

**PATIENT ADHERENCE TO WARFARIN THERAPY AND ITS IMPACT ON
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ABSTRACT**Background:** Medication adherence is crucial for the success of a therapeutic plan, especially in warfarin therapy.**Objective:** This study aimed to measure warfarin-adherence, and to identify their relation to the International Normalized Ratio. **Methodology:** This a descriptive cross-sectional hospital base study was conducted among patient who underwent long-term treatment with warfarin therapy. A study conducted in two cardiac hospitals at Khartoum State. **Results:** The study found that older individuals over 39 years had higher adherence levels than younger individuals under 39 years, and female participants had higher adherence levels than male participant. most participants had a current International Normalized Ratio within normal range, with 66.7% of high-level adherence having a current International Normalized Ratio in the normal range. However, the association between adherence and International Normalized Ratio results was insignificant. Therefore, most participants had a high level of adherence to warfarin therapy. **Conclusions:** Most participants have a normal International Normalized Ratio and a high level of adherence to warfarin therapy.**KEYWORDS:** Medication compliance, INR monitoring, Warfarin therapy, Patient adherence, and Dose adjustment.**INTRODUCTION**

Warfarin is one of the most widely prescribed drugs in the world, it is an effective anticoagulant used to prevent and treat blood clots in various disease conditions.^[1] It is a successful mediator for the therapeutic management of thromboembolic diseases.^[2] Alertness will be taken regarding patients knowledge of warfarin's action, it's possible side effects, interacting drugs and food because it plays a vital role to attain the preferred therapeutic outcome and preventing the undesirable reactions.^[3]

Warfarin has a narrow therapeutic index there for it need regular laboratory test of international normalized ratio (INR) to ensure best therapeutic outcomes and to lessen bleeding complications or thromboembolism.^[4] Previous study done in Sudan at Alshaab Teaching Hospital highlighted that only about 5.4% of the patients were found to be adherent to warfarin therapy.^[4] Safety and effectiveness of warfarin depend critically on maintaining international normalized ratio (INR) within

therapeutic range,^[5] which is recommended by the World Health Organization (WHO) to use of a corrected prothrombin-time ratio.^[6] Duration of treatment and target INR may vary depending on the indication for warfarin therapy. The target INR ranges are between 2.0 to 3.0 for most indications except for mechanical heart valve replacement (2.5 to 3.5).^[7]

Warfarin is known as one of the drugs that most often causes undesirable drug reactions that need hospital entrance and increased length of hospitalization, accounting for extensive morbidity, mortality, and added payment.^[4]

Evaluation of current patient knowledge is the first step to improving the quality of anticoagulation therapy and patient care.^[8] Poor patient knowledge about warfarin therapy has been set up to be related with bad anticoagulation control and increased occurrence of hemorrhagic events.^[5] Many medicines, alcohol, and

herbal products can interact with warfarin.^[6] Achievement a safe condition of stability in warfarin therapy needs a collaborative work involving the patient him/herself, their families, and the medical facilities, and of these the most key factors are the awareness and compliance of the patient with the medical advice. Study done in Malaysia reveal that 56% were unaware of any potential drug interactions, 58% were unaware of any adverse effects, 27% had experienced adverse effects, 12% had been hospitalized because of adverse effects.^[9] The determining rationale in the success of warfarin therapy is patients' adherence to the management.^[9] Obtaining complete patient information is essential for assessing deficient warfarin knowledge and patient's enjoyment with therapy that shown to worsen medication adherence and compromise INR control.^[10] Researchers have recognized non-adherence to therapy as among the multiple causes that expect poor INR control.^[11] Patient counseling and education will progress response to INR; therefore, achieving desired outcomes. Several studies reported that better patient understanding of their therapy will eventually improve outcomes (good INR control).^[10]

An INR result below the target range is linked to risk for a stroke and even an increased risk of mortality.^[12] Study done in Saudi Arabia reveal that 75.2 % had good knowledge of warfarin, but only 33.3 % had good anticoagulation control. An association was seen between patients with no formal education and poor warfarin knowledge.^[13]

METHOD

Study Design and Setting

This research employed a descriptive cross-sectional, hospital-based study design to assess patient's adherence to warfarin therapy. The study was conducted in two Cardiac Hospitals in Khartoum State.

Participants

The study population included the Outpatients aged ≥ 18 years and above, on oral anticoagulation therapy OAT for at least 2 months and visited the outpatient anticoagulant clinic at the period of the study. Patients who were extremely ill or had one of the chronic diseases that affects the INR result, were excluded.

Sampling methods and Sample size

Non-probability Convenience sampling methods used. The sample size calculated according to annual frequency of patients in the outpatient anticoagulant.

Data Collection tools

Two primary tools were and used for data collection.

Tool No. 1 Close Ended Standardize Structured Questionnaire consists of 10 Questions to collect the patient demographic data including age, gender, educational level, duration of taking warfarin and recorded the current INR result.

Tool No. 2 Morisky Medication Adherence Scale 8 items (MMAS 8items)^[17]: To assess patient's adherence level to warfarin therapy. The eight-item Morisky medication adherence scale (MMAS-8) is structured self-reported measure of medication –taking behavior. It was developed from a previously confirmed four-item scale and supplemented with added items addressing the circumstances surrounding adherence behavior^[18] consist of eight questions related to adherence behavior, seven with closed dichotomous responses (yes/no) and the last with three -point response scale: never, sometimes, and always.^[14,16]

Scoring system for Morisky scale

The validated MMAS-8 score was used to evaluate adherence to the medication, each "no" response is rated as "1" and each "yes" is rated as "0" except for item 5, in which each response "yes" is rated as "1" and each "no" is rated as "0". For item 8, if a patient chooses response "0" the score is "1" and if they choose response "2" the score is "0" Total MMAS-8score can range from 0 to 8 and have been categorized into three levels of adherence.^[18] A score of eight showed high level adherence, 6-8 showed moderate adherence and less than 6 showed low level adherence.^[18,19]

Validity and Reliability of the study tools

To ensure the validity and reliability of Close Ended Standardize Structured Questionnaire the following steps taken:

Face and Content Validity (Expert Review)

The Close Ended Standardize Structured Questionnaire evaluated for face and content validity by experienced and educated associate professor experts in the field of medical surgical nursing from Alneelain University. Their expert opinions were used to enhance the face and content validity of the study tool.

Pilot Study

A pilot study conducted in a similar study population who met the criteria of the study, Feedback from the participants collected to evaluate the tool's effectiveness in measuring the intended constructs.

Internal Consistency

The internal consistency of the study Close Ended Standardize Structured Questionnaire was pretested on 10% of the study populations and done in similar stations. The reliability statistics of Close ended Standardize structured questionnaire was (0.81) using Cronbach's alpha test.

Data Collection and Technique

The data collection phase spanned several months; data collected via face-to-face interviews questionnaire conducted by the researchers; the interviews lasted about 8-13 minutes on average. Participants were assured of anonymity and confidentiality to encourage honest and correct responses. The

Statistical Analysis

Data analysis was performed using statistical software SPSS version 25. Descriptive statistics were applied to summarize demographic characteristics and questionnaire responses and associations between the independent variables and the level of adherence using Chi square test p-value of less than 0.05 was considered statistically significant. Univariate analysis used for the background variables and bivariate analysis for dependent and independent variables then presented as tables and figures.

Ethical consideration

This study received approval from the Institutional Review Board of the graduate college, the study proposal reviewed and approved by the Ethics Committee, Ministry of Health, Khartoum State, and the hospitals. Verbal consent was obtained from all study participants. All participants were ensured anonymity, confidentiality, and their privacy and dignity were protected. Participants had the right to refuse to answer any question.

RESULTS

Table 1: Summarizes the demographics and professional details of study participants.

Characteristic	Frequency	Percent
Age		
19 - 39 year	40	26.3
40 - 59 year	58	38.2
60 - 82 year	54	35.5
Total	152	100.0
Gender		
Male	63	41.4
Female	89	58.6
Total	152	100.0
Educational level		
Illiterate	40	26.3
Primary	29	19.1
Intermediate	18	11.8
Secondary	30	19.7
University	32	21.1
Informal education	3	2.0

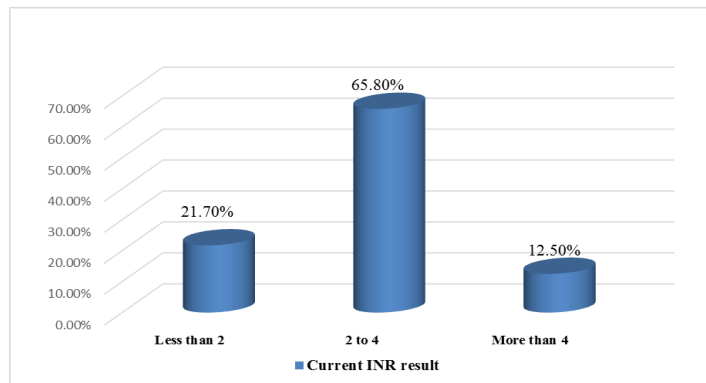


Fig. I: Distribution of current INR result among participants (n=152).

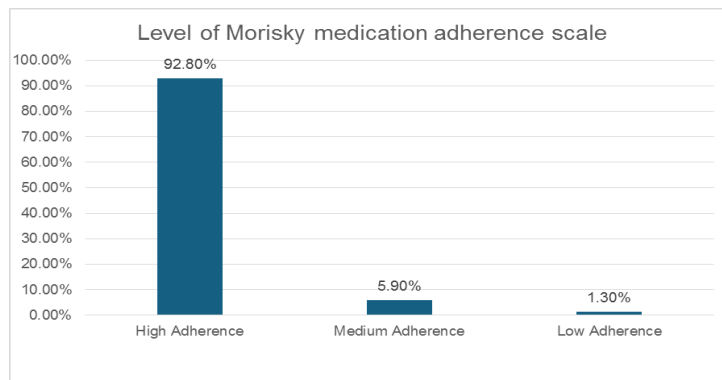


Fig. II: participant's level of adherence according to Morisky medication adherence scale MMAS-8 (n=152).

Table 2: Relationship between participants' level of adherence to their prescribed regimen and their current INR results, sex, and age.

Variables		Level of adherence							
		High Level Adherence		Medium Level Adherence		Low level Adherence		Total	
Age in year	19 - 39	36	25.5%	3	33.3%	1	50%	40	100%
	40 - 59	53	37.5%	4	44.5%	1	50%	58	100%
	60 - 82	52	37%	2	22.2%	0	0.0%	54	100%
	Total	141	100%	9	100%	2	100%	152	100%
(P=0.72)									
Current INR	Less than 2	29	20.6%	3	33.3%	1	50%	33	100%
	2 to 4	94	66.7	5	55.6%	1	50%	100	100%
	More than 4	18	12.7	1	11.1%	0	0.0%	19	100%
	Total	141	100%	9	100%	2	100%	152	100%
(P=0.75)									
Sex	Male	58	41%	4	44%	1	50%	63	100%
	Female	83	59%	5	56%	1	50%	89	100%
	Total	141	100%	9	100%	2	100%	152	100%
(P=0.95)									

DISCUSSION

The safety of warfarin therapy depends on maintaining the INR within the therapeutic range regarding this the researcher found that most of participants (65.8%) their current INR with normal rang (2 – 4) but about 21.7% their INR less than normal that will expose them to re-embolism on the other hand about 12.5% their INR more than normal which can result in serious bleeding. Adherence is patients' voluntary behaviors according to healthcare professionals' advice and includes following the treatment regimen, taking prescribed medications and making recommended lifestyle modifications, to achieve positive treatment outcome concerning this the participants were evaluated according to Morisky medications adherence scale 8 items regarding warfarin therapy the researcher found that the majority of the participant (92.8%) had high adherence to medications, which differ when compared with previous study in a Jordanian survey that reported an adherence rate of participants about 46%. Other study performed in Singapore using MMAS-8 revealed an adherence rate of about 34.5%.^[20] On the other hands previous study done among Sudanese patients which revealed that only 5.4% of the patients were found to be adherent to warfarin therapy.^[4] This result was congruent with study conducted in Sweden found that rates of non-adherence are high among patients on Direct Oral Anticoagulants (DOACs)^[21] When the researcher compare the level of adherence of the participants with age and sex found that the elderly participants (age >39 years) had more adherence than age less than 39, and female had high adherence than male, but this difference is not statistically significant (P=0.72) & (P=0.95) respectively this result is differ when compare with previous study which highlighted that the elderly patients (age>35 years) had a poor warfarin therapy adherence score (05.81).^[22] This result agrees with studies carried out in Thailand and Korea, respectively which revealed that there is no significant statistical difference among the

Adherence level of respondents based on age. At the same time, our finding is disagreeing with study carried out in Kenya that reported there is significant statistical relationship among the Adherence level of sample based on gender.^[23] On the other hands we search about the relationship between participants level of adherence and current INR the researcher found that two third of the participants (66.7%) who had high level adherence their current INR was in normal range and about (20.6%) of high level of adherence had below normal current INR thus the association between level of adherence and result of INR is insignificant (p=0.75). Study aimed to assess the Influence of Patient Adherence on Anticoagulation Control with Warfarin Found that: a significant association between under adherence and under anticoagulation (P<.001).^[24] Moreover, the study reported Knowledge, Medication Adherence and Anticoagulation Control at Warfarin Clinic, Phthalein Hospital -found that the medication adherence was rated at satisfactory level at 93.71% and good INR control at 59.75% Patients' Warfarin.^[25]

CONCLUSION

The study assessed several potential confounding factors, such as age, gender, educational level, and adherence, none of which showed a significant impact on INR control in the sample. Further investigation into other confounders, including detailed patient knowledge, medication interactions, and dietary habits, would be beneficial for a comprehensive understanding of factors affecting INR control.

6. RECOMMENDATIONS

To improve patient adherence to warfarin therapy and manage anticoagulation control, the study recommends enhanced education on warfarin and INR monitoring, personalized counseling, regular follow-ups, and support systems. Utilizing digital tools and telemedicine can aid adherence. Collaboration among healthcare providers

and pharmacist-led interventions are essential. Addressing socioeconomic barriers through financial support and accessible healthcare services is crucial. Continuous research and quality improvement programs are necessary to find confounders and enhance anticoagulation care. These measures aim to improve adherence and reduce complications.

CONFLICTS OF INTEREST

The authors have nothing to declare.

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