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Evaluate the adequacy of Warfarin Treatment among Patients who were on long term Anticoagulation Therapy in Ahmed Gasim Cardiac Center, Khartoum- Suda

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Abstract:

Warfarin therapy for the prevention and treatment of thromboembolic diseases is safe and effective when it is maintained with a narrow therapeutic window measured by the international normalization ratio (I.N.R).Failure to provide adequate anticoagulation consistently predict thromboembolic events(eg stroke and pulmonary embolism), while excessively anticoagulated patients were at risk of bleeding. The management of therapy within this narrow window is complicated by numerous factors including drug interaction, comorbid acute, and chronic diseases, diet, and a variety of patient responses to warfarin therapy. The study was conducted in Ahmed Gasim cardiac center outpatient anticoagulation clinic. The study was carried out in the period from January to December 2012. Patients admitted or attending Ahmed Gasim cardiac center for follow-up of their long-term anticoagulation therapy. From all these results during the follow-up period. We found the percentage of those who were adequately controlled at the normal therapeutic I.N.R range was (54.7%) versus (45.3%) for uncontrolled patients. Of those who were controlled, we found(133) patients (60.7%) of them were fully educated about the interaction between diet and medications, while (31) patients (38.3%) were not receiving education about such interaction. On the other hand, those who were not controlled according to their therapeutic I.N.R (50) patients (61.7%) were not having educated and (86) patients (39.7%) were educated and have knowledge about dietary and drug interaction. P-value (0.01).The study of the adequacy of anticoagulation shows suboptimal control in (45.3%) of patients on patients attending INR clinics, however, the adequacy varies with age group with elderly patients poorly anticoagulated. Finally, the overall research conclude that the adequacy of anticoagulation was suboptimal with (54.6%) adequately controlled versus (45.3%) uncontrolled. In conclusion, the INR range of anticoagulation at the referral clinic mostly falls in the "under anticoagulated range". Areas to be considered are patient attendance, staffing and at the same time increasing the efficiency of services. Improvement should be directed not only toward attaining better patient attendance at the clinic but also to educate patients on the importance of adequate control.

Keywords: warfarin; adequacy; anticoagulation; therapy; khartoum, Sudan.

Introduction:

Warfarin therapy for the prevention and treatment of thromboembolic di seases is safe and effective when it is maintained with a narrow therapeu tic window measured by the international normalization ratio (I.N.R).Fai lure to provide adequate anticoagulation consistently predict thromboem bolic events(eg stroke and pulmonary embolism), while excessively anti coagulated patients were at risk of bleeding. The management of therapy within this narrow window is complicated by numerous factors including drug interaction, comorbid acute, and chronic diseases, diet, and variety of patient responses to warfarin therapy [1]. The integrity of the circulati on is maintained by blood flowing through intact vessels lined by endoth elial cells. Injury to the vessel wall exposes collagen and together with ti ssue injury sets in motion a series of events leading to homeostasis [2]. H emostasis is a complex process depending on interactions between the ve

ssel wall, platelets, and coagulation, and fibrinolytic mechanisms[2].

Platelet adhesion:- When the vessel wall is damaged, the escaping platelets come into contact with and adhere to collagen and the von Will brand factor that is bound below the endothelium. This is mediated through gly coprotein Ib (GPIb) Glycoprotein IIb–IIIa is then exposed, forming a sec ond binding site for VWF. Within seconds of adhesion to the vessel wall platelets begin to change shape, from a disc to a sphere, spread along the subendothelium, and release the contents of their cytoplasmic granules, i .e. the dense bodies (containing ADP and serotonin) and -granules contai ning platelet-derived growth factor, thrombomodulin, fibrinogen, VWF, f ibronectin, thrombospondin, and other factors) [2]. Platelet release:- The release of ADP leads to a conformational change in the fibrinogen recept or, the glycoprotein IIb–IIIa complex (GPIIb–IIIa), on the surfaces of ad herent platelets allowing it to bind to fibrinogen. Platelet aggregation:- A s fibrinogen is a dimer it can form a direct bridge between platelets and s o binds platelets into activated aggregates (platelet aggregation) and furt her platelet release of ADP occurs. A self-perpetuating cycle of events is set up leading to the formation of a platelet plug at the site of the injury. Coagulation:- After platelet aggregation and release of ADP, the exposed platelet membrane phospholipids are available for the assembly of coagu lation factor enzyme complexes (tenase and prothrombinase); this platele t phospholipid activity has been called platelet factor 3[2,3].

There is both parenteral and oral anticoagulant currently the parenteral a nticoagulant include heparin and low molecular weight heparin and the o ral anticoagulant vitamin K antagonist warfarin. For long-term chronic m anagement, oral anticoagulation is preferred over the intravenous or subc utaneous routes due to patient convenience and cost. Warfarin has been i n clinical use for over six decades and it is still one of the most widely us ed oral anticoagulant agents. Warfarin and other vitamin K antagonists (VKAs, eg, acenocoumarol, phenprocoumon, fluindione) are the standard oral anticoagulants used in a variety of clinical settings[4].

Commercially-available warfarin is a racemic mixture of S and R enanti omers. The more potent S form of the drug is metabolized primarily by t he CYP2C9 hepatic microsomal enzyme system. This enzyme system is inducible by many drugs and has several genetic variants, both of which may profoundly alter warfarin in vivo activity. Warfarin is strongly prote in-bound, primarily to albumin; only the non-protein-bound fraction is bi ologically active. Accordingly, any agent that is also bound to albumin m ay displace warfarin from its albumin binding sites and increase its biolo gical activity. Warfarin is water-soluble and completely absorbed after o ral administration. The majority of the drug is absorbed in the proximal s mall bowel, although successful use of the sublingual route has been des cribed in two patients. Excretion is via the urine, primarily as drug metab olites. The long half-life of 20 - 60 hours. The mean half-life is approxim ately 40 hours. The duration of effect is 2 - 5 days. The maximum effect of a dose occurs up to 48 hours after administration and the effect lasts f or the next 5 days. Steady State requires 5-7 days [4].

The anticoagulant effect of warfarin is mediated through inhibition of the vitamin K-dependent gamma-carboxylation of coagulation factors II, VII , IX, and X [4]. This effect of warfarin results in the synthesis of immuno logically detectable but biologically inactive forms of these coagulation p roteins. Warfarin also inhibits the vitamin K-dependent gamma-carboxyl ation of proteins C and S, which have anticoagulant properties through th eir inhibition of activated factors VIII and V [4]. Because of these compe ting effects, vitamin K antagonists such as warfarin create a biochemical paradox by producing an anticoagulant effect due to the inhibition of pro coagulants (factors II, VII, IX, and X) and a potentially thrombogenic eff ect by impairing the synthesis of naturally occurring inhibitors of coagul ation (proteins C and S). The ultimate anticoagulant effect of warfarin is delayed until the normal clotting factors, especially prothrombin, are cle ared from the circulation. The peak effect does not occur until 36 to 72 h ours after drug administration, especially because the plasma half-life of

factor II (prothrombin) is approximately 3 days During the first few days of warfarin therapy, prolongation of the prothrombin time mainly reflect s its action on the extrinsic coagulation pathway, through the depression of factor VII, which has a half-life of four to six hours. The other vitamin K-dependent factors within the common and intrinsic coagulation pathw ays (i.e., factors II, IX, and X) remain relatively unchanged during the fir st few days. Accordingly, the patient is not fully anticoagulated with war farin until these other components are also reduced[5].

Equilibrium levels of factors II (prothrombin), IX, and X, approximately 10 to 35 percent of normal at therapeutic INR levels (11), are reached ab out one week after the initiation of therapy. For this reason, parenteral an ticoagulants and warfarin should OVERLAP by four to five days when w arfarin is initiated in patients with the acute thrombotic disease (eg, veno us thromboembolism, heparin-induced thrombocytopenia) [5].

Many medicines can interact with anticoagulants. Some medicines can in crease the effect of anticoagulants, thus increasing the chances of bleedin g. Some medications can decrease the effect of anticoagulants, thus incre asing the chances of blood clots[6].

Polymorphisms in the genes for the following two enzymes have been as sociated with altered sensitivity to warfarin [7].

Hepatic cytochrome P-450 2C9 (CYP2C9), is involved in the metabolic clearance of warfarin. Vitamin K epoxide reeducates complex 1 (VKOR C1), which recycles vitamin K and is required for gamma-carboxylation of vitamin K-dependent coagulation factors. Cytochrome P-450 2C9 -A well-studied cause for individuality in patient responses to warfarin is th e presence of genetic variation (polymorphisms) in the hepatic cytochro me P-450 2C9 (CYP2C9) isoenzyme, which inactivates both warfarin an d acenocoumarol[8,9].

Materials and methods:

Study design:

Retrospective and prospective observational hospital-based study.

Study area and time:

The study was conducted in Ahmed Gasim cardiac center outpatient anti coagulation clinic. The study was carried out in the period from January t o December 2012.

Study population:

Patients admitted or attending Ahmed Gasim cardiac center for follow-u p of their long-term anticoagulation therapy. Ahmed Gasim center is the cardiac center which is a treachery hospital in North Khartoum for surgic al and medical treatment of cardiac problems.

Study sample:

A sample size of 300 patients was studied.

Inclusion criteria:

Patients who were on long-term anticoagulant therapy for more than thre e months.

Exclusion criteria:

Interrupted or stopped for any reason oral anticoagulant medication. Pati ents who were treated with medication other than oral anticoagulant ther apy e.g., antiplatelet tablet, or those on heparin treatment alone. Period o f anticoagulation less than 3 months duration.

Data collection:

Personal and demographic data from all patients are collected using a dir ect questionnaire (attached)including the indication for anticoagulation, t

he frequency of follow up

Main outcome measure:

The percentage of international normalized ratio (I.N.R) tested below, within, and above the therapeutic range were determined. The patient was classified as adequately anticoagulated if the measured INR was within the therapeutic range for the indicative cause of anticoagulation. On the other hand, the patients were regarded as over anticoagulated or under-coagulated if the measured result of INR lagged by (0.5) above and below the therapeutic range respectively. In addition, the quality of education given to the patient at the start of using anticoagulant therapy was assessed, together with the frequency of bleeding and other complication encountered.

Data processing:

Collected data from the forms entered into a computer at the end of the study and analyzed using the software program SPSS v16. The means, standard deviations, and frequencies were defined. The correlation between the patient's anticoagulation measures to the targeting I.N.R is tested using a chi-square test. The difference between means is tested using an independent t-test. *P-value* >0.05 is said to be significant.

Ethical consideration &clearance:

Verbal consent was taken from all patients after explanation of the study, Ethical clearance from the authorities is taken before the start of the study.

Results:

During the study period (300) patients were enrolled, among them (193) were females (64.33 %) and (107) were males (35.67%). The majority of patients (131) (43.7%) were between the age of (21-40) years followed by (110) patients (37.6%) aged between (41-60) years. There were (29) patients (9.7%) between (61-80) years, (27) patients (9%) at age less than 20 years and (3) patients (1%) < 80 years. Regarding the residence, (45.3%) of patients were from Khartoum state while (54.7%) of patients came from other states. The majority of patients(233) (77.7%) were not working, while 38 patients (12.7%)were manual laborer and (14) patients (4.7%) were officers. There were (15) patients(5%) were students. The indication for anticoagulation in the presence of mechanical valve prosthesis in (174) patients (58%) ,AF in (64) patients (21.3%),cardiomyopathy in (37) patients (12.3%), D.V.T in (7) patients (2.3%), ischemic stroke with AF in (7) patients (2.3%), P.E in (7) patients (2.3%), intracardiac mural thrombi in (5) patients (1.7%),cerebral venous thrombosis in (3) patients (1%) and one patient (0.3%) with antiphospholipid syndrome. During the follow-up period, we found the majority of patients(211) (70.3%) on regular fallow up monthly however there were (67)patients (22.3%) attending fallow up every two months also there were(8) patients (2.7%) attended every 3 months, however, there were (14) patients (4.7%) advised by doctors to be fallowed within two weeks. On direct questioning of the patients, we found the majority of patients attending the clinic (219) patients (73%) were educated about interaction medication and diet compared to (81patients) (27%) who were not educated about such interaction. But the level of education for food interaction was limited in the majority of patients (132) (44%) to green vegetables alone while (82) patients(27.3%) have a good idea about all interactions with food with the aid of a dietitian follow up. However, a significant number of patients (83) patients (27.7%)do not follow dietary advice. Regarding education about the interacting medication, we found (that 172) patients(57.3%) had an idea about interacting medication, while (128) patients(42.7%) did not know about such interaction. Those who were educated well knew the interaction and hazard of over counter use without a prescription of antibiotic with warfarin (53%), aspirin (56.7%), N.S.A.D (37%), and (8.3%) knew other drug interactions with warfarin.

Minor bleeding was the most frequent complication in (44)patients (14.7%), while severe major bleeding (20) patients (6.7%). On the other hand, one patient(0.3%) developed embolic stroke (C.V.A) during the follow-up period. (39) patients (60%) of those patients who develop complications were admitted and managed at the hospital, while(26) patients (40%) were managed at an outpatient clinic. Regarding management of the complications(41) patients (62.9%) needed just an observation and fully recovered, while in (18) patients(27.4%) the bleeding was so severe requiring treatment with F.F.P and (3) patients (4.8%) receive a blood transfusion. In (3) patients (4.8%) management only with Vit K. All those patients who develop complications were fully recovered. A complication of anticoagulation occurs in (48) patients (73.9%) who were not educated about the interacting medication and diet versus (17) patients (26.3%) who were fully educated. We found that the majority of patients (14) patients (70%) who developed major bleeding during the follow-up period were not educated about such interaction (70%), while (6) patients (30%) were educated. *P-value* of (0.75). For patients who develop minor bleeding (33)patients(75%)were not educated (11)patients (25%) were educated *P-value* (0.74). We found only one patient who develop a thromboembolic event (stroke) who was anticoagulated for prosthetic valve and was not fully educated **(Table1).** According to age group, all elderly patients above 80 years (3) patients were uncontrolled. In patients between (61-8o) age group (20) patients (69%) were uncontrolled versus (9) patients (31%) who were controlled. On the other hand, for patients aged (41-60), most of the patients (69) patients (62.7%) were adequately controlled versus (41) patients (37.3%) uncontrolled. In patients in (the 21-40) age group which pick the majority of patients studied we found (72) patients (55%) controlled versus (59) patients (45%) uncontrolled. In patients in (1-20)age group we found (14) patients (51.9%) controlled versus (13) patients (48.1%) uncontrolled .*P value* (0.001) **(Table2).** In this study, 300 patients were followed for three consecutive follow-ups, during each follow up their results of I.N.R were recorded. During the first visit, we found (151) patients (50.3%)within the normal therapeutic I.N.R, while(92) patients (30.7%) were having lower than normal therapeutic I.N.R. and (57) patients (19%) having higher than therapeutic I.N.R. In the second visit there were (169) patients(56.3%) have resulted within normal therapeutic I.N.R, while (81) patients(27%) were having lower than normal therapeutic I.N.R and (50) patients (16.7%) having higher than normal therapeutic I.N.R . In the third visit there were (176) patients(58.7%) have resulted within the normal I.N.R, while (77) patients(25.7%) were having lower than normal therapeutic I.N.R and (47) patients(15.7%) having higher than normal therapeutic I.N.R (15.7%). Regarding the clinical indication of anticoagulation we found that in patients with mechanical valve replacement, the percentage of controlled I.N.R is higher (65.5%) versus those uncontrolled (34.5%). On the other hand, the percentage of uncontrolled patients was high among those anticoagulated because of cardiomyopathy (62.8%) while only (28.3%) were adequately controlled .also in patients with pulmonary embolism (71.4%) were uncontrolled versus (28.6%) of controlled one. In patients with D.V.T, there were (57.1%) uncontrolled versus (42.9%) controlled. The uncontrolled patients predominate over-controlled ones in patients with atrial fibrillation (56.2%) versus (28.3%). From all these results during the follow-up period. We found the percentage of those who were adequately controlled at the normal therapeutic I.N.R range was (54.7%) versus (45.3%) for uncontrolled patients. Of those who were controlled, we found(133) patients (60.7%) of them were fully educated about the interaction between diet and medications, while (31) patients (38.3%) were not receiving education about such interaction. On the other hand, those who were not controlled according to their therapeutic I.N.R (50) patients (61.7%) were not having educated and (86) patients (39.7%) were educated and have knowledge about dietary and drug interaction. *P-value* (0.01)**(Table3).** Regarding the effect of the adequacy of INR control on patients who develop complications during the period of follow up, we found that the percentage of complications of major bleeding was

increased in patients with inadequate INR control (55%) versus (45%) with adequately controlled I.N.R. *P-value* (0.36) (Table4). Also the percentage of minor bleeding was increased in patients with inadequate I.N.R (56.8%) versus (43.2%) with adequately controlled I.N.R *P-*

value (0.98). On the other hand, the only one patient who developed a thromboembolic event during the follow-up was found an inadequate INR control *P-value* (0.27).**(Table5).**

Education About Interacting Medications And Diet		Major Bleeding		Miner Bleeding		Thrombo Embolic Events		Total
		Yes	*No*	*Yes*	*No*	*Yes*	*No*	
No	Count	14	205	33	186	1	72.9%	219
	% within complication	70.0%	73.2%	75.0%	72.7%	100%	81	73.0%
Yes	Count	6	75	11	70	0	27.1%	81
	% within complication	30.0%	26.8%	25%	27.3%	.0%	299	27.0%
Total	Count	20	280	44	256	1	100%	300
	% within complication	100%	100%	100%	100%	100%	72.9%	100.%
	PV	**0.754**		**0.745**		**0.542**		

Table-1: *Effect of education about interacting diet and medication in relation to development of complication.*

Age Groups		Target Control			Total
		Controlled	*Not Controlled*		
1-20	*Count*	14	13		27
	% Within Age Groups	51.9%	48.1%		100.0%
	%Within Target Control	8.5%	9.6%		9.0%
21-40	*Count*	72	59		131
	% Within Age Groups	55.0%	45.0%		100.0%
	%Within Target Control	43.9%	43.4%		43.7%
41-60	*Count*	69	41		110
	% Within Age Groups	62.7%	37.3%		100.0%
	%Within Target Control	42.1%	30.1%		36.7%
61-80	*Count*	9	20		29
	% Within Age Groups	31.0%	69.0%		100.0%
	%Within Target Control	5.5%	14.7%		9.7%
> 81	*Count*	0	3		3
	% Within Age Groups	.0%	100.0%		100.0%
	%Within Target Control	.0%	2.2%		1.0%
Total	*Count*	164	136		300
	% Within Age Groups	54.7%	45.3%		100.0%
	% within Target Control	100.0%	100.0%		100.0%

Table-2: *Adequacy of INR control in relation to age group.*

Education About Interacting Medications And Diet			Target Control		Total
			Controlled	*Not Controlled*	
	YES	*Count*	133	86	219
		%Within education about interacting medications and diet	60.7%	39.3%	100%
		% Within Target Control	81.1%	63.2%	73%
	NO	*Count*	31	50	81
		%Within education about interacting medications and diet	38.3%	61.7%	100%
		% Within Target Control	18.9%	36.8%	27%
Total		*Count*	164	136	300
		% Within education about interacting medications and diet	54.7%	45.3%	100%
		% Within Target Control	100%	100%	100%
		PV= 0.001			

Table-3: *Adequacy of INR control in relation to the education about the interacting medication and diet.*

		Cases						PV
		controlled		*uncontrolled*		*Total*		
		N	*%*	*N*	*%*	*N*	*%*	

D.V.T.	3	42.9%	4	57.1%	7	2.3.0%	.525
Pulmonary embolism	2	28.6 %	5	71.4%	7	2.3%	.16
Atrial fibrillation	28	28.3%	31	.56.2%	59	21.30%	.048
Mural thromdus	1	20%	4	80%	5	1.70%	.116
Cardiomyopathy	14	37.8%	23	.62.8%	37	12.30%	.028
Mechanical heart valve replacement	114	65.5%	60	34.5%	174	58%	.000
Ischemic stroke with AF	2	28.6%	5	71.4%	7	.0%	.161
Cerebral venus simus thrombosis	2	66.7%	1	33.3%	3	.0%	.76
Antiphosoholipid syndrome	1	03%	0	0	1	0.3%	.36
Total	**167**	**54.7%**	**133**	**45,3%**	**300**	**100%**	

Table-4: *Relation of adequacy of INR control in relation to clinical indication of anticoagulation.*

Target Control			Miner Bleeding		Major Bleeding		Thrombo Embolic Events		Total
			Yes	*No*	*Yes*	*No*	*Yes*	*No*	
Controlled		*Count*	19	145	9	155	0	164	164
		% complication	43.2%	56.6%	45.0%	55.4%	.0%	54.8%	54.7%
Not Controlled		*Count*	25	111	11	125	1	135	136
		% complication	56.8%	43.4%	55.0%	44.6%	100%	45.2%	45.3%
Total		*Count*	44	256	20	280	1	299	300
		% complication	100%	100%	100%	100%	100%	100%	100%
PV			**.98**		**.36**		**.27**		

Table-5: *Relation of adequacy of INR control in relation to development of complication.*

Discussion:

During the follow-up in our study, it is found that the quality of anticoagulation control during initiation and maintenance of warfarin treatment is generally unsatisfactory. Compared to a study conducted in 2008 in Canada about the quality of anticoagulation in long term care, where (107) patients who were receiving warfarin (72%) of them were female with a mean age of(65—90 years) (89), Our study also shows female predominance (64.3%) but with younger mean age (mean range 20—40 years). The main indications of anticoagulation were stroke prophylaxis for atrial fibrillation (67%) followed by DVT (18%). While in our study anticoagulation for mechanical valve replacement predominate (58%) followed by anticoagulation for atrial fibrillation (21%). The difference in the predominant age group and the incidence of being mostly in the young age group with anticoagulation for the prosthetic valve is related to the high prevalence of rheumatic heart disease among the young age group in Sudan and hence increase in the rate of prosthetic valve intervention for destructed valves due to R.H.D. During the study period in that research, it is found that the overall result was suboptimal anticoagulation with an INR result (54%) in the therapeutic range while in (46%) was subtherapeutic. This result was similar in range to the suboptimal therapeutic INR result found in our study (54.7%) controlled versus (45.3%) uncontrolled INR. A similar range of results indicates that it is related to facilities other than the presence of well-equipped centers for follow up which is different from our overcrowded small center .it is related to the patient's compliance and education about medication of anticoagulation. In another study conducted in Alberta hospital in Canada about the adequacy of anticoagulation in patients with A.F, Of (375) patients taking warfarin coming to the hospital and having an INR documented in the clinic,(167) patients (44.5%) were subtherapeutic, (137) patients (36.5%) were therapeutically controlled, and (71) patients (18.9%) were supra therapeutic [10]. In our study of (300) patients taking warfarin, the INR results reveal (that 151) patients (50.3%) were therapeutically controlled, and (92) patients (30.7%) were sub-therapeutic and (57) patients (19%) were supra therapeutic. In a study conducted in Africa in Tanzania, about

the adequacy of anticoagulation among patients with MVR, it. is found that only (35.5%) of the measurements were within the recommended therapeutic (normal) range, (33.4%) above therapeutic, and (31.1%) below it [11]. Our study shows a much better percentage in patients with MVR (65.5%) controlled versus (34.5%) uncontrolled. table (3.4). In our study(65) patients from(300) patients develop complication,(44) patients(14.7%) develop minor bleeding ,while (20) patients(6.7%) develop major bleeding and in one patient(0.3%) thromboembolic event was encountered. In another study conducted in South Africa, It is found that in studying (309) patients there were(50) episodes of complications encountered following anticoagulation after MVR(16.2%), (38) bleeding events with (30) patients(9.7%) develop minor bleeding, and,(8) patients (2.6%) develop a major bleeding complication. there were also (12) patients(3.1%) who get a thromboembolic complication[13]. In a meta-analysis study of (45) studies conducted in the U.S about hemorrhagic and thromboembolic complications in patients on long term anticoagulation control, it is found that(23) reported both hemorrhages and thromboembolic; (14) that reported hemorrhages only; and(8) thromboembolic only) involving a median of 208 patients. Of these studies, (64%) were conducted at community practices; the remainder were at anticoagulation clinics. About (69%) of the studies were classed as having moderate or high quality. Overall,(44%) of hemorrhages occurred when INRs were above the therapeutic range, and (48%) of thromboembolic took place when below it [14]. The involvement of patients in the management of anticoagulation therapy was studied in some trials. It was found that patient awareness of the INR values correlated with improved accuracy of anticoagulation control[15]. Our study confirms these data. The patients who had received satisfactory education on anticoagulation had the highest quality of anticoagulation and were less prone to complications. Our study has some limitations including a limited sample size, we conducted the study at a single center, thereby potentially limiting the ability to generalize our data, limiting our ability to explore additional factors that may have contributed to sub-optimal INR such as acute co-morbidities and variability in dietary vitamin K intake One of the most important findings of our study was the significance of the patient's knowledge about anticoagulation. Patient

education is generally performed by the medical staff and includes the purposes of anticoagulation, risk of complications, and information about INR values. The poor quality of such education was the most significant risk factor for complications and the ineffectiveness of anticoagulation. Moreover, insufficient education was more devastating than the total lack of education. Low-quality education resulted in the highest rate of bleeding complications and over coagulation. Poor education on anticoagulation was the most reliable risk factor for adverse outcomes in our study. *P-value* (0.001). Limitations of the study were that it was not an intervention trial and that the education process was not standardized.

Conclusion:

The study of the adequacy of anticoagulation shows suboptimal control i n (45.3%) of patients on patients attending INR clinics, however, the ade quacy varies with age group with elderly patients poorly anticoagulated. The main indication of anticoagulation is MVR which shows a higher pe rcentage of adequately controlled INR (65.5%) Fallowed by anticoagulat ion due to AF and cardiomyopathy which on the other hand shows a high er percentage of sub-therapeutic control of INR (65.2%) and (62.8%) res pectively. The adequacy of anticoagulation is directly proportionate to th e educational aspect about the interaction of medication and diet to warfa rin therapy with a higher percentage under control in patients who were n ot educated (61.7%).versus control rate (38.3%). The complication of w arfarin use in form of major and minor bleeding was encountered in a hig her percentage of patients with uncontrolled high INR (55%) and (56.8%) respectively .with one patient who develop thromboembolic who was u nder control. Finally, the overall research conclude that the adequacy of a nticoagulation was suboptimal with (54.6%) adequately controlled versu s (45.3%) uncontrolled. In conclusion, the INR range of anticoagulation at the referral clinic mostly falls in the "under anticoagulated range". Are as to be considered are patient attendance, staffing and at the same time i ncreasing the efficiency of services. Improvement should be directed not only toward attaining better patient attendance at the clinic but also to ed ucate patients on the importance of adequate control.

Recommendation:

1) Adequacy of anticoagulation in patients with long-term anticoagulant therapy lagged behind actual recommendations. Better control is required.
2) Education of the patient is an essential tool in achieving better control .doctors should advise their patients about dietary and medication interaction with anticoagulant therapy and the impact of such interaction on over and under coagulation state.
3) Improving the anticoagulation state of our patients will reduce the risk of hemorrhagic and thromboembolic complications.

Funding:

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