

# Are Patients on Oral Anticoagulation Therapy Aware of its Effects? A Cross-sectional Study from Karachi, Pakistan

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Ibrahim Zahid

✉ [ibrahim\\_zahid@hotmail.com](mailto:ibrahim_zahid@hotmail.com) *Corresponding Author*  
ORCID: <https://orcid.org/0000-0002-0638-379X>

Syed Wajih UI Hassan  
Dr Ruth KM Pfau Civil Hospital Karachi

Nida Sehar Bhurya  
Dr Ruth KM Pfau Civil Hospital Karachi

Sheena Nadeem Alam  
Dr Ruth KM Pfau Civil Hospital Karachi

Bakht Hussain Shah  
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Dow University of Health Sciences

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Ayesha Ahmed  
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Dow University of Health Sciences

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Dr Ruth KM Pfau Civil Hospital Karachi

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Dow University of Health Sciences

Rabbia Siddiqi  
Dow University of Health Sciences

Kaneez Fatima  
Dow University of Health Sciences

Muhammad Shahzeb Khan  
John H Stroger Hospital of Cook County

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## Abstract

### Objective:

Oral anticoagulants are one of the most frequently used medications. However, these drugs have a range of side effects including potential life-threatening complications. Little is known regarding the awareness of its side effect profile amongst the patients in Pakistan. Therefore, the aim of this study was to assess the knowledge of oral anticoagulant therapy and its side effects among its users.

### Results:

The mean age was  $48.9 \pm 15.2$  years. Mean scores of the participants for knowledge regarding oral anticoagulants and knowledge specific to warfarin were  $49.9 \pm 16.2\%$  and  $14.6 \pm 16.4\%$  respectively. Most notably, the majority of the patients (65.7%) did not know what side effects to be wary of or how to reduce their occurrence; and most of them were unaware of the interaction between oral anticoagulant drugs and over-the-counter substances such as aspirin, herbal medicines and alcohol. Knowledge of International Normalised Ratio (INR) was extremely poor with more than 75% of the population not being aware of the target INR range during warfarin therapy. Higher level of education was significantly associated with better knowledge scores. On the whole, knowledge of oral anticoagulant therapy and INR monitoring is extremely poor among oral anticoagulant users.

## Introduction

With several indications ranging from atrial fibrillation to mechanical heart valves, oral anticoagulants (OAC) use is quite pervasive in modern society<sup>1,2</sup>. OAC, such as warfarin and apixaban impede clotting of blood and hence are used where there is a high risk of thrombosis. However, anticoagulants, especially warfarin, have a narrow therapeutic index which requires careful dosing and monitoring to avoid both ineffectual doses and side effects<sup>3</sup>. Side effects include, but are not limited to, bleeding diatheses, thromboembolism, and hypersensitivity reactions<sup>4</sup>.

Despite the prevalence of their use and risk of serious adverse effects, several studies have shown that most patients do not have adequate knowledge of the OAC they are using<sup>5,6</sup>. Other studies have found that long-term outcomes of OAC are better when patients possess greater knowledge regarding OAC medications<sup>7,8</sup>. The improved outcome has been attributed to several factors such as increased

adherence to dosing schedules, regulation of diet to prevent interactions with the anticoagulants, and closer monitoring of the side effects of anticoagulation therapy. Awareness of INR monitoring is equally important for improved outcomes. Previous studies have shown a positive correlation between the knowledge of patients' warfarin therapy and the INR values lying within the target ranges.<sup>8,9</sup> Poor treatment outcomes were seen in patients with lack of medication adherence and knowledge deficits.<sup>9,10</sup> Considering the scarcity of relevant data in developing countries, our study specifically aims to assess the level of knowledge patients have about their oral anticoagulants.

## Methods

This quantitative, multi-centric, cross-sectional study was conducted from January to June 2019 at Civil Hospital Karachi and National Institute of Cardiovascular Diseases, Karachi Pakistan. Ethical approval was obtained from Institutional Review Board of Dow University of Health Sciences, Pakistan. Patients taking any OAC drugs for at least 1 month were included in the study through non-probability convenience sampling. A written informed consent was taken from the patients, stating the aim of the study and its impact; confidentiality of patients was ensured. Based on the assumption that 74.1% had adequate knowledge regarding OAC<sup>(11)</sup>, and taking a 5% margin of error and 90% confidence level, the calculated sample size was 207. This was increased to 230 to account for any missing or partially filled forms. Patients on OAC therapy were all included in the study except paediatric patients, medical staff, nurses, medical students, healthcare professionals and those unwilling to participate.

Face-to-face interviews were conducted with the patients using the Oral Anticoagulation Knowledge Tool (AKT) which was shown to have acceptable validity and reliability in a previous study.<sup>(12)</sup> The questionnaire is divided into three parts (see Appendix 1). The first section is related to the demographic characteristics of patients. The second part consisted of 20 questions to assess the patients knowledge about OAC (Sect. 2), and the final 8 questions (Sect. 3) of the form were exclusive to patients on warfarin therapy particularly.

For each question, '1' mark was awarded for each correct answer and '0' for each wrong answer,

except for questions '18' and '19' in 'section 2' and '6b' in 'section 3'. In these questions 1 mark was given for each correct point out of 3. Section 2 was scored out of 24, and section B, which was only filled by patients on warfarin therapy, was scored out of 10. Final scores were presented as a percentage of correct answers for all the participants in the study.

Data were analyzed using IBM Statistical Package for the Social Sciences (SPSS) version 22. Knowledge of OAC was evaluated through total oral AKT scores by simply counting the number of correct answers and calculating their percentages. Frequencies and percentages were calculated for all categorical variables. Overall mean and median scores were calculated for both sections, and mean scores of both sections were also reported separately for all demographic groups. Kruskal-Wallis Test was applied to compare mean scores among different demographic groups.  $p < 0.05$  was considered to be significant.

## Results

Out of the 230 participants approached, completely filled forms were obtained from 207 participants giving a response rate of 90%. As presented in Table 1, the mean age was  $48.9 \pm 15.2$ . Half of the study population was male ( $n = 105$ ; 50.7%). More than half of the participants (66.7%) enrolled in the study ( $n = 138$ ) had no formal education ( $P < 0.001$ ) and almost half of the participants ( $n = 98$ ; 47.3%) had a monthly family income of \$100–200.

Table 1  
Demographics of study population

Demographics	Frequency (%)	P-value
Age groups, <i>mean ± SD (years)</i>	48.9 ± 15.2	
≤30	27 (13.0)	0.4
31-50	92 (44.4)	
>50	88 (42.5)	
Gender		0.05
Male	105 (50.1)	
Female	102 (49.3)	
Marital status		0.3
Single	19 (9.2)	
Married	169 (81.6)	
Other	19 (9.2)	
Highest level of education		< 0.001*
High school or equivalent	50 (24.2)	
College	6 (2.9)	
Technical or vocational education	5 (2.4)	
Bachelor's degree	5 (2.4)	
Postgraduate	3 (1.5)	
No formal education	138 (66.7)	
Occupation		0.2
Service & Sales worker	9 (4.4)	
Skilled agricultural, forestry and fishery workers	6 (2.9)	
Craft and related trades workers	12 (5.8)	
Plant and machine operators and assemblers	10 (4.8)	
Elementary occupations	33 (15.9)	
Housewife	84 (40.6)	
Unemployed/Retired	40 (19.3)	
Managers/Professionals/Technicians	13 (6.3)	
Monthly family Income (USD)		0.2
<100	80 (38.6)	
100-200	98 (47.3)	
200-500	26 (12.6)	
>500	3 (1.5)	
* <i>P</i> < 0.05		

When assessed for knowledge, more than half of the participants were using warfarin (n = 147; 71%) (*P* = .002), and about one-quarter (21.7%) were taking rivaroxaban (n = 45). Most of the patients (n = 116; 56%) knew that these drugs actually prevent blood from clotting but more than a quarter (31.9%) of the enrolled participants did not know the drug mechanism (n = 66) (*P* < 0.001). More than half the patients said it is important to take medicine same time each day (n = 139; 67.1%) (*P* < 0.001) and 64.7% (n = 134) disagreed to double the dose if missed (*P* < 0.001). Nearly half of the study population believed that missing a dose could worsen their condition (n = 87; 42%) (*P* < 0.001). Majority of patients believed that they should continue with the drug even if they felt better (n = 111; 53.6%) (*P* < 0.001). Majority was unsure if it is safe to take anti-inflammatory drugs or vitamins,herbal medicines or alcohol with their OAC (*P* < 0.001).

There was a positive response from the patients regarding informing their physician or dentist about

their OAC (n = 161; 77.8%) ( $P < 0.001$ ). Most of the patients were unaware about main side effects of their anticoagulant or over all three side effects to watch out for (n = 113; 54.6%) ( $P < 0.001$ ). When patients were asked about the best step if they consume too much of this medicine, most of them opted for consulting their doctor (n = 110; 53.2%) ( $P < 0.001$ ). This is displayed in Table 2.

Table 2  
Knowledge of OAC

Knowledge Questions	Frequency (%)	P-value
Name of OAC		0.002*
Warfarin	147 (71)	
Rivaroxaban	45 (21.7)	
Don't know the name	15 (7.2)	
Why has your doctor prescribed this medicine		< 0.001*
Arrhythmias	14 (6.8)	
Blood thinning	47 (22.7)	
Cardiac issue/ chest pain	20 (9.7)	
DVT	15 (7.2)	
MI	39 (18.8)	
Prosthetic valve	26 (12.6)	
Don't know	26 (12.6)	
Others	20 (9.7)	
How does this medicine work in your body		< 0.001*
Lowers BP	16 (7.7)	
Prevents blood from clotting	116 (56.1)	
Lowers heart rate	9 (4.3)	
Don't know	66 (31.9)	
How many times a day do you need to take this medicine		0.02*
Once	171 (82.6)	
Twice	22 (10.6)	
Thrice	4 (1.9)	
Don't know	10 (4.8)	
For how long do you need to take this medicine		< 0.001*
3 months	15 (7.2)	
6 months	18 (8.7)	
1 year	19 (9.2)	
Lifelong	89 (43)	
Don't know	66 (31.9)	
Why is it important to take this medicine exactly as the doctor has told you		< 0.001*
Too much of this can cause bleeding	44 (21.3)	
Skipping a dose can cause bleeding	2 (1)	
It interacts with food, so changing the dose/timing can be hazardous	6 (2.9)	
Don't know	155 (74.9)	
Is it important to take this medicine at the same time each day		< 0.001*
Yes	139 (67.1)	
No	31 (15)	
Not sure	37 (17.9)	
Is it okay to double the next dose of this medicine if you missed a dose		< 0.001*
Yes	23 (11.1)	
No	134 (64.7)	
Not sure	50 (24.2)	
Could missing one dose worsen your condition		< 0.001*
Yes	87 (42)	
No	68 (32.9)	
Not sure	52 (25.1)	
Is it appropriate to stop taking this medicine once you feel better		< 0.001*
Yes	46 (22.2)	
No	111 (53.6)	
Not sure	50 (24.2)	
Is it safe to take anti-inflammatory meds while on OAC		< 0.001*
Yes	67 (32.4)	
No	41 (19.8)	
Not sure	99 (47.8)	

Is it safe to take vitamins, herbal meds without consulting doctor		< 0.001*
Yes	66 (31.9)	
No	64 (30.9)	
Not sure	77 (37.2)	
Is it beneficial to take more medicine than prescribed		< 0.001*
Yes	11 (5.3)	
No	126 (60.9)	
Not sure	70 (33.8)	
Will drinking too much alcohol increase the risks of this med		< 0.001*
Yes	70 (33.8)	
No	10 (4.8)	
Not sure	127 (61.4)	
Would you inform surgeon, dentist, doc about your meds		0.001*
Yes	161 (77.8)	
No	19 (9.2)	
Not sure	27 (13)	
Is it imp that all healthcare practitioners know about this med		0.01*
Yes	161 (77.8)	
No	23 (11.1)	
Not sure	23 (11.1)	
Most important side effect of this medicine		< 0.001*
Bleeding	49 (23.7)	
Others	20 (9.7)	
Don't know	136 (65.7)	
Correct Side Effects Identified		< 0.001*
All Three	56 (27.1)	
Two correct	22 (10.6)	
One correct	7 (3.4)	
None	5(2.4)	
Don't Know	117 (56.5)	
Side Effect Identified		
Bleeding Gums	72 (19.7)	
Prolonged Nosebleeds	50 (13.7)	
Severe Bruising	32 (8.8)	
Blood in urine	64 (17.5)	
Insomnia	10 (2.7)	
Loss of Appetite	20 (5.5)	
Don't Know	117 (32.1)	
How to reduce Side Effects		
Monitor INR regularly	15 (4.9)	
Monitor	44 (14.4)	
Sleeping on time	21 (6.9)	
Eating less food	14 (4.6)	
Avoid things that could cause cuts/injuries	31 (10.1)	
Proper Dosing	53 (17.3)	
Don't Know	128 (41.8)	
Best step if you take too much of this medicine		< 0.001*
Skip the next dose	35 (16.9)	
Consult my doctor	110 (53.1)	
Be alert for signs of side effects	15 (7.2)	
Don't Know	47 (22.7)	
OAC, oral anticoagulants; INR, international normalized ratio		
*P < 0.05		

Table 3 shows knowledge of participants specific to warfarin therapy. More than three-quarters of the study population (n = 116; 78.9%) did not know about the target INR range during warfarin therapy ( $P < 0.001$ ). Most of the patients were unaware of their last INR reading (53.1%). Only 16.4% believed that regular INR tests were necessary to know if the medicine is working ( $P < 0.001$ ). More than half of the participants (66.7% n = 98) were not sure if diet had any effect on their warfarin therapy, and a fairly small percentage agreed to this idea (n = 24; 16.3%)( $P < 0.001$ ).

Table 3  
Knowledge specific to Warfarin therapy

	Frequency (%) (n = 147)	P value
What is your target INR range		< 0.001*
<1.0	17 (11.6)	
1.0 to 1.9	5 (3.4)	
2.0-3.0	9 (6.1)	
Don't Know	116 (78.9)	
Last INR reading		0.02*
<1.0	1 (0.7)	
1.0-2.0	49 (33.3)	
2.1-3.0	14 (9.5)	
>3.0	5 (3.4)	
Don't know	78 (53.1)	
Are Regular INR tests necessary to know that the medicine is working		< 0.001*
Yes	34 (23.1)	
No	8 (5.4)	
Not sure	105 (71.4)	
Is an INR above target good for health		< 0.001*
Yes	8 (5.4)	
No	20 (13.6)	
Not sure	119 (81.0)	
Is an INR below target bad for health		< 0.001*
Yes	16 (10.9)	
No	10 (6.8)	
Not sure	121 (82.3)	
Is it possible what you eat to affect your Warfarin therapy		< 0.001*
Yes	24 (16.3)	
No	25 (17.0)	
Not sure	98 (66.7)	
Vitamins that can affect your OAC therapy		0.008*
Vitamin A	1 (0.7)	
Vitamin B	5 (3.4)	
Vitamin K	6 (4.1)	
Don't Know	131 (89.1)	
Others	4 (2.7)	
INR, international normalized ratio		
*P < 0.05		

Table S1 further elaborates on the mean knowledge scores of the population. Only 41.5% of people were able to score above 50% mark when assessed for knowledge about their OAC, and less than 2% were above this mark when assessed for knowledge specific to Warfarin. Having a minimum of postgraduate level education was significantly related to higher knowledge scores as shown in table S2

## Discussion

Similar to researches conducted by Shrestha<sup>5</sup> et al, Hu<sup>13</sup> et al and Baker<sup>11</sup> et al, our study showed that patients have low knowledge with regards to their prescribed OAC. Taking the demographics into account, one can reasonably attribute the lack of higher education and a language barrier as the primary causes of this gap in knowledge. However, previous literature regarding the association of knowledge with age has mixed findings. Some researchers conclude that participants of younger age and higher level of education scored better,<sup>14,15</sup> whereas others showed older age to positively

influence the scores.<sup>16</sup> Our study does not show any significant relation of knowledge with participants' age.

Findings of our study indicate that only 27.1% of the participants correctly identified bleeding as the most important side effect of this medication, particularly bleeding from gums, prolonged nosebleeds and blood in urine. The majority of the sample (65.7%) did not know what side effects to be wary of or how to reduce their risk. These findings prove to be an alarming indicator of lack of awareness as most of these participants had been asked to continue this medicine for life and their lack of knowledge about possible side effects is concerning. This gap in knowledge is common in reference to many studies, one of which reported only 42% of their sample population to be aware of any possible side effects of warfarin therapy.<sup>17</sup>

Another particular area of concern was the inadequate patient understanding of warfarin's interactions. Majority of the participants were unaware of the interaction of OAC drugs with over the counter pills like aspirin, herbal medicines and alcohol. Drugs such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and aspirin inhibit platelet function therefore when coupled with oral anticoagulants, they may increase the risk of bleeding.<sup>18</sup> There is a high prevalence of multiple NSAIDs prescription in Pakistan<sup>19</sup>, an alarming fact when considering that NSAIDs increase the risk of gastrointestinal bleeding when used in combination with warfarin, and that only a minority of our sample was aware of this interaction. Alcohol, on the other hand, interacts with the cytochrome P450 system, responsible for metabolizing warfarin. Only one third of the study population understood the risk of concurrent use of alcohol and an even smaller percentage to that with NSAIDs. A similar finding was obtained by Shrestha et al<sup>5</sup>, who reported that 94.1% of their sample did not know which drinks could decrease warfarin's effectiveness. This is particularly worrying when taking into consideration the fact that excess alcohol can increase the risk of major bleeding when taken with warfarin, and only 23.7% of our sample could identify bleeding as the most important side effect of oral anticoagulants. These findings were similar to results obtained by Roche<sup>6</sup> et al, Yahaya<sup>20</sup> et al and Campbell et al<sup>21</sup>. The sample population barely knew about INR, its target values and the importance of therapeutic INR

range; attaining a mean score of only 14.6( $\pm$  16.4)%. Furthermore, a research also found that even though young and educated people are likely to have better knowledge about their anticoagulant medicines, this does not affect their INR control or episodes of bleeding and/or thrombosis.<sup>23</sup> On the contrary, a research in Saudi Arabia showed INR control to be positively influenced by knowledge about their OAC.<sup>24</sup> Maintaining a stable INR is an important indicator of adequate anticoagulation in the body, because suprathreshold value increases the probability of bleeds and subtherapeutic value may cause thrombosis.<sup>25</sup> Within our sample population, the ability to self-monitor is likely to be reduced due to their lack of adequate knowledge about INR, increasing the probability of patients being under or over treated.

A positive result identified in our patient population indicated that over three quarters of people agreed it was important for their healthcare providers to know they were taking an OAC, and the similar proportion of people said that they would usually inform their doctors about their drug history. In contrast, Khudair et al<sup>26</sup> found that most participants did not know the importance of informing healthcare professionals if they were on warfarin.

## Conclusions

The findings show that majority of the patients have poor level of knowledge about oral anticoagulant therapy and knowledge about INR monitoring with warfarin therapy is highly substandard.

## Limitations

The study only included 207 participants and a larger sample size from different hospital settings is required to generalize the findings. Most patients were admitted in government hospitals, with little data obtained from private setups, and the majority of our sample population belonged to a low socioeconomic background and received little to no formal education, which could influence the results. Second, the data was not divided according to the hospital it was collected from. This could have provided us with some insight into the effectiveness of patient counseling in the different setups. Furthermore, our questionnaire did not assess level of knowledge with duration of therapy or calculate a passing rate for the proportion of people with adequate knowledge.

## Abbreviations

OAC

Oral Anti Coagulant

INR

International Normalised Ratio

AKT

Anticoagulation Knowledge Tool

NSAIDs

Non-Steroidal Anti-Inflammatory Drugs

Declarations

### **Ethics approval and consent to participate**

The study was approved by the Ethical Review Committee of Dow University of Health Sciences, Pakistan and written informed consent was taken from each participant prior to data collection.

### **Consent for publication**

Informed consent was obtained from the study participants for publication of data.

### **Availability of data and material**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare that they have no competing interests.

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None.

### **Authors' contributions**

IZ, RaS, KF and MSK were involved in study design. IZ, BHS, FBF and CAH were involved in data analysis. IZ, SWUH, NSB, SNA, BHS, FBF, CAH, AA, SSUH, JH, AZ, RS and MA performed data collection, article writing and compilation of the manuscript. All the authors contributed to article writing. All authors have read, reviewed and approved the final manuscript.

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