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INFLUENCE OF PHARMACEUTICAL CARE ON ANTI-COAGULATION KNOWLEDGE, MEDICATION ADHERENCE AND INTERNATIONAL NORMALIZED RATIO (INR) CONTROL IN PATIENTS OF A TERTIARY CARE HOSPITAL

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ABSTRACT

Anticoagulants are the cornerstone therapy for thrombosis prevention and treatment. While anticoagulants are commonly employed, their use is often associated with adverse drug events and increased readmission rates.A prospective observational study was carried out for 6 months with a sample size of 49 patients. 8-Item Morisky Medication Adherence Scale (MMAS-8) was used to assess medication adherence and Anti-coagulation knowledge Assessment (AKA) questionnaire was used to assess the knowledge of the patients. Total study patients were divided into two groups [Control group i.e. without pharmaceutical care (n = 22) and Pharmaceutical care group (n=27)]. International Normalized Ratio (INR) and activated Partial Thromboplastin Time (aPTT) were observed at baseline, first follow-up and second follow-up in the patients. The AKA scores of pharmaceutical care group and control group were analyzed by one way ANOVA followed by Dunnet t test. Results indicated AKA score has not significantly altered at base line, first follow-up and second follow-up. The AKA scores of pharmaceutical care group and control group were analyzed by one way ANOVA followed by Dunnet test. Results indicated that AKA score has significantly ($p<0.001$ increased in first follow-up and second follow-up in comparison to base line scores.The study showed that INR and aPTT value of the patients can be kept within the recommended range when physicians and pharmacist collaboratively manage patients' anti-coagulation therapy.Since, clinical pharmacist can effectively manage anticoagulation therapy and provide optimal care to the patients and there is a strong need for physician-pharmacist collaboration in health care setup which will empower patients to improve quality of care and to achieve better therapeutic outcome with improved safety in patients who receives anticoagulation therapy.

Key Words:-Anticoagulation, INR, aPTT, MMAS-8, AKA, Physician-Pharmacist.

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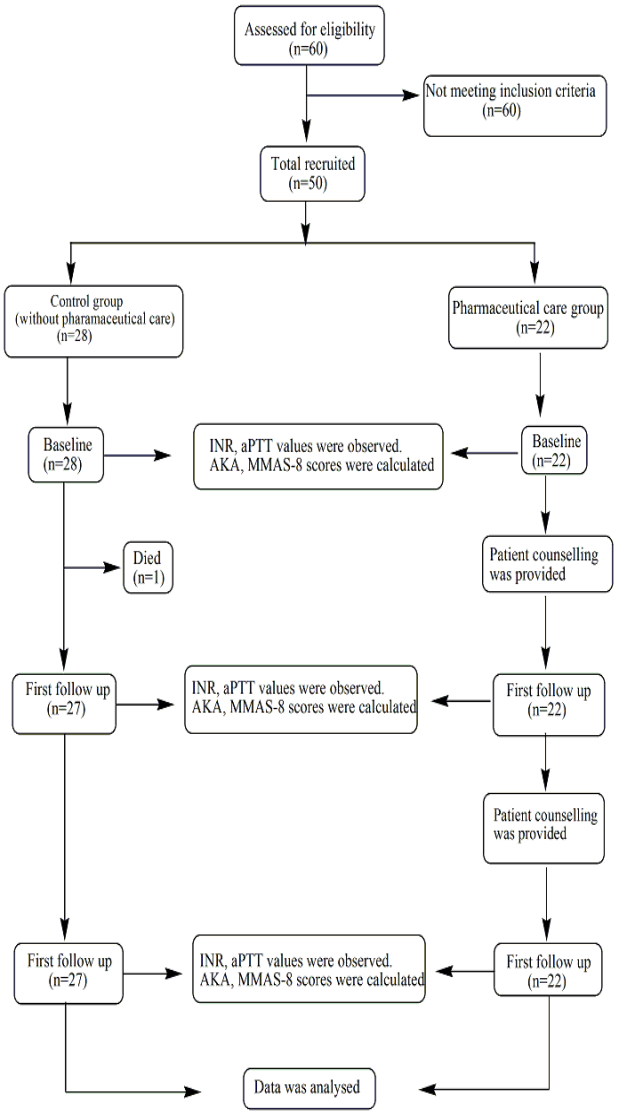
INTRODUCTION

Anticoagulants are the cornerstone therapy for thrombosis prevention and treatment. While anticoagulants are commonly employed, their use is often associated with adverse drug events and increased readmission rates. Despite novel anticoagulants being touted as replacements for warfarin and heparin products, rivaroxaban has been associated with serious thrombotic events while dabigatran has been associated with serious bleeding. Warfarin has been utilized as an anticoagulant drug for about 60 years but still causing a variety of adverse effects. Routinely, warfarin is monitored by measuring the International Normalized Ratio (INR). The target INR range for most indications of warfarin therapy is 2–3 or 2.5–3.5 (Keeling *et al.*,

2011; Holbrook *et al.*, 2012). Pharmacists provide essential information, education, and services, yet they could expand their practices to address substance abuse and other issues requiring input from community health workers. Pharmacists who provide patient counseling increase adherence to drug regimens. Some chronic diseases require lengthy treatment, and pharmacists are the health professionalsbest positioned to help improve outcomes.

The pharmacist develops an individualized patient-centered care plan, in collaboration with other health care professionals and the patient or caregiver that is evidence based and cost effective.

Figure 1: Schematic representation of Experimental designas per STROBE guidelines



Increased incidence of ADRs associated with anticoagulation therapy necessitates the involvement of Pharmacist in order to provide pharmaceutical care including patients counseling, careful monitoring of monitoring parameters and management of ADRs. Hence, thestudy was aimed to assess clinical outcomes by physician - pharmacist collaboration on anti-coagulation therapy management in tertiary care hospital which leads to safer and more effective initiation of anticoagulation therapy.

MATERIALS AND METHODS:

Ethical approval

The study protocol was approved by Institutional Ethics Committee of Dr. Pinnamaneni Siddhartha Institute of Medical Sciences & Research Foundation (Dr. PSIMS & RF) (CDSCO Reg. No: ECR/804/Inst/AP/2016). IEC protocol approval number is PG/235/2017.

Funding

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Study design and Participants:

This is aprospective observational study was carried out for a period of 6 months during October 2017 to March 2018 in patients admitted to Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation which is an 850-bedded tertiary-care teaching hospital at Chinaoutpalli, GannavaramMandal, Krishna district, Andhra Pradesh (India). Total 60 patients were assessed for eligibility. Out of 60 patients, 50 patients were recruited into the study. The experimental design was shown in a flow chart [Figure 1].

Inclusion criteria:

- Patients with age >18 years old
- Patients who are willing to participate
- Patients who were admitted as in-patients in the study duration (6 months)
- Patients who are currently on anticoagulation therapy.

Exclusion criteria:

- Patients whose admission duration is less than 24 hrs
- Pregnant women
- Psychiatric patients
- Patients who are on ventilator and who couldn't respond to study.

Study Procedure:

A total of 49 patients (*n* =49) who met the inclusion criteria were recruited in the study. A suitable data collection form was designed as per the NICE guidelines for use in the study. All the necessary data including the patient demographic details, disease history, past medication, allergic status, diagnosis, treatment chart, case notes and data on laboratory investigations were collected from patient interview, patient case reports ,Treatment chart, NICE guidelines, MMS-8 scale anticoagulation knowledge assessment scale and documented in a suitably designed data collection form for the study. All the recorded data was reviewed independently. The collected data were analysed and was compared with that of the data from the case sheets collected by the physician's interpretation for anticoagulation therapy. Data analysis was carried out using standard databases like Micromedex, knowledge assessment scale, adherence scale etc.

Statistical analysis:

The categorical variables were expressed as percentages whereas continuous variables were presented as mean ± standard deviation (mean ± SD).For all analyses, *p<0.05, **p<0.01 and ***p<0.001 were regarded as statistically significant. Data was analysed using statistical tools like Graph pad prism version 5.0.

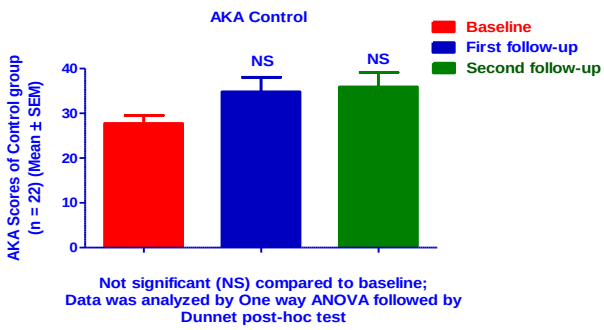
RESULTS:

AKA scores of pharmaceutical care group and control group

The AKA scores of pharmaceutical care group and control group were analyzed by one way ANOVA followed by Dunnet t test. Results indicated AKA score has not significantly altered at base line, first follow-up and second follow-up.

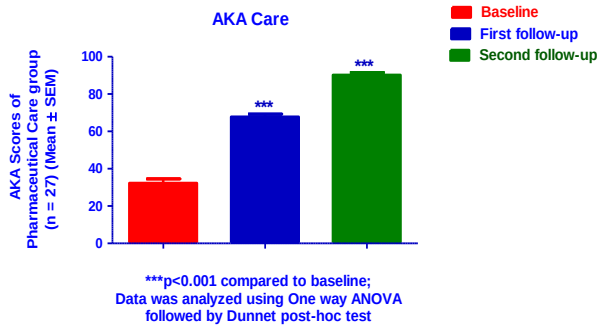
In control group, the AKA score was 27.76 ± 1.780 at baseline, 34.81 ± 3.249 at first follow-up, 35.93 ± 3.184 at second follow-up and MMAS-8 score was 3.636 ± 0.5487 at baseline, 3.273 ± 0.4798 at first follow-up in control group patients.

Fig.2: frequency distribution of AKA scores of control group of study population



In pharmaceutical care group, The AKA score was 32.33 ± 2.249 at baseline, 67.78 ± 1.523 at first follow-up, 90.21 ± 1.337 at second follow-up and MMAS-8 score was 2.00 ± 0.4169 at baseline, 0.6296 ± 0.1427 at first follow-up in pharmaceutical care group patients.

Fig.3. frequency distribution of AKA scores of pharmaceutical care group of study population



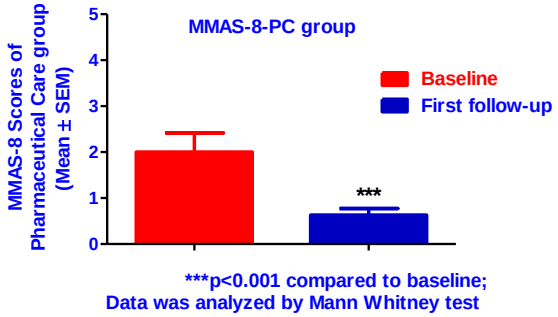
The pharmaceutical care given by the student pharmacist remarkably improved the knowledge of patient's with respect to anticoagulant therapy.

MMAS-8 Scores of pharmaceutical care group and control group

In pharmaceutical care group, MMAS-8 scores of baseline, first follow-up were 2.00 ± 0.4169 and 0.6296 ± 0.1427 respectively.

MMAS-8 Scores of pharmaceutical care group were analyzed by Mann Whitney test. Results indicated that MMAS-8 Score has significantly (p<0.001) decreased in first follow-up in comparison to base line scores. This further implied that medication adherence substantially improved as it is clearly evident from the decreased MMAS-8 Scores. (Decreased scores indicates increased medication adherence as per MMAS-8 scale).

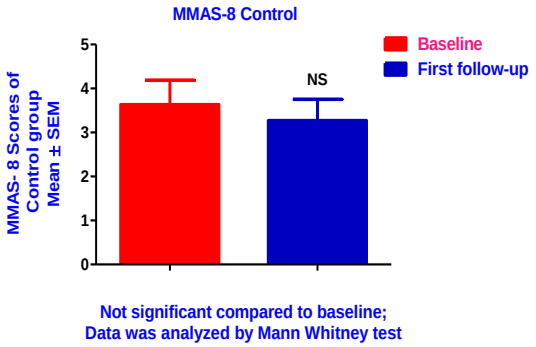
Fig.4. frequency distribution of MMAS-8 scores of pharmaceutical care group of study population



In control group patients, MMAS-8 scores of baseline and first follow-up were 3.636 ± 0.5487 and 3.273 ± 0.4798 respectively. MMAS-8 Scores of control group were analyzed by Mann Whitney test. Results indicated

that MMAS-8 Score has not significantly decreased in first follow-up in comparison to base line scores. This further implied that medication adherence not altered.

Fig.5. frequency distribution of MMAS-8 scores of control group of study population.

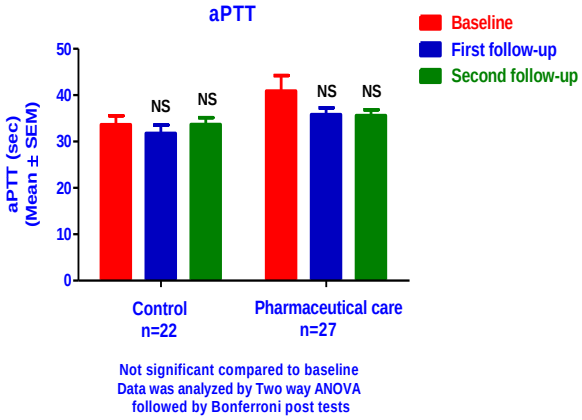


aPTT (Pharmaceutical care group Vs control group)

In pharmaceutical care group (27 patients), aPTT values at base line, first follow-up and second follow-up were 40.88 ± 3.358 seconds, 35.80 ± 1.470 seconds and 35.60 ± 1.239 seconds respectively. In control group (22 patients), aPTT values at base line, first follow-up and second follow-up were of 33.63 ± 1.947 seconds, , 31.75 ± 1.815 seconds and 33.67 ± 1.485 seconds respectively.

The aPTT values of pharmaceutical care group and control group were analyzed by two way ANOVA followed by Bonferroni post tests and results of first follow up and second follow up were not significant in either group when compared to baseline.

Fig.6.frequency distribution of aPTT of study population.



We observed a significant improvement in population (n=27) within range in first follow-up and second follow-up when compared to the baseline values of aPTT.

Fig.7.frequency distribution of aPTT within range in the study population.

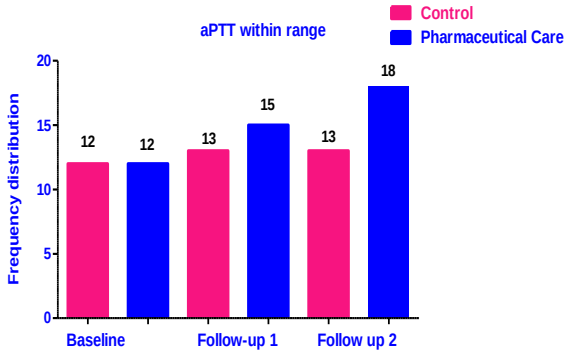
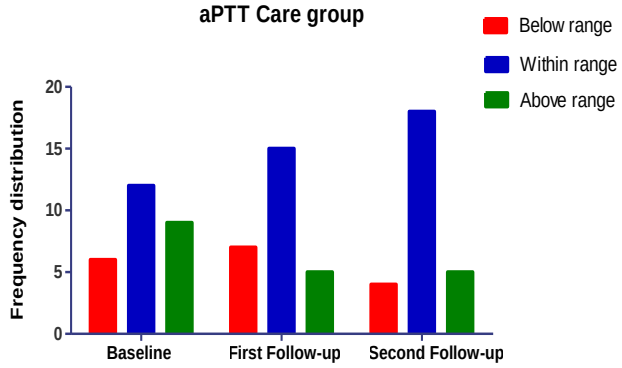
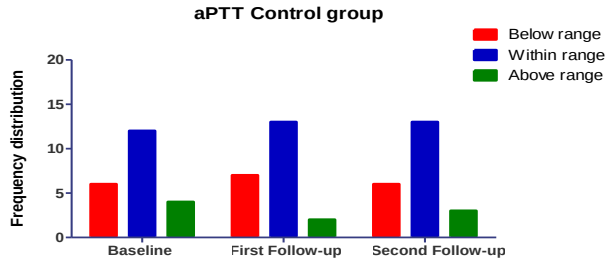


Fig.8. frequency distribution of aPTT care group in the study population.



When comparison with care group population, there is no significant increase in control group population (n =22) within range which may be due to lack of poor medication adherence and adequate knowledge on anticoagulation medication.

Fig.9. frequency distribution of aPTT control group in the study population



INR (Pharmaceutical care group Vs control group)

INR values of pharmaceutical care group (27 patients) at base line, first follow-up and second follow-up were 1.528 ± 0.1582, 2.131 ± 0.1473 and 2.523 ± 0.1040 respectively. INR values of control group (22 patients) at base line, first follow-up and second follow-up were 1.345 ± 0.09763, 1.817 ± 0.1722 and 2.185 ± 0.1239 respectively.

The INR values of pharmaceutical care group and control group were analyzed by two way ANOVA followed by Bonferroni post tests and results of first follow up ($p<0.05$) and second follow up ($p<0.001$) were significantly increased in control group when compared to baseline. Similarly, in care group, results of first follow up ($p<0.01$) and second follow up ($p<0.001$) were significantly increased in control group when compared to baseline.

Fig.10. frequency distribution of INR in the study population

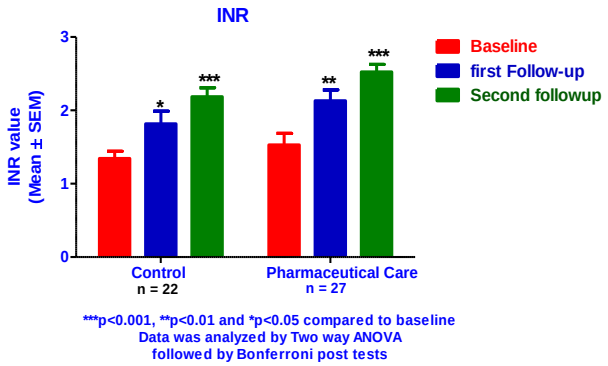
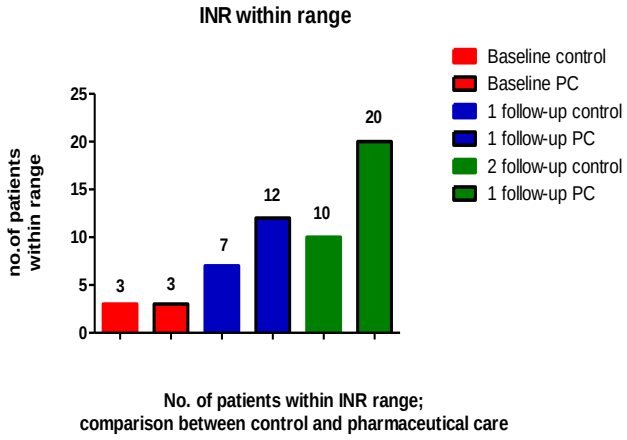
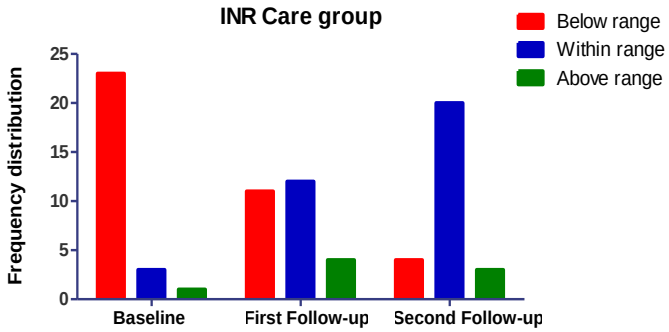


Fig.11. frequency distribution of INR within range in the study population



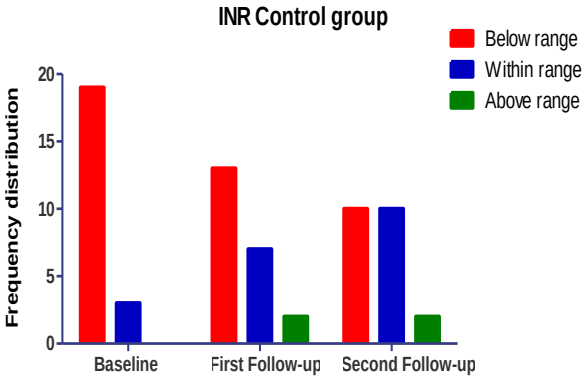
Among the pharmaceutical care group (n=27), we observed a significant anti-coagulation control, this may be due to the physician –pharmacist collaboration which lead to the improvement in the anti-coagulation knowledge and medication adherence.

Fig.12. frequency distribution of INR (care group) in the study population



We observed that there is no significant INR control in the control group (n=22) which may due to poor knowledge and medication adherence towards anti-coagulation therapy.

Fig.13. frequency distribution of INR (control group) in the study population



DISCUSSION:

Anticoagulation management is a challenging task for healthcare professionals especially for clinical pharmacists. It is because of the individual variability in response to the anticoagulants, alterations in a patient's consumption of vitamin K-rich foods and alcohol, change in medications, or change in health status all of which can alter the INR values. Proper educational guidance and monitoring of the INR status regularly and proper dose titrations is the only step for the successful anticoagulation. Several other studies (Chiquette *et al.*, 1998; Bounde *et al.*, 2009; Witt *et al.*, 2005; Dager *et al* 2007; Wilt *et al.*, 1995) have showed the effectiveness of clinical pharmacists in outpatient and in-patient anticoagulation management.

Demographics:

Our study population includes 40.81% were illiterate, 44.89% passed primary level, 10.20% passed secondary level and 4.08% were graduated and above. This is probably due to rural back ground (73.46%) of study population. It is quite common that illiterates and drop outs are more in rural area. Since our study population belongs to rural area, farmers accounted for 28.57% and house wives accounted for 32.65%. Large number of study population (46.93% had barely sufficient income, 14.28% had no sufficient income) have poor economic back ground. Previous studies report that economic status of patients could influence anti-coagulation therapy management. Majority of study population is using anticoagulation therapyfor atrial fibrillation, deep vein thrombosis (DVT), myocardial infarction and valvular heart diseases. Anticoagulation therapy is major therapy that is considered for all the above conditions. There is growing evidence that pharmacist could play an important role in anticoagulation management.Most of study patients take fruits either occasionally, monthly once or no habit of taking fruits. Hence, it is very unlikely that fruit intake could influence Warfarin therapy.

Anticoagulation Knowledge Assessment (AKA):

Anticoagulation is a well-established and crucial intervention for the prevention and treatment of thromboembolic events. It is important for patients to have an understanding of their risk of future vascular events to improve adherence to therapeutic and lifestyle modifications.

AKA score was assessed by a validated questionnaire. Counseling regarding oral anticoagulants was given to patient and / their caregivers and were also provided with patientinformation booklets. The doubts were cleared throughout their stay in the hospital. Contact number of the anticoagulation service was given to patients and caregivers on discharge to report INR results, get their dose titrated and for clarification of any doubts regarding anticoagulation. During the follow up of our study, the knowledge on anticoagulation was reassessed and the average score of patient knowledge assessment scores were remarkably improved after counseling. It is evident that the clinical pharmacist's intervention improved the patient's knowledge on oral anticoagulation. A good communication and contact was maintained with the patients by the clinical pharmacist who helped the patients to clarify their doubts and discuss the matters regarding anticoagulation therapy and it was difficult for them to reach the physicians directly. Better levels of the knowledge of the patients may also be achieved if the information is reinforced by simple measures such as repetition of knowledge assessing questionnaires to make patients/ caregivers answer it or use of written materials like leaflets/booklets. The availability of anon-physician counselor such as a clinical pharmacist has shown to increase the patient's knowledge about their health and disease condition, treatment undertaken/required, medications, importance of adhering to therapy etc (Yahaya *et al*., 2009).

In our study, most patients (62.9%) were ignorant about the target PT/INR value. Similarly, in a study from Brazil (Rocha *et al*., 2010). 50% of the patients did not know their target INR. Half of the patients in our study were having poor knowledge score, whereas about one-third (36.7%) of them had average knowledge, and 13.3% patients had good knowledge scores regarding OAT. A lack of knowledge regarding OAT was found even in patients attending an anticoagulation clinic in Malaysia (Yahaya *et al*., 2009), where 46% of the patients had poor level of knowledge, 33% had moderate, and 20% had good knowledge in contrast with a study from New York (Davis *et al*., 2005) where 37% of the patients demonstrated good knowledge of anticoagulation. The lower level of knowledge of patients in our study can be attributed to the lack of a formal education regarding medication management. Our study further revealed that knowledge gap was most prominent in the domains of dietary interactions followed by drug interactions, adverse effects, and PT/INR monitoring. This finding is in agreement with other studies from Germany (Jank *et al*., 2008) and Jordan (Yassien *et al*., 2012) where the incorrectly answered topics most often included drug and food interactions. Most patients (67.9%) in the present study knew that the purpose of anticoagulant drugs is to prevent clotting of blood. However, only a limited number of the patients knew that PT/INR test measures how long it takes the blood to clot and that if PT/INR value is more than normal, there is increased risk for bleeding. A previously reported study (Yassien *et al*., 2012) also found that less than 30% of the patients knew what INR test is used for and 44% of the patients reported that if PT/INR value is more than normal, the risk of bleeding is increased. As observed in the present study, higher education is associated with better knowledge (Rocha *et al*., 2010; Yahaya *et al*., 2009).

CONCLUSION:

Especially INR regular monitoring is required during the initiation or discontinuation of the medications. Clinical pharmacist collaboration with physician is important to: recognize, analyse and manage potential anti-coagulant drug interactions during hospitalizations; prescribe other medications or change doses of anti-coagulants based on changes of INR and aPTT.

The study showed that INR and aPTT value of the patients can be kept within the recommended range when physicians and pharmacist collaboratively manage patients' anti-coagulation therapy. Since, clinical

pharmacist can effectively manage anticoagulation therapy and provide optimal care to the patients and there is a strong need for physician- pharmacist collaboration in health care setup which will empower patients to improve quality of care and to achieve better therapeutic outcome with improved safety in patients who receives anticoagulation therapy.

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