ORIGINAL RESEARCH

Determining the level of anti-hypertensive drugs and factors associated among patients with hypertension at a government tertiary care centre: A cross-sectional study

[1]Dr. Indrashis Mukerjee, [2]Dr. Amod Kumar Sachan, [3]Dr. Narsingh Verma, [4]Dr. Kauser Usman, [5]Dr. Anuradha Nischal, [6]Dr. Kamal Kumar Sawlani

[1]Research Scholar, [2]Professor & Head, [5]Professor, Department of Pharmacology & Therapeutics, King George's Medical University, Lucknow, UP, India

[3]Retd Professor & Head, Department of Physiology, King George's Medical University, Lucknow, UP, India

[4,6]Professor, Department of Internal Medicine, King George's Medical University, Lucknow, UP, India

Corresponding author: Dr. Indrashis Mukerjee, Research Scholar, Department of Pharmacology & Therapeutics, King George's Medical University, Lucknow, UP, India

Email: indrashish.mukhopadhya@gmail.com

ABSTRACT

Introduction:-Hypertension is a persistent systemic blood pressure reading of 140/90 mm Hg or greater which is a known cause of cardiovascular disease morbidity and mortality and Hypertensive heart disease is a major public health issue worldwide.Noncommunicable diseases (NCDs) pose a significant global health threat, claiming the lives of more than 50 million people annually.Interventions designed to improve medication adherence, and blood pressure control have not been fully effective globally.Despite decades of attention, noncompliance with HTN therapy is still a key cause in poor BP control.There is limited comprehensive understanding regarding the level of drug adherence to antihypertensive medications particularly in our country. Individual's risk of heart disease and stroke is increased due to uncontrolled blood pressure

Methods:-A total of 425 patients were enrolled from the Department of Internal Medicine at King George's Medical University (KGMU), Lucknow. Both male and female patients of age between 35-75 years on anti – hypertensive medications , providing written consent were included in the study. An institutional-based cross-sectional study was conducted among hypertensive patients. A simple random sampling technique was used to select the study participants from the study population.Sociodemographic data, medication adherence, factors affecting adherence were collected using a structured questionnaire and aMorisky Medication Adherence Scale questionnaire was used to assess the level of adherence. The questionnaire had 8 questions and a score of 7 or 8 was classified as good adherence, 6 as moderate, and less than 6 as nonadherence. On each visit at the OPD the questionnaire was provided to the patients.

Results:-A total of 35 patients were lost to follow-up, resulting in 390 patients out of 425 having hypertension further completed the study. The sample comprised 56.9% of females and 56.4% of participants aged 60 years or older. Approximately 80% of participants were currently married, and 46.7% had a higher education level. The MMAS-8 questionaire response indicated good adherence in 63.8% of participants. The findings showed that several factors were significantly associated with higher adherence rates, including older age (COR = 3.41, 95% CI = 1.10– 10.54, p = 0.03), higher educational level (COR = 1.72, 95% CI = 1.05– 2.83, p = 0.03), regular blood pressure monitoring (COR = 1.90, 95% CI = 1.10– 3.30, p = 0.03), and knowledge about their medications (COR = 2.12, 95% CI = 1.14– 3.94, p = 0.02).The mean (±SD) age of the study participants was 52.5 (±10.6) years.Chi-square/Fisher's exact test and non-parametric tests were used for statistical analysis. Prevalence of non-adherence was found in 24.3% study participants. Present study found statistically significant association between socio-demographic factors (age, religion, marital status, occupation, substance abuse, education and family history of HT) with treatment adherence of hypertension among study participants. The other factor associated to non-adherence was therapy factor 32.9% (P=0.001) from the total non-adherence, in this case patients were supposed to unwanted effect of the drug and they were not able to take the medication.

Conclusion:-The main possible reasons for non-adherence were 'refuse to take regular treatment , cost of treatment', 'poor patient-doctor relation', 'unwanted side effect of drugs' and other factors like age, marital status, occupation, education level, family H/O, substance abuse also played supporting role to develop non-adherence to treatment. Patient education and counselling shouldbe focused on older age, rural residents, single, and patients with lower monthly incomes.This study finds good adherence among the patients taking anti-hypertensive medications. However, with the improved education, lesser number of pills and physical fitness help to adhere with the anti-hypertensive therapy.

Keywords: Hypertension, Medical compliance, Patient-physician interaction,Treatment adherence.

INTRODUCTION

Hypertension is the most common , frequent and known cardiovascular disorder ,whichisanidenticalriskfactorforcoronaryarterydisease found in adults worldwide [1]. The World Health Organization (WHO) reports that over 1.3 billion individuals worldwide suffer from hypertension, contributing to more than 7 million annual deaths. Alarming projections anticipate more than 30% surge in global hypertension prevalence by 2025, particularly affecting low- and middle-income countries [2].It has been found that despite the availability of effective medical therapy, more than 50% hypertensive don't take any treatment and more than 50%of those on treatment have elevated blood pressure which remains constant over the140/90mmHg threshold. World health oganization(WHO) describes poor adherence to drug therapy , the identical cause of uncontrolled blood pressure and one of the main obstacles in the management of hypertensive patients and estimates that 50-70% of people do not take any antihypertensive medications as prescribed [3] [4]. Number of doses also play a very important and valuable role , single dose has been found to improve compliance, but 24-hour anti-hypertensive activity should be provided by the drug.Controlling hypertension primarily relies on medication treatment jointly combined with lifestyle modifications. However, the asymptomatic nature of hypertension poses a challenge, as patients may underestimate the importance of adhering to their prescribed treatment therapy [5].Adherence towards treatment affected by factors such as age, gender, low socio - economic status and severity of disease, classes of drug prescribed, number of pills per day, side effects of medication,patient's inadequate understanding of the disease and importance of the treatment, co-morbid medical conditions,lackof social support, poor patient provider relationship, cost, forgetfulness, and presence of psychological problems, especially depression . Patient’s non compliance with the therapeutic regimen has long been a challenge for practitioners,hence this study has been undertaken to investigate the adherence and persistence of anti hypertensive drugs in Indian rural population as well as monitoring adverse drug reactions and its relation to compliance . Studies investigating medication non-adherence among hypertensive patients consistently highlight the role of education and sociodemographic status. Higher education levels and income are associated with improved adherence [6] [7] [8]. Research findings indicate a direct correlation between patients’ educational levels and their medication knowledge. Many studies specifically revealed a significant association between patients’ education levels and all facets of medication knowledge, encompassing medication recognition, understanding medication indications, dosage schedules, and awareness of potential side effects. The higher education levels, intertwined with enhanced medication knowledge, play a pivotal role in fostering medication adherence among patients [9]. Additionally, age emerges as a significant factor, with younger patients exhibiting higher adherence rates [10].

Methodology

This cross-sectional study was conducted using data that was collected between June 2021 to June 2023 through face-to-face interviews and using a questionnaire sheet. The study protocol was approved by the Institutional ethics committee of the institution and informed consents were obtained from all the study participants. Patients were recruited by simple random sampling on visiting the hypertension clinic (OPD) of Department of Internal Medicine at King George's Medical University (KGMU), Lucknow . As a tertiary medical centre, KGMUprovides health care services to approximately half a million patients annually from various regions across the country and state.On an average, 150 to 200 outpatients

suffering with hypertension , diabetes , and other cardiovascular diseases attend the clinic daily. Free and low-cost services at this facility alsoattract a large number of patients.
The study participants were selected on the basis of the following:-

Inclusion criteria

1) Subjects having hypertension and diagnosed according to AHA guidelines.
2) Patients with hypertension and with at least one anti-hypertensive medication for at least 6 months.
3) The patients who were aged 30 years or above.
4) The patients who were non-pregnant or non-puerperal at the time of the interview (for female patients).
5) Those who gave informed consents to participate in the study.

The patients who were excluded from the study:-

Exclusion criteria

1) Patients with a critical illness or cognitive impairment.
2) Newly diagnosed patients with hypertension at the first visit to the hospital.
3) Patients not willing to give consent.
4) Patients with kidney transplant or end stage renal disease.

The hypertension OPD clinic runs from Tuesday to Friday i.e. 4 days per week. Subjects on anti-hypertensive medications for atleast 6 months and follow up patients having hypertension were screened & were recruited according to the inclusion & exclusion criteria respectively & it took complete2 years to complete the sample size. Data of each participant was collected by using a pre-designed, pre-tested, structured enrollment form which included socio-demographic variables like age, sex, the educational and the marital status, the per-capita monthly income, and specific questions on the duration on diabetes, the type of medications which were prescribed, the compliance to anti-hypertensive drugs, the diet plan and the exercise schedule, and associated complications of hypertension.The level of Medication adherence was assessed by using a structured , pretested & validated Hill Bone, Morisky 8-item Medication Adherence Scale (MMAS-8) with a high reliability and validity, which has been particularly useful in chronic conditions like hypertension. Each of the 8 item was scored 0 or 1 [11].MMAS-8 was scored as 1 point for each no answer and 0 points for each yes. The total score ranged from 0 points (completely nonadherent) to 8 points (completely adherent). An MMAS-8 score of 7 or 8 was classified as good, a score of 6 as moderate, and a score less than 6 as nonadherent. It highlights forgetfulness of medication, measures medication use , stops to take medication when feel worse, forget to take medication when travel or go out of home, measures medication use in yesterday, stops to take medication when feel better, feeling dissatisfaction due to daily commitment to take hypoglycemic medicine , facing difficulties to remember to take all medications. A lower score means a lowerdegree of adherence and a higher score means ahigher degree of adherence to treatment regimens.

Statistical analysis

The data analysis was carried out by using Statistical Package for Social Science (SPSS) for Windows IBM SPSS Statistics 28.0.1 version 2022. Data were analyzed as descriptive statistics (proportions, percentages, ratios, and frequency distribution tables) and expressed as mean (SD) or as percentages. For qualitative data (gender, education level, marital status, duration of the disease, comorbidities, drug regimen, income, smoking, committed to follow-up, relationship with prescribers, suffering from side effects, adherence level), frequency and percent were used. The categorical data such as for qualitative data (gender, education level,

marital status, duration of the disease, comorbidities, drug regimen, income, smoking, committed to follow-up, relationship with prescribers, suffering from side effects, adherence level), frequency and percent were used. sex, race, age, duration of disease, body mass index, family history, comorbidities, and level of education are presented as frequency and percentage. Pearson Chi-square or Fisher's exact test were utilized to investigate the association between the Hill-bone adherence level, Chi-square test was used to Statistical significance was accepted at the 95% confidence level. Bivariate analysis was performed with a P value of less than .05 considered significant and was used to establish an association between adherence to hypertension medication and patient-related, drug-related, disease-related, and service-related factors. For bivariate analysis, we categorized frequency of determinants among patients reporting good adherence (MMAS-8 score 7 or 8) and those reporting moderate or nonadherence (MMAS-8 score ≤6) to antihypertension therapy. Multivariate regression analysis was performed to identify independent predictors of adherence by using adherence status as the outcome variable and the other factors as predictor variables.Binary logistic regression analysis was conducted to identify factors associated with non-adherence, while adjusting for covariates.A p-value < 0.05 was considered statistically significant.

RESULTS

The analysis encompassed a total of 390 patients meeting the inclusion criteria. Among them, 249 individuals demonstrated good adherence (63.8%), while 141 patients exhibited poor adherence (36.2%). The mean age of participants was 61.9 + 10.8 year, and slightly more than half of the patients were female (56.9%) and were 61 years or older (56.4%). The majority were married (80%), had a BMI of 25.0 or higher (86%), and residing in Urban areas (92.6%). In addition, almost half of the patients had completed a bachelor's degree or higher (46.7%), and just over half reported a family monthly income of less than Rs 10000 (54%). The majority of patients in this study were non-smokers (82.8%). Regarding comorbidities, around half of the patients had diabetes (49%). Notably, close to a quarter of the patients (28.2%) were taking three or more antihypertensive medications.Significant associations with better medication adherence were observed in older patients, specifically those in the age groups 40-59 (COR = 3.21, 95% CI= 1.03-10.06, p = 0.04) and 60 years or older (COR = 3. 41, 95% CI= 1.10-10.54, p = 0.03), as well as those who had completed higher education (COR= 1.72, 95% CI=1.05-2.83, p = 0.03).

Table 1. Sociodemographic and Adherence-Related Characteristics of Participants

Variable	Median n %	Poor adherence score	Good adherence score	COR 95% CI	P-Value
Age Groups					
18-39	14 (3.6)	9 (64.3)	5 (35.7)	3.21	0.04
40-59	156 (40)	56 (35.9)	100 (64.1)	3.41	0.03
>60	220 (56.4)	76 (34.5)	144 (65.5)		
BMI					
<25	55 (14)	22 (40)	33 (60)		
>25	335 (86)	119 (35.5)	216 (64.5)	1.21	0.52
Gender					
Female	222 (56.9)	79 (35.6)	143 (64.4)		
Male	168 (43.1)	62 (36.9)	106 (63.1)	0.95	0.83
Area of residence					
Urban	361 (92.6)	130 (36)	231 (64)		

Rural	29 (7.4)	11 (37.9)	18 (62.1)	0.92	0.84
Level of education					
Primary school	111 (28.5)	46 (41.4)	55 (58.6)	0.93	0.79
Secondary school	97 (24.9)	42 (43.3)	55 (56.7)		
Higher education	182 (46.7)	53 (29.1)	129 (70.9)	1.72	0.03
Marital Status					
Single	78 (20)	33 (42.3)	45 (57.7)		
Married	312 (80)	108 (34.6)	204 (65.4)	1.39	0.21
Family Monthly Income					
Less than 10000	211 (54)	81 (38.4)	130 (61.6)		
More than 10000	179 (46)	60 (33.5)	119 (66.5)	1.24	0.32
Smoker					
No	323 (82.8)	112 (34.7)	211 (65.3)		
Yes	67 (17.2)	29 (43.3)	38 (56.7)	0.70	0.21
Diabetes					
No	199 (51)	71 (35.7)	128 (64.3)	0.96	0.87
Yes	191 (49)	70 (36.6)	121 (63.4)		
No of HTN Medications					
Less than 2	280 (71.8)	101 (36.1)	179 (63.9)		
3 or more	110 (28.2)	40 (36.4)	70 (63.6)	0.98	0.95

Patients' attitudeand their MMAS scores are presented in Table 2 below . Patients who measured their blood pressure periodically (COR = 1.86, 95% CI 1.23-2.83, p = 0.004), those who measured their blood pressure regularly twice daily compared to patients who measured randomly throughout the day (COR = 1.64, 95% CI 1.03-2.60, p = 0.03), those who measure their blood pressure at home (COR = 1.90, 95% CI 1.10-3.30, p = 0.03), and those who knew that their medications were effective and had a role in maintaining their health (COR = 2.12, 95% CI 1.14-3.94, p = 0.02) had increased odds of having good adherence. On the other hand, patients who changed their dose of medication or stopped taking their medication without consulting their doctor (COR = 0.54, 95% CI 0.39-0.96, p = 0.04) and (COR = 0.081, 95% CI 0.037-0.18, p < 0.001), respectively, and patients that had ever felt unwilling to take their treatment (COR = 0.45, 95% CI 0.29-0.69, p < 0.001) were more likely to have poor adherence.

Table 2. Patients adherence level and score on MMAS-8 Questionnaire

Statements	Total n %	Poor adherence score	Good adherence score	COR 95% CI	P-Value
Measure BP periodically					
No	164 (42.1)	73 (44.5)	91 (55.5)		
Yes	226 (57.9)	68 (30.1)	158 (69.9)	1.86	0.004
Time of BP Measurement					
Random	234 (60.5)	90 (38.5)	144 (61.5)	1.64	0.03
Regularly twice daily	134 (34.6)	37 (27.6)	97 (72.4)		
Do not measure at all	19 (4.9)	12 (63.2)	7 (36.8)	0.37	0.04
Location of BP Measurement					

Outside Home	61 (15.6) 329 (84.4)	30 (49.2) 111 (33.7)	31 (50.8) 218 (66.3)	1.90	0.03
Change dose of medication without consulting doctor No Yes	 337 (86.4) 53 (13.6)	 115 (34.1) 26 (49.1)	 222 (65.9) 27 (50.9)	 0.54	 0.04
Stop BP medication as BP normal & don't feel symptoms No Yes	 341 (87.4) 49 (12.6)	 100 (29.3) 41 (83.7)	 241 (70.7) 8 (16.3)	 0.081	 <0.001
Forget to take medicine while travelling No Yes	 260 (66.7) 130 (33.3)	 85 (32.7) 56 (43.1)	 175 (67.3) 74 (56.9)	 0.64	 0.06
Use a medication regulator No Yes	 310 (79.5) 80 (20.5)	 119 (38.4) 22 (27.5)	 191 (61.6) 58 (72.5)	 1.64	 0.09
Ever felt unwilling to take the treatment No Yes	 261 (66.9) 129 (33.1)	 78 (29.9) 63 (48.8)	 183 (70.1) 66 (51.2)	 0.45	 < 0.001
Medication is effective and maintains my health No Yes	 46 (11.8) 344 (88.2)	 24 (52.2) 117 (34)	 22 (47.8) 227 (66)	 2.12	 0.02

The mean MMAS was18.23 ± 4.95, the minimum recorded score was 14, and the maximum was 36. The Hill-Bone CHBPTS is comprised of multiple subscales, contribute to the reduced sodium intake subscale, exhibiting a mean (SD) of 5.28 ± 1.87. The subsequent two questions pertain to the appointment-keeping subscale, with a mean (SD) of 3.58 ± 1.43. Finally, the last eight to nine questions form the medicine-taking subscale of the Hill- bone MMAS score, demonstrating a mean (SD) of 12.37 ± 1.37.

Table 3. Patients Hill Bone, MMAS-8 Questionnaire adherence summary.

	Never	**Sometime**	**Frequently**	**Always**	**Mean±SD**
Reduced Sodium Intake					
Eat Salty food	146(37.4)	**156 (40)**	**62 (15.9)**	**26 (6.7)**	**1.92 ± 0.89**
Shake salt on your food before you eat it	244 (62.6)	**80 (20.5)**	**46 (11.8)**	**20 (5.1)**	**1.59 ± 0.89**
Eat fast food	154 (39.5)	185 (47.4)	40 (10.3)	11 (2.8)	1.76±0.75
Appointment Keeping					
Get the next appointment before you leave the clinic	**74 (19)**	**42 (10.8)**	**74 (19)**	**200 (51.3)**	**1.97±1.18**
Miss Schedule appointments	227 (58.2)	**107 (27.4)**	**37 (9.5)**	**19 (4.9)**	**1.61±0.85**
Medicine Taking					
Forget to take your BP medicine	**196 (50.3)**	**133 (34.1)**	**49 (12.6)**	**12 (3.1)**	**1.68±0.81**

Decide not to take your medicine	**277 (71)**	**67 (17.2)**	**35 (9)**	**11 (2.8)**	**1.44±0.77**
Forget to get prescriptions filled	**318 (81.5)**	**42 (10.8)**	**14 (3.6)**	**16 (4.1)**	**1.30±0.73**
Run out of BP pills	**290 (74.4)**	**67 (17.2)**	**27 (6.9)**	**6 (1.5)**	**1.36±0.68**
Skip your BP medicine	**305 (78.2)**	**36 (9.2)**	**21 (5.4)**	**28 (7.2)**	**1.42±0.89**
Miss BP pill when feel better	**326 (83.6)**	**20 (5.1)**	**16 (4.1)**	**28 (7.2)**	**1.35±0.86**
Miss BP pill when feel sick	**322 (82.6)**	**34 (8.7)**	**22 (5.6)**	**12 (3.1)**	**1.29±0.71**
Take someone's else BP pills	**348 (89.2)**	**28 (7.2)**	**10 (2.6)**	**4 (1)**	**1.15±0.49**
Miss taking your BP pills when careless	**292 (74.9)**	**59 (15.1)**	**29 (7.4)**	**10 (2.6)**	**1.38±0.73**

DISCUSSION

This study aimed to assess the adherence of patients to antihypertensive medication in our population. According to the WHO, inadequate adherence is identified as the primary factor contributing to uncontrolled blood pressure [12]. Sustained and consistent adherence to medication over the long term is essential for managing and sustaining control over this chronic condition [13]. In hypertensive patients, suboptimal drug adherence is a key factor associated with inadequate blood pressure control, contributing substantially to a growing and noteworthy public health challenge [14].The non-adherence to medications carries both human and economic implications, with estimates suggesting that adhering to treatment recommendations could potentially save around 8% of global overall health costs [15]. The findings of this study revealed that 63.8% of the sample exhibited commendable adherence to their antihypertensive medications, while 36.2% demonstrated subpar adherence, which indicates relatively a better adherence to hypertensive medications compared to other studies. This finding surpassed a study conducted in the Middle East, where only 55.9% of patients adhered to their antihypertensive medication [16]. Similarly, a study in Malaysia reported a lower adherence rate of 53.4% among participants [17]. Our results also outperformed two previous Jordanian studies [18] [19] . The Lebanese study utilized the validated 8-item Modified Morisky Medication Adherence Scale (MMMAS)and found that out of 210 patients, 50.5% demonstrated good adherence to medicine, 27.1% had medium adherence, and 22.4% had low adherence[20].

However, our study's adherence rate was lower than those reported in developed countries such as the United States and Scotland, where adherence rates reached up to 91% for each [21]. This difference could be attributed to the fact that the latter research used a subjective method to assess adherence levels, which may have inflated the results.

Our findings revealed that older patients exhibited a higher level of medication adherence compared to their younger counterparts, particularly among patients aged 40–59 and above 60 years. This observation aligns with the results of a retrospective cohort study involving approximately 950,000 patients, which assessed the persistence with antihypertensive drugs over 10 years and concluded that older patients demonstrated greater persistence than their younger counterparts [22] Several other studies have also reported a positive correlation between age and medication adherence [23] [24] It is theorized that this trend may be attributed to the fact that older patients often experience a higher severity of illness compared to their younger counterparts, leading to increased awareness of their health status, which, in turn, positively influences adherence [25]. We hypothesized that older patients exhibit

higher rates of medication adherence due to specific factors. Firstly, their possession of more established and consistent daily routines facilitates the seamless incorporation of medication-taking into their daily activities [26]. More, often family members or caregivers, play a crucial role in providing support and this proves instrumental in reminding and assisting with medication adherence [27].

We contend that younger patients exhibit a lower adherence rate to their medications for several reasons. Firstly, a sense of invincibility prevalent among younger individuals may lead them to underestimate the potential consequences of non-adherence, fostering a lax attitude toward medication adherence [28]. Furthermore, the dynamic and fast-paced lifestyles common among younger individuals contribute to forgetfulness in regularly taking their medications, particularly when routines change due to travel or irregular work hours [29] [30] Side effects or concerns about medication that the younger patients may be more sensitive to potential side effects or have concerns about the long-term effects of medications, leading to lower adherence rates [31].

Furthermore, this study showed that patients with higher level of education exhibited a greater level of adherence to their medications. This finding aligns with a study conducted in South Korea which aimed to identify factors linked to self-reported non-adherence to antihypertensive regimens and found that patients with lower educational level had higher rates of non-adherence [32].Similarly, a study in the USA showed that individuals with higher levels of education demonstrated higher rates of medication adherence [33].

Our study illustrated that patients who monitored their blood pressure regularly, specifically those who checked their blood pressure twice daily, and individuals who measured their blood pressure at home, had higher odds of maintaining good medication adherence. This observation aligns with a separate study conducted in Jordan, where 85% of participants reported monitoring their blood pressure, and nearly 79% maintained a record of their blood pressure at home [19].

Monitoring blood pressure at home is of significant importance as it demonstrates significant results of blood pressure and also for various reasons brings numerous advantages to individuals dealing with hypertension or other cardiovascular conditions. One key factor underlining the significance of home blood pressure monitoring is its ability to provide an accurate assessment of blood pressure in a familiar and relaxed environment. This helps mitigate the “white coat syndrome”, ensuring a more precise reflection of an individual’s typical blood pressure [34]

Furthermore, home monitoring enables healthcare providers to compile a more comprehensive and personalized dataset on a patient’s blood pressure patterns. This wealth of information assists in tailoring treatment plans to address the specific needs of each individual, taking into account factors such as time-of-day variations and responses to medications [35].

Our findings indicated that patients who adjusted their medication dosage or discontinued their medication without consulting their doctor, as well as those who expressed reluctance to take their medications, were more likely to exhibit poor adherence. There is a growing body of evidence emphasizing the importance of the patient-clinician relationship in this context. Practices that prioritize patient-centeredcare, exhibit professional and non-judgmental communication skills, and foster patients’ trust and confidence in the clinician’s knowledge have been shown to effectively enhance medication adherence [36].

This study also indicated a significant association between patients who could correctly identify the names of all their medications and exhibiting good adherence. A study conducted in Ethiopia yielded similar findings, where 60% of patients with low adherence faced difficulties remembering their medications[37].Other studies have identified low education as a risk factor for inadequate medication-related knowledge. Logistic regression analyses

revealed that patients with comprehensive knowledge were ten times more likely to demonstrate high medication adherence. Specifically, patients who were knowledgeable about their medication names, administration instructions, what to do in case of a missed dose, and how to address potential side effects exhibited a significant association with improved medication adherence [38].

The strength points of this research paper lie in its robust methodology, notably the inclusion of a substantial number of patients and the utilization of a reliable scale for assessment. The study benefits from a large and diverse patient sample, enhancing the generalizability of the findings and bolstering the statistical power of the analyses. Furthermore, the use of a validated and reliable scale ensures the accuracy and consistency of the measurements, contributing to the overall reliability of the study. Additionally, the research is conducted in a tertiary medical center renowned for its specialization and role as a referral center. This aspect adds a layer of credibility to the study, as the hospital's expertise and patient population make the findings more representative and applicable to broader clinical contexts. The combination of a robust methodology, a significant number of patients, and the study setting in a tertiary medical center reinforces the strength and reliability of the research outcomes.

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