTS

Our study was quite similar to local studies carried out in India that showed 15%, 39%, and 46% were high medium, and low adherent [12]. Different studies across the world reported less adherence to antihypertensive medications. A study done in Northern China showed 79% non-adherence [13]. 57% non-adherent result was found in a study carried out in Lima Peru [14]. 54% no adherence in non-Congo [15]. Research carried out in Eastern Nepal showed 43.5% of the participants were found to be non-adherent [16].

77%, 91%, and 77% of medication adherence were reported in studies carried out in Egypt, Scotland, and Pakistan[17]. Similarly, the Rate of adherence was found to be 53.4% in a study carried out in Malaysia [18]. Variations between studies may occur due to variations in the studied population, assessment tools, tests, and cutoff point's used [19]. The inclusion criteria for age were>18 years of age, however, we found no individuals of 18, 19 years so we took the age group of vicenarians to nonagenarians [20]. In our study, medication adherence for the age group 50-60 was found to be high adherent insignificantly which is in contrast to the study done in Iraq where compliance was observed high among 70 years and more [21]. The probable reason for this might be in old patients 'adherence to medications tend to decrease for many reasons, one of them being progressive cognitive decline or depression or developing with age [22]. A study carried out at Duke University significantly showed that lower age was associated

with lower adherence [23]. In Nepal, the possible reason for low medication adherence could be socioeconomic factors, demographic factors, poor and irregular follow-up patterns and difficulty accessing medication, simple forgetfulness, and low level of seriousness of consequences of missing medications. Geographic factors, sometimes within a country, support rendered by caretakers can modulate the association between age and adherence under the influence of local traditions [24]. Our study showed males were insignificantly high adherent than females similar to the study done in Maharashtra which also showed insignificant results [25].Our study showed the insignificant and same level of adherence of literate and illiterate people.

Different studies suggest a Disability to Read and Understand medication instructions, with low literacy difficulty understanding instructions ultimately results in decreased adherence [26]. Patient education affected adherence; people omitted doses as time increased [27]. Moreover, Patient education: Omission of doses and delays in time of dose may also influence adherence [28]. Our study showed insignificant results with the profession while comparing with medication adherence.

Our study significantly revealed that Nonsmokers are 60% no adherent and 12% adherent to medicines, and smokers are 62.9% low adherent to their medicines which is, in contrast, to a study done in Tamil Nādu which showed insignificant association to smokers [29]. The variations in the result might be due to choosing of the variable of interest, we chose smoker, nonsmoker, and past smoker as our choice of interest but other studies have taken smoker, non-smoker, and past smoker (at least 12 months of withdrawal [30]. Our study revealed no significant association with alcoholic intake. Which is a contrast to a study done in southern Ethiopia which showed a significant association with alcoholic intake [31]. The variations might be due to differences in the choice of interest in the selection of variables. Further different studies showed results in contrast to our study showing a significant association of alcohol intake with antihypertensive medicines [32] association with an increase in blood pressure [33]. Our study showed a significant association between family histories with hypertension showing people with a family.

history of hypertension showed less high adherence and lower adherence to medications whereas people with no family history showed results just reverse to it. Our study showed insignificant results for follow-up patients with high adherence, but a study done in Brazil significantly predicted adherence to antihypertensive medicines [34]. However, another study was similar to our investigation showing that patients with no regular follow-up had low adherence [35].

CONCLUSION: The adherence level to the prescribed anti-hypertensive medications was found and a high proportion of patients had low adherence, half of the respondents were no adherence to antihypertensive medicines. The study's findings showed a significant association between smoking behaviors, diabetes mellitus, and a family history of hypertension.

These findings open multiple avenues that healthcare providers should pay due attention to the importance of adherence and the influencing factors of adherence. There should be approaches in place in hospitals and healthcare centers in Nepal that would improve Medication adherence. Drug adherence is a crucial issue in the pharmacotherapy of chronic disease at all ages.

In old patients adherence tends to decrease for many reasons, one of them being the progressive cognitive decline or depression developing with age. In order to avoid frequent and costly hospitalization healthcare professionals should periodically reassess the pertinence of all prescribed medications. Moreover, regular follow-up, Patient education, and improved social behavior can be the contributing factors to improving medication adherence.

Limitations:

- As there are wide ranges of factors that can affect medication adherence, we were not able to study all the possible factors such as marital status, dietary habits, and psychological factors.

- Another limitation includes the fact that the study was conducted from a single center with a modest number of individuals, which might limit the generalization of the findings to a wider center.

- The questionnaire tool used is a self-reporting tool, thus there is a risk of reporting bias and social desirability bias.

- Our study did not use direct methods like Blood serum or Urine analysis to detect medication adherence or indirect methods like pill count to precisely determine medication adherence.

Recommendation:

- It would be a good idea to design a questionnaire to include physical, psychological, therapeutic, and social factors related to healthcare management and economic issues of patients who are suffering from another comorbid disease besides HTN while studying Medication Adherence.

- Studying other important factors such as medication cost, differences between generic and brand forms of a single medication, visual acuity of patients, and the role of the pharmacist seems necessary for a better understanding of adherence.

- Interventional studies using medication chart pill count and direct assessment measures can be carried out in the future to improve medication adherence.

CONFLICTS OF INTEREST: There are no conflicts of interest.

REFERENCES:

1. Mohamed SF, Uthman OA, Caloyachetty R, Chumo I, Mutual MK and Asiki G: Uncontrolled hypertension among patients with comorbidities in Sub-Saharan Africa: protocol for a systematic review and meta-analysis. Syst Rev 2020; 9(1): 1-5.
2. Shareinia H, Sadeghmoghadam L, Mokhtarzadeh MR, Zahrayi SM, Jafari N and Noori R: Relationship between polypharmacy and medication adherence in hypertensive elderly patients. Disease and Diagnosi 2020; 9(4): 153-57.
3. Wang J, Ma JJ Liu J, Zeng DD, Song C and Cao Z: Prevalence and risk factors of Co morbidties among hypertrensives patients in China. Int J Med Sci 2017; 14(3): 201-212.
4. Shakya R, Shrestha S, Gautam R, Rai L, Maharjan S and Satyal GK: Perceived illness and treatment adherence to

hypertension among patients attending a tertiary hospital in Kathmanndu, Nepal. PPA 2020; 14: 2287-2300.

5. Chaudhary AM, George J, Khadowade K, Faizya L, Anjun R and Uma VM: Evaluation of medication and associated factors in hypertensive patients in Banglore, India; A cross-sectional study. IJPI 2021; 11(4): 426-431.

6. Cha AHY, Home R, Hankins M and Chisari C: The Medication adherence report scale: A memasurement tool for eliciting patients' report of non-adherence. Bristish Jour of Clin Pharm 2020; 86(7): 1281-1288.

7. Lyles A, Culver N, Ivester and Potter T: Effects of Health Literacy and Pharmacology on Medication adherence. The Consultant Pharmact 2013; 28(12): 793-799.

8. Kubica A, Kosobucka A and Michalski P: Self reported questionnaire for assessment adherence to treatment in patients with cardiovascular diseases. Medical Research J 2017; 2(4): 115-22.

9. Naing L, Wim T and Rusli BN: Practical Issues in Calculating the sample size for prevalence studies. Arch of Orf Sci 2006; 1: 9-14.

10. Beyhagi H, Reeve BB, Rodgers JE and Stearn SC: Psychometric Properties of the four- item Morisky Levin Medication Adherence Scale among Artherosclerosis Risk in Communities (ARIC) Study Participants. Val in Health 2016; 19(8): 998-1001.

11. Chaudhary GP, Khadka RB, Lamichhane A, Dhakal B, Das N, Tharu NS, Karki K and Pandey J: Impact of COVID-19 pandemic on learning status of student in Nepal. J of Educat and Health Promotion 2022; 11(1): 314.

12. Satish S, Rose AJ and Shabaraya AR: A study to assess the impact of comorbidities and polypharmacy in non-adherence to antihypertensives. IJRR 2021; 8(2): 222-227.

13. Ma C: A cross-sectional survey of medication adherence and associated factors for rural patients with hypertension. Appl Nurs Res 2016; 31: 94-99.

14. Fernandez-Aries M. Acuna-Villaorduna A, Miranda JJ, Diez-Canseco F and Malaga G: Adherence to Pharmacotherapy and medication-related beliefs in patients with hypertension in Lima, Peru. Plos One 2014; 9(12): 1-11.

15. Lulebo AM, Mutombo PB and Mapatano MA: Predictors of non-adherence to antihypertensive medication in Kinshasa, Democratic Reublic of Congo: a cross-sectional study. BMC Res Notes 2015; 8: 1-8.

16. Bhandari B, Bhattarai M, Ghimire A, Pokharel PK and Morisky DE: Adherence to Antihypertensive Medications: Population Based Follow up in Eastern Nepal. J Nepal Health Res Counc 2015; 13(1): 38-42.

17. Youseff RM and Moubarak II: Pattern and determinants of treatment compliance among hypertensive patients. East Mediterr Health J 2002; 8: 579-592.

18. Ramli A, Ahmad NS and Paraidathathu T: Medication adherence among hypertensive patients of primary health clinics in Malasiya. Patients Prefer and Adher 2012; 8: 613-622.

19. Hashmi SK, Afridi MB and Abbas K: Factors ssociated with adherence to anti hypertensive treatment in Pakistan. PloS One 2007; 2(3): 1-8.

20. Dahaba A, Xiao Z and Zhu X: Age progression from vicenarians (20-29 year) to nonagenarians (90-99 year) among a population pharmacokinetic/ pharmacodynamic (PopPk-PD) covariate analysis of propofo;-bispectral index (BIS) electroencephalography. J of Pharmacokinetics and Pharmacod 2020; 47(4): 145-161.

21. AI-Dabbagh SA and Aswad SM: Compliance of hypertensive patients to management in Duhok governorate using Morisky-green test. Duhok Med J 2010; 4: 28-39.

22. Burnier M, Polychronopoulou E and Wuerzner G: Hypertension and drug adherence in the elderly, Frontiers in Cardiovascular Medicine 2020; 7: 1-9.

23. Granger BB, Ekman I and Granger CB: Adherence to medication according to sex and age in the CHARM programme, Europ J of Heart Fail 2009; 11(11): 1092-98.

24. Han Y, Saran R, Erickson SR, Hirth RA, He K and Balkrishnan R: Environmental and Individual predictors of medication adherence among elderly patients with hypertension and chronic kidney diseases geospatial approach. Res Soc Adm Pharm 2019; 16(3): 422-430.

25. Nagarkar AM, Gedhave SA, Sharma I, Choure A and Morisky D: Factors influencing medication adherence among hypertension patients in a tertiary care hospital. PUne, Maharastra. NJCM 2013; 4(4): 559-563.

26. Praska JL, Kripalani S and Seright AL: Identifying and assisting low-literacy patients with medication use: a survey of community pharmacies. Ann Pharmacotherapy 2005; 39(9): 1441-1445.

27. Saadat Z, Nikdoust F and Aerab-Sheibani H: Adherence to Anti-hypertensives in Patients with Co morbid Condition. Nephrourol Mo. 2015; 7(4): 1-6.

28. Burnier M: Long term compliance with anti hypertensive therapy: another facet of chronotherapeutics in hypertension. Blood Pressure Moniterin 2000; 5(1): 31-34.

29. Venkatachalam J, Abrahm SB and Singh Z: Determinants of patients adherence to hypertension Medications in a Rural Population of Kancheepuram Districts in Tamil Nadu, South India. IJCM 2015; 40(1): 33-37.

30. West R: Tobacco smoking: Health impact prevalence correlates and interventions, Department of Behavioural Science and Health 2017; 32(8): 1018-1036.

31. Asgedom SW, Atey TM and Desse TA: Antihypertensive medication adherence and associated factors among adult hypertensive patients at Jimma University Specialized Hospital Southwest Ethiopia. BMC Res Notes. 2018; 11(1): 1-8.

32. Rai BB, Kabra PR and Sreedahar M: Factor associated with adherence to antihypertensive treatment among hypertensive persons in urban slum area of Hyderbad, India. Indian J Basic Appl Med Res 2014; 4: 471-477.

33. Sharma SK: Prevalence of hypertension, obesity, diabetes, and metabolic syndrome in Nepal. Int J Hypertens 2011; 821-971.

34. Albuquerque NLS, Oliveira ASS, Silva JMD and Araujo TL: Association between follow-up in health services and antihypertensive medication adherence. Rev Bras Enferm. 2018; 71(6): 3006-3012.

35. Feriato KT, Gusmao JL, Silva A, Santos CAD, Pereira RSF and Amendola F:; Antihypertensive treatment adherence in workers of a General Hospital. Rev Bras Enferm 2018; 71(4): 1875-82.