

# Warfarin Knowledge and Patient-reported Outcomes Regarding Warfarin Adverse Events

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## Abstract

**Background:** This study evaluated the association between warfarin knowledge and patients' reported outcomes (PROs) among warfarin patients. **Methods:** A cross-sectional study was performed among warfarin patients in Pakistan. Warfarin knowledge was evaluated using a self-developed and pre-validated instrument. Descriptive and inferential statistics were applied to observe patients' demographic features and to determine the correlation among different PROs regarding the adverse events among warfarin patients. Spearman's rank-order correlation matrix was used to determine the association between knowledge mean scores and the PROs of adverse events. **Results:** Among total 295 patients, females were more than males ( $n = 184, 62.4\%$  and  $n = 111, 37.6\%$ , respectively). The mean knowledge score was  $6.62 \pm 2.68$  and the correlation coefficients between the mean knowledge score and the studied PROs were statistically significant. **Conclusion:** Statistically, a significant positive correlation ( $P < 0.05$ ) was observed between the mean knowledge score of the participants and the adverse events' PROs.

**Key words:** Pakistan, patients reported outcomes, warfarin knowledge, warfarin

## INTRODUCTION

Anticoagulant therapy (ACT) has been widely used by millions of cardiac patients due to its safety and proven efficacy.<sup>[1]</sup> ACT is not only used to treat various diseases such as tissue or mechanical prosthetic heart valves, atrial fibrillation, acute myocardial infarction, peripheral arterial disease, and stroke but also as prophylaxis of myocardial infarction.<sup>[2]</sup> Among oral anticoagulants (OACs), warfarin is preferred in conditions requiring prolonged anticoagulation therapy.<sup>[2,3]</sup> Warfarin like OAC is used to treat and prevent cardiac, thromboembolic, and hypercoagulable disorders because of its convenient administration as compared to its parenteral counterpart heparin.<sup>[3-5]</sup> As warfarin is a narrow therapeutic window drug, it requires close and cautious monitoring when used for long periods.<sup>[5]</sup> Contrary to its advantageous use warfarin has also been associated with several adverse effects, drug and food interactions, and complications like prolonged bleeding.<sup>[3-5]</sup>

Warfarin is prescribed to treat various cardiovascular diseases (CVDs) because of its optimum therapeutic advantages and perceived

cost-effectiveness.<sup>[6]</sup> Conversely, warfarin's optimal therapy also poses a greater challenge to the health-care providers due to its varied dose-response, narrow therapeutic index, multifactorial regimens, drug and food interactions, adequate dose adjustments, and international normalized ratio (INR) monitoring.<sup>[4]</sup> Knowledge about warfarin regarding its mechanism of action, duration of action, potential side effects, and food and drug interactions is a success key in achieving desired therapeutic outcomes with minimal interactions and adverse events.<sup>[7]</sup> Undeniably, provision of adequate knowledge about warfarin's apposite usage is a valuable approach to decrease its possible adverse events, drug interactions, and various other associated complications.

Proper knowledge about warfarin therapy also helps patients attaining significant anticoagulation control, decrease hospitalizations, less frequent INR checks, and improve

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health-related quality of life (HRQoL).<sup>[7,8]</sup> Few studies from different countries are evident in the literature regarding warfarin knowledge<sup>[3,8]</sup> but nothing is reported regarding the association of warfarin knowledge and its association with patient-reported outcomes (PROs) regarding adverse events in Pakistan. Therefore, this study was designed to examine the association between warfarin knowledge and PROs regarding adverse events among warfarin patients in Pakistan.

## METHODS

### Study design, sampling technique

A cross-sectional study was conducted among warfarin patients in Pakistan in June 2018–August 2018. Although to date, there is no ethical approval requirement for non-clinical and observational studies in Pakistan,<sup>[9]</sup> yet this study was performed following the international clinical guidelines and to the principles of the Helsinki Declaration, version 2013.<sup>[10]</sup> All aspects of the study protocol were strictly confidential.

### Participants and data collection

All of the participants were on warfarin and  $\geq 18$  years. A written consent according to the Declaration of Helsinki 1964 and its amendments on comparable ethical standards was taken from all the participants. Patients who gave written consent and familiar with Urdu (National language of Pakistan) were included in the study. For exclusion criteria, patients unable to understand Urdu, aged below 18 years, pregnant women or planning to become pregnant, having documented psychological issues, mental sickness, and those who refused to sign the consent forms were excluded from the study. The convenience sampling technique was used to select research subjects and those who were unable to give consent for any reason were also excluded from the study.

### Study instrument

The knowledge among warfarin patients was assessed using a new research instrument comprising of three diverse sections. The instrument was developed in English after an extensive literature review. The instrument consisted of warfarin basic information, INR control information, and warfarin adverse event sections. The items of the tool were translated into Urdu language using a forward-backward translation method (two independent translations). The obtained Urdu questionnaire was again back-translated into English (two independent translators) and both of the dual translations were facilitated by native speakers of both languages. Each correct answer was given a score of 1 and the incorrect answer was given 0 scores. All obtained scores for each patient were summed to get a total score, ranging from 15 to 0. The research tool was cutoff into two categories based on the obtained knowledge

scores. A patient who scored  $\leq 7$  correct answers was considered having poor knowledge and  $>7$  correct answers as good or appropriate knowledge.

### Statistical analyses

Descriptive statistics were used to evaluate the demographic and disease characteristics of the patients. Frequencies and percentages ( $n$ , %) were used for the categorical variables, while means and standard deviations (SD) (Mean  $\pm$  SD) were calculated for the continuous variables. Independent samples  $t$ -test, one-way ANOVA, and Spearman's rank correlation coefficient were used to evaluate correlations (agreements) between the studied variables.  $P < 0.05$  was considered statistically significant. Data from the questionnaire were analyzed using Statistical Package for the Social Sciences (SPSS) version 24.0.

## RESULTS

Table 1 shows the demographic data of the study participants. More females than males ( $n = 184$ , 62.4%, and  $n = 111$ , 37.6%,

**Table 1: Demographic characteristics of the study participants ( $n=295$ )**

Characteristics	Frequency (%)
Gender	
Male	111 (37.6)
Female	184 (62.4)
Age	
<30 years	118 (40.0)
$\geq 30$ years	177 (60.0)
Marital status	
Single	115 (39.0)
Married	180 (61.0)
Educational status	
<Primary level	10 (3.4)
$\geq$ Secondary level	285 (96.6)
Work status	
Working	181 (61.4)
Not working	114 (38.6)
Comorbidities	
Yes	103 (34.9)
No	192 (65.1)
Warfarin indication	
AF/valve replacements/stroke	133 (45.1)
DVTs/PEs	162 (54.9)
Warfarin duration	
<1 year	126 (42.7)
$\geq 1$ years	169 (57.3)

respectively) were reported. Around 177 (60.0%) were above 30 years and 118 (40.0%) were <30 years. Out of a total of 295 patients, 285 (96.6%) had a higher level of education, whereas 10 (3.4%) had a primary level of education. One hundred and ninety-two had no comorbidity and 103 (34.9%) had comorbidities.

Table 2 represents the key findings for knowledge of warfarin among the participants. A total of 184 (62.4%) patients showed poor knowledge and 111 (37.6%) of the patients showed good or appropriate knowledge of warfarin. The mean knowledge score for the study population was  $6.62 \pm 2.68$ .

Table 3 illustrates the major indications among the studied patients for which the warfarin was prescribed. According to the study findings, 67% of the patients were suffered from deep vein thrombosis, 52% with atrial fibrillation, 44% from cardiac (prosthetic) valve replacement, and 43% were diagnosed having a stroke. Some of the indication percentages were shared among studied patients.

**Table 2: Warfarin knowledge among patients**

Warfarin knowledge	Yes n (%)	No n (%)
Warfarin basic information		
Reason for taking warfarin	110 (37.7)	185 (62.7)
Familiar with daily dose	073 (24.7)	222 (75.3)
Familiar how to take warfarin	090 (30.5)	205 (69.5)
Know the consequences of missing a dose	167 (56.6)	128 (43.4)
INR information		
Familiar with INR test	170 (57.6)	125 (42.4)
Know the normal INR range	123 (41.7)	172 (58.3)
Know what INR control means	114 (38.6)	181 (61.4)
Warfarin adverse events		
Know duration of warfarin therapy	121 (41.0)	174 (59.0)
Familiar with warfarin interactions	192 (65.1)	103 (34.9)
Familiar with bleeding effects of warfarin	080 (27.1)	215 (72.9)
Spinach/Broccoli is safe to consume with warfarin	139 (47.1)	156 (52.9)
Warfarin interacts with common cold medicines/supplements	200 (67.8)	095 (32.2)
Warfarin interacts with antibiotics/pain killers/multivitamins	123 (41.7)	172 (58.3)
Know what to do in a thromboembolic emergency	159 (53.9)	136 (46.1)
Know thromboembolic emergency could be life-threatening	093 (31.5)	202 (68.5)

Table 4 represents the relationship between the mean knowledge score and PROs regarding adverse events. The knowledge score for males was  $06.71 \pm 2.79$ , and for females, it was  $06.46 \pm 2.50$ . There was a statistically significant correlation ( $P < 0.05$ ) observed between the knowledge mean score and PROs regarding adverse events.

## DISCUSSION

Patients' appropriate knowledge about warfarin is important in improving PROs, especially reducing drug interactions and decreasing adverse drug reactions.<sup>[11,12]</sup> The present study aimed to evaluate the effect of warfarin knowledge on PROs regarding adverse events among warfarin patients in Pakistan. Undeniably, adequate knowledge and precise therapy information about is a valued approach to decrease possible adverse events, drug interactions, and drug-related problems of warfarin.<sup>[6]</sup> Appropriate knowledge of warfarin therapy also helps patients attaining significant anticoagulation control, decrease hospitalizations, less frequent INR checks, and improve HRQoL.<sup>[12-14]</sup>

According to our study, the younger patients (age <30 years) had better warfarin knowledge ( $06.74 \pm 2.90$ ) as compared to the  $\geq 30$  years old patients, but this difference was not statistically significant ( $P = 0.525$ ). Warfarin is often prescribed to treat various CVDs because of its optimum therapeutic advantages and perceived cost-effectiveness.<sup>[6]</sup> In

**Table 3: Major indications for warfarin therapy**

Warfarin indications	n (%)
Deep vein thrombosis	67
Atrial fibrillation	52
Cardiac valve replacement	44
Stroke	43

**Table 4: Association of mean knowledge with PROs regarding adverse events**

Items	P-value
Know duration of warfarin therapy	<0.001*
Familiar with warfarin interactions	<0.001*
Familiar with bleeding effects of warfarin	<0.001*
Spinach/broccoli is safe to consume with warfarin	<0.001*
Warfarin interacts with common cold medicines/supplements	0.044*
Warfarin interacts with antibiotics/pain killers/multivitamins	0.017*
Know what to do in a thromboembolic emergency	<0.001*
Know thromboembolic emergency could be life-threatening	<0.001*

\*Correlation was significant at 0.05 level (two tailed)

terms of total knowledge score for the marital status attribute, a statistically non-significant difference ( $P = 0.179$ ) was observed between singles ( $06.88 \pm 2.57$ ) and married patients ( $06.45 \pm 2.74$ ). Likewise, better therapy understandings can lead to greater compliance with warfarin therapy that might result in good anticoagulation control and better PROs. Our study findings were almost in line with two studies regarding warfarin food interactions and warfarin interactions with other medicines.<sup>[15-17]</sup> These similarities could be due to the demographic characteristics, especially in gender, as in their study, more participants were male and in our study also male participants were more than females.<sup>[16,17]</sup>

Our study findings were also in line with two other studies in terms of knowledge about possible side effects of warfarin and drinks that can decrease warfarin effectiveness.<sup>[3,18]</sup> These obtained results definitely emphasize the need for proper patient counseling and general education to increase warfarin therapy knowledge among warfarin patients. There could be many reasons which may justify this lack of knowledge about warfarin therapy. An important and leading factor was the absence of a standardized health-care education program, especially for warfarin patients.<sup>[18]</sup> Furthermore, another reason could be that usually a very short time is given to each patient by the health-care providers which could affect patient counseling regarding the appropriate way to use warfarin and avoid adverse events.<sup>[18-20]</sup>

Statistically, a significant positive correlation ( $P < 0.05$ ) was observed between the knowledge of warfarin and the PROs regarding adverse events of the warfarin. The findings of this verified that adequate knowledge among the patients could lead to less adverse events which ultimately much help in achieving better PROs among warfarin patients. Thus, the provision of warfarin's optimal therapy knowledge also poses a greater challenge to the health-care providers for better counseling. Warfarin therapy is a bit complicated due to its varied dose-response, narrow therapeutic index, multifactorial regimens, drug and food interactions, adequate dose adjustments, and INR monitoring.<sup>[20-23]</sup> The findings of this study could help physicians, pharmacists, allied health-care professionals, and the family members of the patients to better understand the physical, psychological, social, and environmental problems patients usually face while on warfarin.

This was a self-reported study and in cases of illiterate patients, the tool was filled with the help of patients' caregivers, nurses, or the attendants that may report some biases. For this reason, data reporting may be a confounding factor in this study. The second limitation was the lack of the control group because there was no control group to make applicable comparisons for the results of the current study. This study recommends an extensive psychological exploration either using a qualitative probe, multivariate analysis, or factor analysis to obtain accurate and specific factors affecting the association of warfarin knowledge and numerous PROs among warfarin patients in Pakistan.

## CONCLUSION

The present study showed that there was a statistically significant association present about warfarin knowledge and PROs regarding adverse events among warfarin patients. This positive association between warfarin therapy knowledge and PROs was likely to be influenced by plentiful aspects that can be further explored by multivariate analysis to get pure determinants of adverse events among warfarin patients in Pakistan.

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