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EVALUATION OF A DESIGNED COMMUNITY-BASED POST -DISCHARGE WARFARIN MANAGEMENT PROTOCOL ON IRAQI PATIENTS

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Keywords:

Warfarin Anticoagulation, pharmacist-managed warfarin protocol, usual medical care, warfarin-monitoring service

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ABSTRACT: Introduction: The warfarin management programs include mainly routine INR measurement, dosing protocols, clinical management protocols for excessive anticoagulation, and patient education. There have been numerous investigations to explore the most appropriate model for outpatients, accordingly different Anticoagulation Management Programs have been emerged in practice. **Aims and objectives:** This study is an attempt to develop concise warfarin protocol that expands role for the community pharmacist in Iraq. **Patients and methods:** A prospective case-controlled carried out on patients discharged from the hospital on warfarin therapy in combination to their prescribed medications. The follow up was achieved by four visits starting from 8-10 days after hospital discharge until 90 days. patients who were allocated into Intervention group received designed warfarin management program , and control group on 'usual care' monitoring. **Results:** The percentage of patients with international normalized ratio (INR) levels is within therapeutic/target range in the intervention group was significantly higher than that in the control group (66.67% vs. 34.78%) after 90 days of monitoring program ($p<0.05$). During 90 days of follow up, the total percentage of time therapeutic range (TTR) for the intervention group was (57.68%), and (44.92%) for the control group. Patient adherence to warfarin was (100%) in intervention group compared to control group ($p<0.05$). **Conclusions:** The intervention group demonstrated higher percentage of patients with INR levels within therapeutic/target range, following the management program, and significant improvement in time therapeutic range (TTR) from admission to 90 days post discharge. Accordingly, many promising strategies emerged from pharmacist warfarin- management program.

INTRODUCTION: The necessity to provide more precise dosage adjustment of warfarin may be of clinical importance in respect to current recommendation for higher-intensity warfarin therapy and maintenance of acceptance INR values [1]. Poor adherence was significantly associated with under anticoagulation or out-of-range INRs [2].

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The interventions to improve adherence are most effective if implemented by physicians, pharmacists, nursing staffs, and behavioral specialists throughout the course of therapy [3]. The warfarin management programs include mainly routine INR measurement, dosing protocols, clinical management protocols for excessive anticoagulation, and patient education [4]. The key endpoint evaluated is usually the control of a patient's INR (estimated as the time the patient's INR is maintained within the target range) [5]. There have been numerous investigations to explore the most appropriate model for anticoagulant management, accordingly different Anticoagulation

Management Programs have been emerged in practice [6-9]. This study is an attempt to develop concise protocol that expands role for the community pharmacist in Iraq to work closely with general practitioners in managing, monitoring and educating patients receiving anticoagulant therapy with the overall goal of improving outcomes for patients receiving warfarin.

Patients and method:

Study design: This study is a prospective Case-controlled carried out on patients discharged from the hospital. The patients were in warfarin therapy in combination to their prescribed medications. The candidate patients received warfarin therapy according to the clinical indication by Consultant cardiologist. The ethical approval was obtained from the institution ethical committee, and a written consent was given by each patient participated in the current study.

As per study design, the follow up for all patients was achieved by four visits and interview starting from 8-10 days after hospital discharge which is considered as visit number (1).Thereafter; visits number (2,3 and 4) were programmed after 30, 60 and 90 days after hospital discharge, respectively. Each visit involves the following keynote from standard of practice:

1. Review the risks and benefits with the patients observed when starting warfarin therapy.
2. Patient instructions and education according to the patient level of education and understanding about warfarin therapy (adverse effects, drugs and herbal interactions, food and dietary (Vitamin K) interaction, smoking and alcohol drinking, and female menstrual cycle.
3. INR monitoring.
4. Home medicine review to identify and resolve any post discharge medications related issues.
5. Communication with prescriber physician for warfarin dose adjustment if any.

The results of the patients outcomes gained by the follow up program were compared with the results obtained from control patients. The control patients were on usual medical care and follow up achieved by the medical staff rather the clinical pharmacist conducted the current management program.

Patients: The sample size of the present investigation involved of 50 patients who were allocated into two groups as follow:

1. Intervention group; included 27 patients who were eligible for anticoagulation therapy, matches the inclusion criteria, and received designed warfarin management program in collaboration with health care team.

This group is subdivided into:

A. Medical group; included 14 patients who were diagnosed as deep vein thrombosis, pulmonary embolism and atrial fibrillation.

B. Surgical group; included 13 patients who were undergoing cardiac surgery for atrial valve replacement, mitral valve replacement, and double valve replacement.

2. Control group; included 23 patients eligible for anticoagulation therapy and matches the inclusion criteria to be continued on 'usual care' monitoring and don't receive designed warfarin management program. Usual care monitoring is a patient routine visit to a physician working in the center for INR monitoring and dose adjustment without warfarin-clinical pharmacist intervention.

Inclusion criteria:

1. **Indications for anticoagulation;** including atrial fibrillation, venous thromboembolism (deep vein thrombosis and/or pulmonary embolism), and prosthetic valve replacement from (internal medicine and surgery wards).
2. Hospitalized patients who were discharged on warfarin therapy.
3. Intended duration of anticoagulation of a minimum of 3 months.

Exclusion Criteria:

1. Patients without a regular visits and community pharmacist through which a home medicine review could be arranged.
2. Patients with dementia, or otherwise unable to answer basic questions about their therapy.
3. Pregnancy and lactation.

Methods: Warfarin -management program include the following checklist:

A. Patient data sheet:

1. Patient demographics and baseline data sheet [10-12].
2. Anticoagulant referral form [13].

B. Comprehensive warfarin monitoring:

1. Flexible warfarin initiation nomogram (this nomogram is useful in hospitalized patients in whom an INR can be checked on a daily basis) [10, 12].
2. Complicating factors influence warfarin sensitivity [14].
3. Warfarin pharmacokinetic / pharmacodynamics interaction [10, 14- 18].
   - **a)** Warfarin - drug interaction
   - **b)** Warfarin - food interaction
   - **c)** Warfarin - laboratory interaction

C. HMR (Home Medicine Review):

1. Patient counseling for warfarin [14-16, 19].
2. Laboratory monitoring [11, 19].

Patients should be assessed for factors that influence interpretation of laboratory results and determine warfarin dosing. The INR was calculated using specific equation [20], and the time therapeutic range (TTR) was calculated using Rosendaal linear interpolation method by addition each patients time within the therapeutic range and divided by the total time of observation [21].

RESULTS AND DISCUSSION:

Patient demographics and disease characteristics: The implementation of pharmacist- management programs for anticoagulation approach may provide a safe and effective collaborative care compared to individual patient appointments. It would be able to reduce health care expenditure as well and improving therapeutic outcomes. These programs can provide different models like development of pharmacist-managed inpatients services for anticoagulation initiation and titration, anticoagulation protocols for long- term care pharmacist, pharmacist-management of anticoagulation in multi- physician family clinics on outpatient based, or sub-specialized programs like clinical pharmacist interventions in optimization oral anticoagulation use in stroke patients or undergoing dental procedures.

Several models had been implemented earlier worldwide [10-17], and to the best knowledge this is the first maneuver to assess such program on Iraqi patients.

Table (1) presented the baseline demographic data of all patients on warfarin indications enrolled with study groups.

TABLE 1: PATIENTS DEMOGRAPHICS AND DISEASE CHARACTERISTICS OF THE CONTROL AND INTERVENTION GROUPS

Characteristics		Study groups		Total	*P* value
		Control group	Intervention group		
Gender	Male	9(39 %)	15(55 %)	24(48 %)	0.27
	Female	14(61 %)	12(45 %)	26(52 %)	
	Total	23(100 %)	27(100 %)	50(100 %)	
Age (years)	Mean ±SD	52.78 ±10.49	46.96 ± 12.06	49.87 ± 11.27	0.92
BMI (kg/m^2)	Mean ±SD	29.26 ± 3.77	29.36 ± 6.61	29.31 ± 5.19	0.07
Drug allergy	Yes	3(13 %)	4(14 %)	7(14 %)	0.59
	No	20(87 %)	23(86 %)	43(86 %)	
Number concomitant chronic diseases	0	7(30.4 %)	4 (14.8 %)	11(22 %)	0.07
	1	8(34.8 %)	4 (14.8 %)	12(24 %)	
	2	5(21.7 %)	9 (33.3 %)	14(28 %)	
	≥3	3(13.1 %)	10(37.1 %)	13(26 %)	
Smoking status	Smoker	1(4.3 %)	6(22.2 %)	7(14 %)	0.07
	non smoke	22(95.7 %)	21(77.8 %)	43(86 %)	

Data presented as number of patients (n) and percentage (%), or as mean ±SD
Independent sample t test for numerical variables, chi- square test
P value > 0.05 is considered non-significant, *P* * value< 0.05 is considered significant

Fifty patients enrolled to represent the sample size of this study including 24 male (48%), and 26 female (52%). Those patients were then allocated into control group (including 9 male patients (39%) and 14 female patients (61%)), and intervention group (including 15 male patients (55%) and 12 female patients (45%)). The mean±SD age of all patients involved in this study was (49.87±11.27) years. The mean age of the control group was (52.78±10.49) years, and the mean age of the intervention group was (46.96±12.06) years.

The mean body mass index (BMI) of all patients was (29.31±5.19) Kg/m². The mean BMI of control group was (29.26 ±3.77) Kg/m² and the mean BMI for the intervention group was (29.36±6.61) Kg/m².

The allergy of drugs among control group was documented in (13%) of patients, while intervention group presented drug allergy in (14%) of patients.

The numbers of the concomitant diseases among the study groups were divided into 4 categories: patients, who are free of concomitant chronic disease, patients whom had one chronic disease, patients whom had two chronic diseases and patients whom had more than three chronic diseases. A (30.4%) of patients in the control group were found to be free of concomitant chronic diseases in comparison with (14.8%) of patients in the intervention group. A (34.8%) of patients in the control group had one chronic disease and (14.8%) of patients in the intervention group. The patients with two chronic diseases were (21.7%) in the control group and (33.3%) of patients in the intervention group. Three and more chronic diseases were found in (13.1%) of patients in the control group and (37.1%) of patients in the intervention group.

Smoking status among study groups was divided into; currently smoking which was found in (4.3%) of patients and non smoked was in (95.7%) of patients in the control group. On the other hand, the current smokers were (22.2%) of patients, and the non smoked were (77.8%) of patients in the intervention group.

Process of matching for the variables mainly (age, gender, and body mass index) between participants in the control and the intervention group showed no significant differences ($p > 0.05$).

The percentage of patients with INR within the target range for intervention and control groups according to each intervention visit

The intervention group demonstrated higher percentage of patients with INR levels within therapeutic/target range (which is determined according to each indication for warfarin) among study population (27 patients) in comparison to the control group (23 patients) in all intervention visits. However in visit 3, the percentage of patients with INR levels within therapeutic/target range was slightly higher in control group compared to the intervention group (60.87% vs. 59.26%) respectively. From statistical point of view, no significant differences were found between the intervention and the control groups in all the intervention visits. Nevertheless, significantly higher percentage of patients with INR levels within therapeutic/target range was clear of visit 4 ($p=0.03$), interestingly, which was nearly double that recorded in the control group (66.67% vs. 34.78%) respectively, as shown in **Table 2, Fig. 1.**

TABLE 2: THE PERCENTAGE OF PATIENTS WITH INR WITHIN THE TARGET RANGE FOR INTERVENTION AND CONTROL GROUPS ACCORDING TO EACH INTERVENTION VISIT

	Study groups		
Intervention visits	**Control (%)**	**Intervention (%)**	***P* value**
Visit 1(8 days)	9 (39.13 %)	12 (44.44 %)	0.54
Visit 2(30 days)	9 (39.13 %)	13 (48.15 %)	0.40
Visit 3(60 days)	14 (60.87%)	16 (59.26 %)	0.40
Visit 4(90 days)	8 (34.78 %)	18 (66.67 %)	0.03*

Data presented as number of patients (n) and percentage (%)
Independent sample t test
P value > 0.05 is considered non-significant, *P**value < 0.05 is considered significant

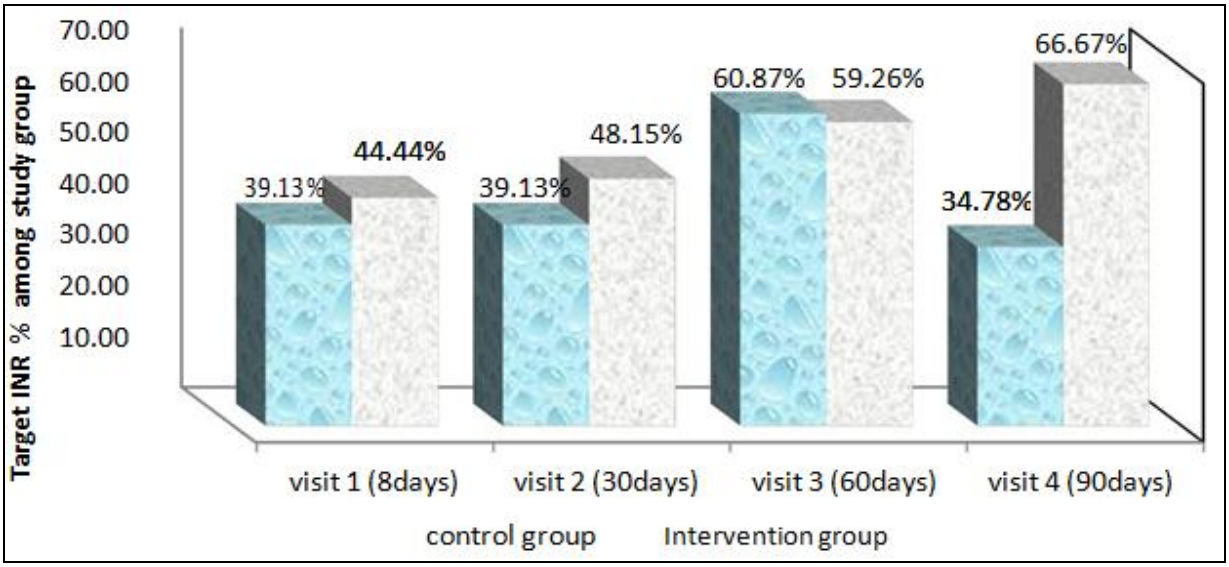

FIG. 1: THE PERCENTAGE OF PATIENTS WITH INR WITHIN THE TARGET RANGE FOR INTERVENTION AND CONTROL GROUPS ACCORDING TO EACH INTERVENTION VISIT

The current finding is supported by several previous investigations [22- 25]. A very recent study conducted by Hazem et al. (2016) demonstrated that the percentage of patients with INR levels within therapeutic/target range was higher for the patients managed by clinical pharmacists intervention in comparison to the patients under doctor based advices and intervention (76.5% vs. 71.2%) respectively [22]. Similar results was presented by Dib JG et al. (2014) [23] in which higher target range of INR in patients with warfarin therapy managed by clinical pharmacists intervention compared to those obeying usual conventional pharmacy practice (59% vs. 48%) respectively. Several other clinical programs reveal high percentage of target range INR in both intervention and control group as follow; (76% vs. 48%) [28], (67.2 % vs. 54.6%) [24], (82.9 % vs. 34.3%) [25] respectively clearly support the results of the present study. All evidences necessitate the collaborative role of clinical pharmacist intervention in order to achieve optimal INR levels in the patients with warfarin therapy. The total percentage of time therapeutic range (TTR) for the intervention and control groups from discharge to day 90 following warfarin therapy

The percentage of TTR reflect the time interval during which the patients are kept within the therapeutic target range of INR level relative to over all time interval for follow up of the patients which was 90 days in the current study from hospital discharge. The percentage TTR for the intervention group was 57.68% that is to say that the patients were kept within the therapeutic target range of INR level for 52 days from 90 days follow up, and the TTR was found to be 44.92% (40.5 days) for the control group during 90 days, **Table 3.**

TABLE 3: THE TOTAL PERCENTAGE OF TIME THERAPEUTIC RANGE (TTR) FOR THE INTERVENTION AND CONTROL GROUPS FROM DISCHARGE TO DAY 90 FOLLOWING WARFARIN THERAPY

Intervention visits	Study groups	
	Control (%)	Intervention (%)
TTR from discharge to day 90 %	44.92%	57.68%

Data presented as percentage (%)
P value < 0.05 is considered significant

The results of the present study matched several recent studies [22, 26]. A very recent study by Hazem *et al*. (2016) reported a % TTR of 81.8% versus 69.8% ($p< 0.05$) when comparing pharmacist based anticoagulant management to doctor-based management, respectively [22]. In other recent study by Entezari *et al*., (2016) the percentage TTR was 72.1% versus 56.7% ($p<0.05$) for two common models for management of warfarin therapy (pharmacist-led service versus usual medical care) respectively [26].

Applying the pharmacist-managed anticoagulation program within a family practice clinic achieved better INR control with TTR over 60% for pharmaceutical care [27]. Many other studies explore significant differences between pharmacist intervention and the usual care in warfarin management therapy (73.7% versus 61.3%) (p<0.05) [24] and (62.7% vs. 53.9%), (p<0.05) respectively [28]. According to all these findings from the present study and the previous literature, it can be said that the clinical pharmacist intervention play a vital role to elevate the percent TTR in the patient and consequently achieve optimal warfarin therapy via maintaining higher actual TTR.

Warfarin monitoring for intervention and control groups following warfarin therapy: **Table 4** presented the details of warfarin monitoring during the intervention visits. These include bleeding events, total number of drugs prescribed, number of interacting drugs with warfarin, daily dosing of warfarin, change in warfarin dose, mean INR measurement, the classification of INR level and patient adherence and instructions to warfarin therapy.

TABLE 4: DETAILS OF WARFARIN MONITORING CRITERIA DURING INTERVENTION VISITS FOR BOTH GROUPS FOLLOWING WARFARIN THERAPY

Details of intervention visits		Control group				Intervention group				*P* Value
		Visit 1 (8days)	Visit 2 (30days)	Visit 3 (60days)	Visit 4 (90days)	Visit 1 (8days)	Visit 2 (30days)	Visit 3 (60days)	Visit 4 (90days)	
Bleeding events(n)	Minor	4(17.39%)	1(4.34%)	1(4.34%)	1(4.34%)	1(3.7%)	3(11.11%)	1(3.7%)	2(7.4%)	
	Major	0(0%)	0(0%)	0(0%)	1(4.34%)	0(0%)	0(0%)	0(0%)	0(0%)	> 0.05
Total Number of drugs	Means±SD	3.3±2.36	3.3±2.36	3.3±2.36	3.3±2.36	4.92±2.99	5.14±3.13	4.88±2.83	4.63±2.81	0.042*
Number of interacting Drugs	Means±SD	0.87±1.14	0.87±1.14	0.87±1.14	0.87±1.14	2±1.77	1.56±1.62	1.19±1.38	0.96±1.12	> 0.05
Daily dose of warfarin (mg)	Means±SD	3.93±1.66	3.66±1.53	4.17±1.67	4.25±1.92	4.83±1.5	4.03±2.05	4.03±1.85	3.99±1.85	> 0.05
Change in warfarin dose (n)	Yes	15(65.2%)	13(56.5%)	9(39.1%)	11(47.8%)	10(37%)	18(66.7%)	15(55.6%)	16(59.3%)	
	No	8(34.8%)	10(43.5%)	14(60.9%)	12(52.2%)	17(67%)	9(33.3%)	12(44.4%)	11(40.7%)	> 0.05
INR	Means±SD	2.65±1.15	2.28±1.04	2.56±0.69	2.75±0.96	3.24±1.39	2.64±0.94	2.71±0.95	2.42±0.78	> 0.05
Classification of INR level (n)	Under	8(34.78%)	11(47.83%)	6(26.09%)	8(34.78%)	5(18.52%)	7(25.93%)	5(18.52%)	8(29.63%)	
	Supra	1(4.35%)	2(8.70%)	3(13.04%)	4(17.39%)	3(11.11%)	5(18.52%)	3(11.11%)	0(0%)	
	≥ 4	5(21.74%)	1(4.35%)	0(0%)	3(13.05%)	7(25.93%)	2(7.41%)	3(11.11%)	1(3.70%)	0.3
	Target	9(39.13%)	9(39.13%)	14(60.87%)	8(34.78%)	12(44.4%)	13(48.1%)	16(59.2%)	18(66.6%)	
Patients adherence (n)	Yes	20(87.0%)	20(87.0%)	20(87.0%)	19(82.6%)	27(100%)	27(100%)	27(100%)	27(100%)	
	No	3(13.0%)	3(13.0%)	3(13.0%)	4(17.4%)	0(0%)	0(0%)	0(0%)	0(0%)	0.002*

Data presented as number of patients (n) and percentage (%), or as mean ±SD
ANOVA test for numerical variables, chi- square test
P value > 0.05 is considered non-significant, *P** value< 0.05 is considered significant

The bleeding events are divided into minor and major bleeding. Minor bleeding was found in (17.39%) of patients after 8 days post discharge in the control group. The number of patients was reduced to (4.34%) throughout the study period. But one major bleeding event occurs after 90 days in control group. In the intervention group, no patient developed major bleeding events, but minor bleeding was noticed in several visits. The total percentage of minor bleeding between the groups throughout the monitoring program was (7.6% vs. 6.48%) for control and intervention group respectively. While In major bleeding, the total percentage was 1% in the control group and 0% in the intervention group. Thus, difference was found between the two study groups in respect to the bleeding events (p>0.05). Previous study observed that minor and major adverse events of warfarin therapy occurred in 10% and 1.5% patients between usual care and pharmacist intervention program, respectively [23].

Additionally, the major bleeding events in pharmacist-led service model for management of warfarin therapy were (0.6% vs. 1.7%) for the usual medical care compared to management model [26]. Bleeding frequency due to warfarin has been estimated to occur (15%-20%) per year, and the life threatening or fatal bleeding, the rates was estimated to be (1%-3%) per year [29].

The mean numbers of drugs used by patients in the control group overall the intervention visits were (3.3±2.36), Whereas, the mean number of drugs used in the intervention group were higher compared to control patients was as follow: (4.92±2.99), (5.14±3.13), (4.88±2.83), and (4.63±2.81) respectively. The total mean of the drug used by intervention group patients throughout all visits was (4.89±2.94) and for control group (3.3±2.36) with statistical significant difference between them (p=0.042). As mentioned earlier, several drugs significantly interact with warfarin by different mode. In the present study, the control group showed similar mean of interacting drugs throughout all visits (0.87±1.14), whereas mean drug interaction in interventional group varies from visit to another with total mean of (1.42±1.47). This is due to large number of drugs used by patients in the intervention group that interact with warfarin compared to control group. However, the result was non-significant (p>0.05). Castro et al. in his study mentioned that major of drug interactions with warfarin are very common in inpatients resulting in INR outside the The range and he concluded through pharmaceutical interventions providing more information to clinician and can improve the patient safety [30].

There was increase in the mean daily doses of warfarin in control group patients throughout the visits with total mean of (4.00±1.70) mg. While, the mean daily doses of warfarin in intervention group was decreased as follows (4.83±1.5) mg, (4.03±2.05) mg, (4.03±1.85) mg and (3.99 ±1.85) mg in visit 4 (90days) respectively with mean total daily dose of (4.22±1.80) mg (p>0.05), **Fig. 2**.

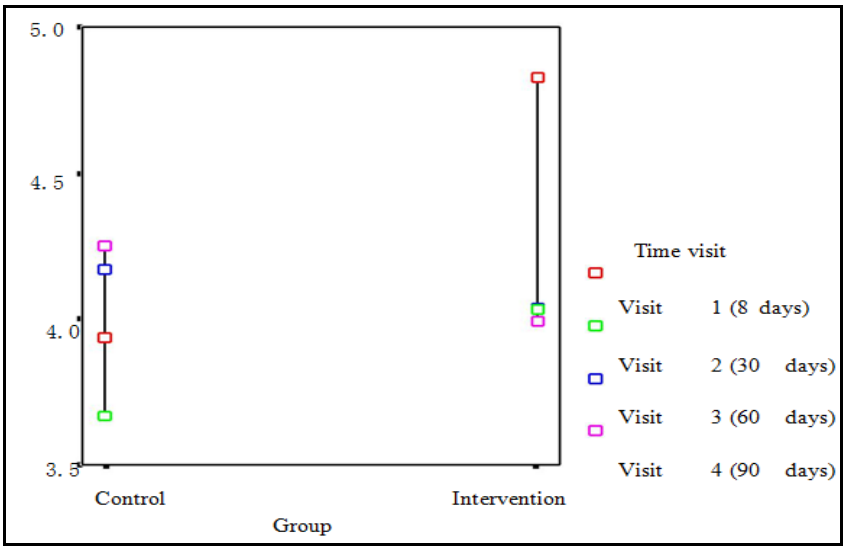

FIG. 2: MEAN DAILY DOSE OF WARFARIN THERAPY (MG) IN THE CONTROL AND INTERVENTION GROUPS ACCORDING TO EACH VISIT

There is wide inter-individual variation in the requirement of warfarin dosing to raise the INR to a therapeutic level. The mean dose is approximately 4.3 mg and the range is (0.5-15) mg/day [31]. Changing warfarin dose was scheduled in each visit to reach target level and avoid warfarin complications. Changing dose of warfarin in the intervention group was more frequent than that in control group (54.62% vs. 52.17%), but still the difference was not statistically significant (p>0.05). INR levels were recorded throughout the study visits after each change in warfarin dose in both study groups. The total mean of INR measured during all visits was higher among intervention group compared to control group (2.75 vs. 2.56); however, the result was not significant. The mean INR levels are illustrated in **Fig. 3** for both study groups.

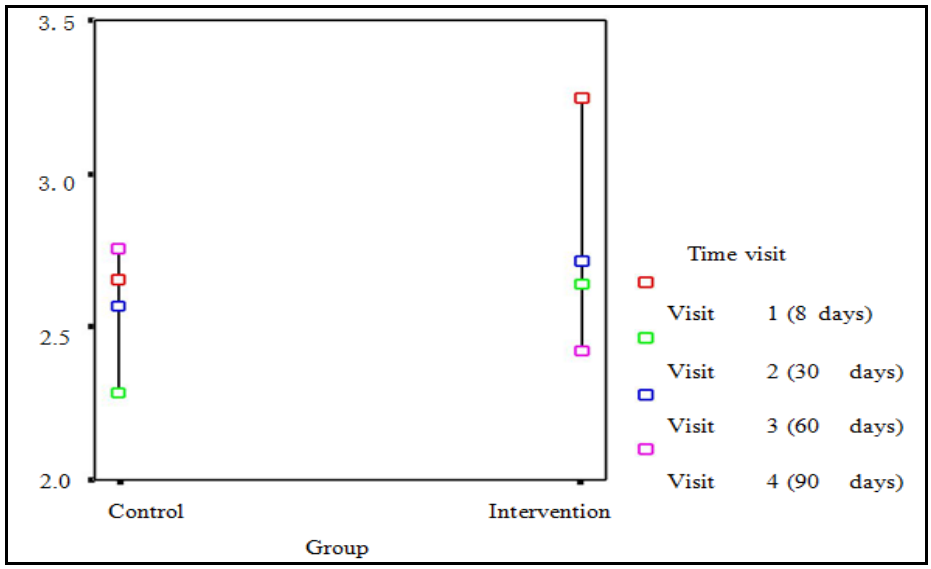

FIG. 3: MEAN INR LEVELS IN CONTROL AND INTERVENTION GROUPS ACCORDING TO EACH VISIT

Therapeutic range of INR levels which was classified into four categories (under therapeutic range, supra therapeutic range, equal or more than 4 INR level, patients reaching target therapeutic range). The overall number of patients in the control group with under therapeutic INR level was (35.87%). The % of patients with supra therapeutic INR was (10.87%) and % of patients of INR ≥ 4 was (9.78%). Whereas, the total percentage of patients within the target/therapeutic range was (43.48%).

On the other hand; in the intervention group, the overall number of patients with under therapeutic range was (23.15%). The % of patients with supra therapeutic range was (10.18%) then % of patients with INR ≥ 4 was (12.04%).Whereas, the total percentage of patients within the target/therapeutic range was (54.63%). These results highlighted the role of pharmacist interventions in monitoring the INR level within the target/ therapeutic range following warfarin dosing in a frequency of patients higher in the intervention group (54.63%) compared to control group (43.48%), although statistically no significant difference was noticed probably due to small sample size of the present study.

Despite of increasing in total daily dosing of warfarin, changing in the dose throughout the intervention visits, increase of total number of drugs used by patients and increase in total number of interacting drugs, showed target INR with higher levels throughout the intervention visits compared to control group, **Fig. 4.**

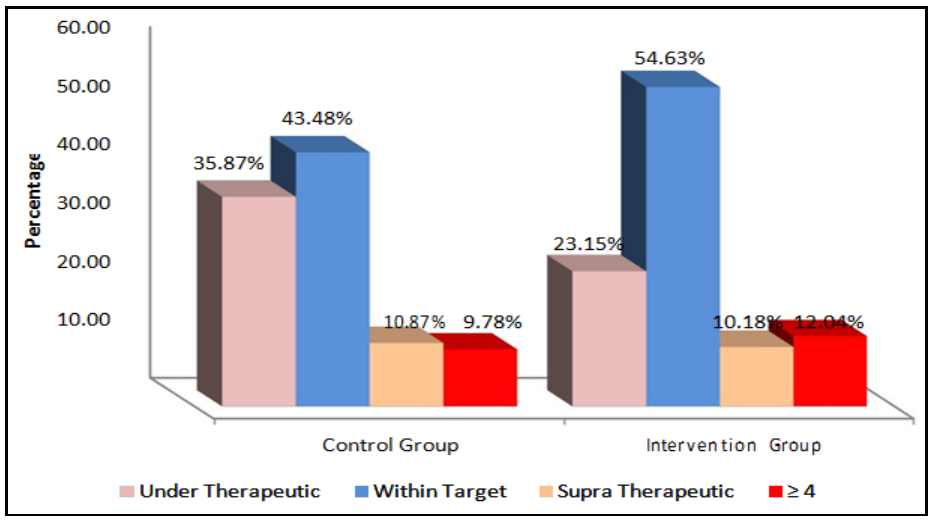

FIG. 4: INR EVALUATION IN THE CONTROL AND INTERVENTION GROUPS IN ALL VISITS

Previous study explore that the involvement of clinical pharmacist in the anticoagulation management improved the therapeutic outcome of patients by decreasing the percentage of sub- and supra-therapeutic from (28.4% and 18.4%) to (18.5% and 8.45%), respectively. Whereas, the percentage within therapeutic target range was elevated from (53.2% to 73.45%) 32. Moreover warfarin management program by clinical pharmacist supply effective and safe services for patients in which it produced significantly better anticoagulation control by reducing total bleeding and warfarin related emergency accidents. Besides, it effectively reduced over anticoagulant without increasing under anticoagulant and improved outpatient and inpatient warfarin therapeutic outcomes [33-39].

The patient adherence to warfarin was (87%) of patients throughout the study visits. Meanwhile all patients in intervention group showed (100%) adherence to warfarin therapy. The difference between the control and the intervention groups was statistically significant (p=0.002).

The implementation of warfarin management program led to better monitoring of patients receiving warfarin, and increased patient education. Educating patients are mostly suboptimal but may improve treatment outcomes. Patient education provides focus on drug-drug and drug food interactions as stated in previous study [40-43].

Clinical pharmacists can play an important role in managing anticoagulation therapy through continuous (inpatients and outpatients) education and counseling, enhancing drug use and adherence, minimizing drug related problems, improving quality of life and knowledge outcomes for patients, accordingly the percentage of sub-therapeutic warfarin level in patients counseled group was(9.16%) and supra-therapeutic was (8.33%), whereas the percentage of sub-therapeutic warfarin level in patients non-counseled group was (27.5%) and supra-therapeutic was (44.16%) [44].

From the present intervention and previous studies, it can be said that increasing patient education, improving dosing schedules, and developing greater communication are potential ways to maximize patient adherence.

CONCLUSION: In the present study many promising monitoring strategies emerged from the available results that can be supplied by clinical pharmacist via warfarin management program for inpatients and outpatients services. The intervention group demonstrated higher percentage of patients with INR levels within therapeutic/ target range, and significant improvement in time therapeutic range (TTR) from admission to 90 days post discharge. There was significant improvement in patients' laboratory parameters following the 90 days warfarin management. Accordingly, many promising strategies emerged from pharmacist warfarin- management program.

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