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Study on Utilization Evaluation of Anticoagulants Therapy in Cardiovascular and Cerebral Ischemic Disorders

[1]student, Niharika, [1]student, K Mohsina Banu, [1]student, Shivani J Prajapati, [1]student, K Nikhil Kumar Reddy, [2], Dr. Bassy K Alias,

Tvm college of pharmacy, ballari, karnataka
Tvm college of pharmacy, ballari, karnataka
Tvm college of pharmacy, ballari, karnataka
Tvm college of pharmacy, ballari, karnataka
Asst. Professor Tvm college of pharmacy, ballari, karnataka
Corresponding Author: Dr. Bassy K Alias

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ABSTRACT: Background: Drug use assessment (DUE) is a review to determine drug use variability and to promote measures that would increase clinical outcomes for patients. Drug use measures are used in a hospital or community facility to assess particular aspects of health care professionals and drug use. The medications used to avoid thrombus extension and embolic complications by decreasing the rate of fibrin formation are anticoagulants. They do not dissolve pre-formed colts, but prevent the development of thrombi in the veins, artery, or intra-cardium and cause local obstruction complications, distant embolism in distal microcirculations, and hemostatic material intake. The main objective is to compare the effectiveness and protection of systemic and direct oral anticoagulant used in patients with cardio and neurological disorders. **Method**: It is a prospective observational study conducted during six months period in which 130 sample size were included of age groups above 18 and below 60 of both genders. **Result**: Heparin was mostly used anticoagulant followed by Acenocoumarol, Warfarin, Enoxaparin and Dabigatran were other commonly used drugs. The duration of the therapy varied from disease to disease. Laboratory tests like prothrombin time (PT), International normalized ratio (INR), Activated partial thromboplastin time (aPTT) were performed to monitor the therapy. **Conclusion**: The pharmacotherapy with anticoagulant drugs should be cost effective and with minimum risks involved. The study highlights the importance of following the guidelines for appropriate use of anticoagulants.

Keywords: Anticoagulants, Drug utilization evaluation, aPTT, INR, PT, Drug interactions, and ADR.

I. INTRODUCTION:

[1] Drug use assessment (DUE) is a review to determine drug use variability and promote measures that enhance the treatment results of patients. Drug use measures are used in a hospital or community facility to assess particular aspects of health care professionals and drug use. It will provide health care administrators with knowledge about drug use and prescription habits.

[16] Anticoagulants have been a staple of the evolving care of patients with acute ischemic stroke for several years. In an attempt to prevent neurological worsening, many doctors prescribe anticoagulants, probably by halting the development of thrombosis, helping to preserve collateral flow and circulation, and preventing early recurrent stroke, especially among patients with cardio-embolism and large-artery atherosclerosis.

[23] To avoid stent thrombosis, double antiplatelet therapy with aspirin and clopidogrel is indicated in these cases. However, the combination of oral anticoagulants and antiplatelet medication is associated with a high annual risk of fatal and non-fatal bleeding events (4–16 percent). Therefore, the appropriate care following PCI is uncertain when both thrombotic and bleeding complications are taken into account..

[24] The medications used to avoid thrombus extension and embolic complications by decreasing the rate of fibrin formation are anticoagulants. They do not dissolve pre-formed

International Journal of Pharmaceutical Research and Applications
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colts, but avoid the formation of thrombi in the veins, artery, or intra-cardium, causing local obstruction complications, distant embolism in distal microcirculations, and hemostatic material intake. They do not dissolve already established colts directly, but they avoid recurrences and devastating medical complications by allowing them to.[2] Atherosclerosis is most often caused by peripheral arterial disease and is an indication that widespread atherosclerotic artery disease is present. There is a risk of myocardial infarction , stroke, or cardiovascular mortality in patients with peripheral arterial disease that is three times as high as in people without peripheral arterial disease. In patients with peripheral arterial disease, antiplatelet therapy decreases the occurrence of significant cardiovascular events.

[2] The pathway of coagulation plays a pivotal role in both arterial and venous thrombi development and progression. Drugs engineered to suppress this mechanism are therefore a significant strategy for the production of novel antithrombotic agents..

[2] Anticoagulants are primarily used in hospital settings for diseases like deep vein thrombosis (DVT), pulmonary embolism (PE), myocardial infraction (MI), unstable angina, rheumatic heart disease, cardiac surgery, prothetic heart valve, thrombosis of the retinal artery, extra corpuscular circulation, acute coronary syndrome, NSTEMI, AWMI,.

[7] There are only a few research of neurology patients that determine the status of anticoagulants. For their care, neurology patients are often dependent on their families and INR studies are carried out in developing countries in particular. The quality and stability of INR in neurological patients receiving OAC was analysed in the current study, as well as the effect of adjustment of corrective factors on these parameters.

[3] Anticoagulants (AC) are important life-saving medications used to avoid arterial, venous and intra-cardiac thromboembolic events as well as to treat them. Coronary artery disease (CAD) is the major cause of cardiovascular disease (CVDs), accounting for 35 percent of the disease burden, according to the global burden of disease analysis in India. Oral anticoagulant (OAC) pharmacotherapy is prescribed for long-term thrombo prophylaxis in patients at high risk of stroke complications due to atrial fibrillation(AF). Thromboembolic disorder therapeutic treatment is sometimes focused solely on a prescriber 's professional decision, irrespective of the availability of standardised guidelines. 6 Guidelines for the treatment of patients with artial fibrillation from the American College of Cardiology / American Heart Association / European Society of Cardiology (ACC / AHA / ESC) consider chronic oral anticoagulation therapy a Class I indication in all patients with heart failure and atrial fibrillation. If this treatment is contraindicated, aspirin is prescribed for use at a dosage of 325 mg daily.

[24] In patients with coronary artery disease, oral anticoagulant agents with or without antiplatelet therapy minimize the incidence of significant cardiovascular events. In patients who have had a myocardial infarction with ST elevation, oral anticoagulation in combination with aspirin is seen by the American College of Cardiology and the American Heart Association as an effective alternative to aspirin alone.

[4] There are, however, two major problems associated with its use: one related to under-anticoagulants with attended clinical thromboembolism and the other over-anticoagulation with specific bleeding complications. 2 The main objective of OAC therapy is to establish an international normalised ratio (INR) of 2-3 that provides the best balance between preventing thromboembolic events.

[5] Novel anticoagulants (NOACs), dabigatran, rivaroxaban, and apixaban are currently approved for the prevention of stroke or systemic embolism and for the prevention and treatment of VTE in patients with nonvalvular AF. Dabigatrone is approved for the treatment of VTE in previously treated patients.

[5] NOAC dosing is dependent on indication and may involve modification based on age-weight concomitant drugs and/or renal function. By directly blocking the Xa effect on a single factor within the coagulation cascade, rivaroxaban was created. With maximum plasma concentration reached within 2–4 h, it absorbs easily. With or without food, a 10 mg (mg) dose has 80-100 percent oral bioavailability and about 60 percent bioavailability for doses of 15 mg and 20 mg if a patient is fasting.

II. OBJECTIVES:

To study on utilization evaluation of anticoagulants therapy in management of cardiovascular and cerebral ischemic disorders.

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 07-15 www.ijprajournal.com ISSN: 2249-7781

To compare the efficacy and safety of systemic and direct oral anticoagulant used in patient with cardio vascular and cerebral ischemic disorders.
To access the degree of compliance with (ACCF/AHA) guidelines for anticoagulant in patients with cardio and cerebral ischemic disorders.
To identify possible drug - drug interactions with concomitantly administered agents.
To identify ADR of anticoagulants in patients with cardiovascular and cerebral ischemic disorders.

III. METHOD:

It is a prospective observational study carried out in the Department of General medicine, Vijayanagar Institute of Medical Science,Karnataka, India. The study was conducted for a period of six months with the proposed sample size of 130 patients. The material used wereSelf designed data collection form, Informed consent form, Microsoft Excel sheet, ACCP Guidelines. Patient information was collected from patient medical records or case sheets and by treatment chart review.
The study was carried out by considering the following inclusion and exclusion criteria.

Inclusion criteria:

Patient of either gender of age between 18 to 65 years. Patient diagnosed with any cardiac or cerebral ischemic disorders and prescribed with anticoagulants.

Exclusion criteria:

Who were not willing to sign inform consent form.
Patients diagnosed with any cardiac or cerebral ischemic disorders but not treated with anticoagulants.

Patients who were undergoing hemodialysis. The data wascollected by studying patient case sheet and Medication history interview. The result was obtained by using simple mean median method. The study didn’trequire any investigation on patients or other humans or animals. The protocol was submitted to the institutional review board to obtain ethical committee clearance before starting the study.

IV. RESULT:

A total of 130 patients were enrolled in this study, who were administered with anticoagulants. Out of them 75 (57.6%) were males and 55 (42.4%) were females as presented in Table 1.

GENDER	TOTAL (N=130)	PERCENTAGE %
Males	75	57.6%
Females	55	42.4%

Table1 Gender-wise distribution of study populations

The majority of patients with cardiovascular disorders were 83 (63.95%) in the age group between 46–65 years, followed by 32 (24.61%) in the age group of 31-45 years and least 15 (11.54%) with the age group between 18-30 years (Table 2).

AGE GROUP	MALE (N=75)	FEMALE (N=55)	TOTAL , N=130 (%)
18 -30	8	7	15 (11.54%)
31 -45	17	15	32 (24.61%)
46 -65	50	33	83 (63.85%)

Table2 Age-wise distribution of study populations

Study population were distributed according to the alcoholic and non-alcoholic status (Table 3). Of 130 patients, 55 patients were found to be alcoholic. Male patients with alcoholic were 52 (40%) and females were 03 (2.4%). However, 75 patients were non-alcoholic. Of them 23 (17.6%)were male and 52 (40%) were female non-alcoholic habits.

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 07-15 www.ijprajournal.com ISSN: 2249-7781

CATEGORY	GENDER	TOTAL (N=130)	PERCENTAGE %
ALCOHOLIC	Male	52	40%
	Female	3	2.4%
NON-ALCOHOLIC	Male	23	17.6%
	Female	52	40%

Table 3 Distribution of study populations according to Alcoholic and Non alcoholic

Evaluation of INR in patients who were alcoholic: in our study it was found that 55 patients were alcoholic in which 20 were below INR range and 10 were showing elevated INR and the remaining 25 were having stable INR(Table 4).

Below INR	Stable INR	Above INR
20 (36%)	25 (45.5%)	10 (18.1%)

Table 4 Evaluation of INR in Alcoholic Patients

In this study totally 130 patients of cardiovascular and neurological disorders were included of which common reasons for admissions are given below in **Table 5.**

Of 130 patients, 96 patients were admitted with co-morbidities in which 48 (50%) were male where23 (67.65%) were male and 11 (32.35%) were female

.

Comorbidities	Frequency
Comorbidities present in patients with Cardiovascular disease	
LVF, Sub acute infraction, MV Function Partial	2
Arterio Ventral Wall, MI with Pulmonary Edema	7
AF with Interior wall MI	9
Stroke Post Aortic Valve Replacement stats with IHD	2
ACS	15
ACS with IHD per DCM with MI	12
ACS with NSTEMI, Unstable Angina	13
Dilated Cardiac Myopathy with MI	1
RHD	1
IHD with Type -2 DM with CKD	12
C orpulmonary with LVT	2
RHD, AF with Ventricular rate	10
ACS with Anterior Wall Acute Pulmonary Edema	5
Anterior Wall MI	2
ArtialSeptal Defect	1
AF with CVA with HTN, IHD	5
AF with LBBB	1
LVF with Sub acute Infarction	5
CCF	1
Comorbidities presented in patients with Neurological disorders	
CVT with Right Thalamic Bleed	10
CVA	9
CVST	5
Ischemic heart disease(IHD); Rheumatic heart disease (RHD); Left ventricular failure(LVF); myocardial infarction(MI); Acute coronary Syndrome (ACS); Arterial fibrillation(AF); Congestive cardiac failure(CCF); diabetes mellitus(DM); Left bundle branch blocker(LBBB); Hypertension(HTN); Cerebrovascular thrombosis(CVT); Cerebrovascular accident(CVA);Cerebral venous sinus thrombosis(CVST)	

Table 5: Comorbidities presented among study populations

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 07-15 www.ijprajournal.com ISSN: 2249-7781

Prameters	Data done	Not done
Clotting time • INR • PT, aPTT	 102 99	 28 31
Liver Function Test • SGOT, SGPT, Bilirubin Level	86	44
Hb%	125	5
Platelet Count	120	10
CT Scan	Not done	Not done

Table 6 Laboratory Parameters of Baseline data

In hospital setting most commonly used anti-coagulants were Heparin followed by the LMWH, direct thrombin inhibitors and coumarin derivatives. Of these 103(79.23%) cases were administered with parenteral drugs and in 28(21.5%)received oral administration. The details on anticoagulants drugs uses were presented in **Table 7.**

Types of anticoagulant used	Route	Duration	Number
Heparin & Its Derivatives Heparin	 IV	 2-8 days	 101
Low Molecular Weight Heparin(LMWH) Enoxaparin	I.V	2-12 days	2
Direct thrombin inhibitor Dabigatran	 P.O	 4 days	 1
Coumarin Derivatives Acenocoumurol Warfarin	 P.O P.O	 2-21 days 3-7 days	 23 4

Table 7 Types and frequency of anticoagulants drugs used among study population

In our study totally three combination of anticoagulants were used both with parental and oral i.e single drugs were (inj. Heparin, tab. Acenocumerol, tab. Warfarin) and double therapy like (inj. Heparin+ tab. Acenocumerol) triple therapy includes(inj.heparin+ tab. Acenocumerol+ inj. Enoxaparin) as presented in Table 8

Monotherapy	104
Inj Heparin	90
Tab Acenocoumarol	8
Tab Dabigatran	1
Tab Warfarin	4
InjEnoxparin	1
Double Therapy Inj Heparin plus Tab. Acitrom	25
Triple Therapy Inj. Heparin + Tab. Acitrom + Inj. Enoxaparin	01

Table 8 Monotherapy and Combination therapy used to achieve effective INR

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 07-15 www.ijprajournal.com ISSN: 2249-7781

Out of 130 subjects, coagulation test was not performed in 28 patients, remaining 102 patients the coagulation test was performed repeatedly 1 to 2 times during the hospital stay in order to monitor efficacy of Anticoagulant.It was found that most of the patients INR was sub therapeutic range, i.e. INR <2(N =46; 35.38%). Merely, (N=30; 23.07%) achieved target INR, rest of the patients attained supra therapeutic level >3 (N=26; 20%). The pattern of INR monitoring frequency indicates that (N=28; 21.5%)0f the study population was not advised for INR monitoring after initiation of therapy. And out of 130 cases 99 patients were done with PT and aPTT and 31 were not.

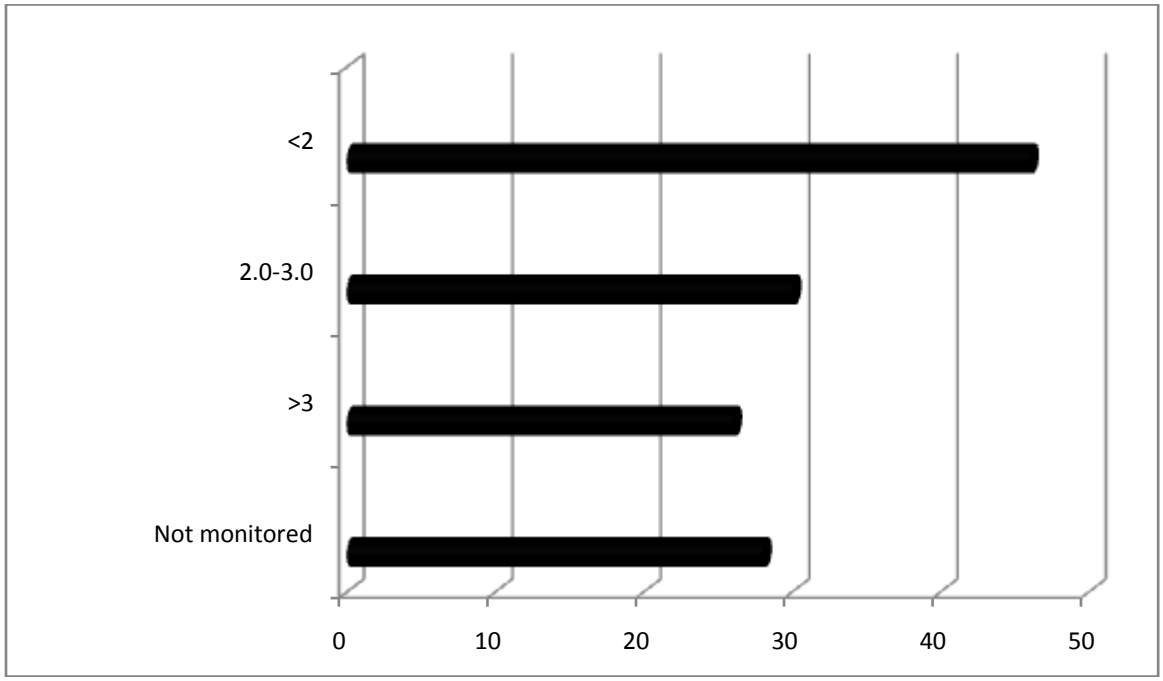

Fig: 1: monitoring pattern and achievement of target INR level

Concurrent use of Antiplatelet was also observed during this study, mostly in combination with Aspirin and Clopidogrel or Clopidogrel alone.

As another objective of this study, the patients medication chart was evaluated for drug interactions involving anticoagulants. A total of 95 interactions were identified. In that 88 interactions were of anticoagulants (heparin & acenocumerol, warfarin) with antiplateletes (Aspirin & Clopidogrel) and 7 interactions were observed involving heparin with drugs like streptokinasae and warfarin with tramadol, aldacton, azithromycin and acenocoumarol with glimipride, acetaminophen. The pharmacokinetic drug interaction between acenocoumarol & aminodarone is due to the mechanism that acenocoumarols acts by inhibiting vitamin K synthesis and amiodarone acts by inhibiting the action of cytochrome P450 isozymes, both of this action results in increased anticoagulants activity. The pharmacodynamic interactions were found to be a synergistic activity involving drug like acenocoumarol with enoxaparin, acetaminophen and glimipride.

Totally 3 ADR were found of which 2 were with warfarin, and one with heparin

At the time of discharge 33 patients were prescribed with anticoagulants; 27 patients were prescribed with acenocoumarol and the rest 5 patients with warfarin and 1 with heparin; and 52 were prescribed with antiplateletes with aspirin and Clopidogrel. And remaining 45 have not been followed up.

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 07-15 www.ijprajournal.com ISSN: 2249-7781

PATIENTS	TOTAL
Anticoagulants • Acenocoumarol - 27 • Warfarin - 05 • Heparin - 01	33
Antiplatelets • Aspirin • Clopidogrel	52
Not followed up	45

Table 9 Discharge Medication In Patients With Cardio And Cerbrovascular Disorders

V. DISCUSSION:

A prospective observational study had been conducted in tertiary care teaching hospital, Vijayanagar Institute of Medical Sciences, Karnataka, India. The current study showed that the anticoagulants are very commonly used for treatment and prophylaxis.The pattern of use was based on clinician's judgment and experience and in few situations the usage pattern deviated from American college of chest physicians (ACCP) guidelines based on patient's requirements.Over 6 months of study on patients ranging from age above 18 below 60 of both genders.In Meeraet.al;'s the maximum used Anticoagulant was Acenocoumarol which is a coumarin derivatives followed by Enoxaparin which is LMWH whereas , in our study Heparin which is administered parentally was most commonly prescribed followed by Acenocoumarol which is a oral anticoagulant.The maximum observed co morbid conditions is Acute Coronary Syndrome whereas in Meeraet.al;'s study the maximum observed co-morbid condition is Ischemic heart disease.UFH was mostly used parenteral in our study were the initial dose was 5000IU where ACCP guidelines suggest 5000IU initially followed by 1000U/hour.The usual ordered laboratory parameter and investigation were PT, INR, aPTT which goes along with Meeraet.al;'s.In our study we found that UFH was preferred in 101 cases and in many cases apttwas not performed as per the laid down guidelines and this can result in administrating an inappropriate dosage to the patients resulting in bleeding and thrombosis. UFH as a therapeutic doses the test value did not reach a desired aptt level necessitating repeat PT test to be performed, it is very important to check the aptt levels to decide the dose of UFH to be given as in adequate dose can lead to patient developing DVT.The poorer quality of OAC therapy in our study compared to that reported in other prospective studies maybe due to less INR testing. Several studies suggest that adverse events can be reduced and optimal INR may be maximized by more frequent INR testing, the optimal INR can be achieved in 90 percent on alternate day monitoring compared to 50 percent when monitored monthly. Therapeutic INR is difficult to achieve. The type of OAC and co medication may also affect the quality of anticoagulation.Stable INR was obtained in 23.7% patients and patients with unstable INR that is 61% were due to use of multiple drugs and associated co-morbidities. Warfarin was used only for proplylaxis and closer monitoring of patients was recommended. It was observed that in many cases Acenocumerol was given along with parenteral anticoagulants and monitoring was done one every second day of therapy to avoid risk of bleeding with high dose of parenteral anticoagulants.In addition the few studies directly compared aspirin with oral anticoagulants have found no difference between them either in the pre and post thrombolytic periods since aspirin is inexpensive and requires no monitoring.In our study the NOAC'S used were Enoxaparin and Dabigatran, although there are fewer drug interactions and significantly less bleeding than conventional therapy the main finding of our study was that three - fourth of patients had no contraindications with anticoagulant therapy. Use of oral antiplatelet was more in discharge medications and fewer anticoagulants were prescribed during discharge. This may be due to regular use of antiplatelet agents in patients with chronic ischemic heart disease.

VI. CONCLUSION:

Anticoagulant drug utilization pattern follows very commonly ACCP guidelines. NOAC'S were prescribed only in fewer patients though these were cost effective and significantly cause less bleeding risk and fewer interactions, but NOACs causes economic burden to the patients.The primary objective of our study was to

compare the efficacy of older and newer Anticoagulant agents, whereas we failed to fulfill it as the used of newer agents in our hospital was very limited.It was found that the stability of INR was disturbed due to the presence of alcoholic consumption in few patients which effect the efficacy of treatment.Repeat monitoring of parameters helps to evaluate the safety of Anticoagulant drug use. Therapy of anticoagulant need to be cost effective and reduce the complications associated with their use. Our study conclude that the use of monotherapy anticoagulants were effective when compared to the combination therapy since use of combination therapy was limited. Use of oral anticoagulant with antiplatelets in discharge medication, prevents the further reoccurrence of thrombo embolic events and effectiveness of therapy.

REFERENCES:

[1]. Raffaele De Caterina, Steen Husted . Anticoagulants in Heart Disease : Current Status and Prspectives, European Heart Journal (2007) 28, 880-913

[2]. Vijay Singh, Krishnappa Gopinath, Amirali Behzadpour and Neelathahalli Kasturiranagan Meera. Anticoagulant Utilization Evaluation in a Tertiary Care Teaching Hospital : An Observational Prospective Study in Medical in Patients, Indian Journal of Pharmacy Practice, Vol 8, Issue 2, Apr- June, 2015

[3]. Singh Prabhat, Kalita J. &Misra U.K. Quality of anticoagulation therapy in neurological patients in a tertiary care hospital in North India, Indian J Med Res 143, April 2016, pp 428-433

[4]. Patrick D. Brophy, Michael J. G. Somers. Multi centre evaluation of Anticoagulant in patients receiving Continuous renal replacement therapy (CRRT) : Nephrology Dialysis Transplantation, 26 April 2005

[5]. Reshma Elsa Jeny, Jenny Susan Sabu, Mamatha Krishna Murthy, Nagamalesh Udigala Madappa. Oral anticoagulant prescription analysis for utilization pattern in pattern patients at a tertiary care hospital, International Journal of Pharmacy and Pharmaceutical Science Volume 10, Issue 3, 2018

[6]. Ahmed YacoobMayet, Ahmed Ibrahim Alsaqer. Rivaroxaban prescribing in a Saudi tertiary Care Teaching Hospital, Saudi Pharmaceutical Journal :26 (2018) 775- 779.

[7]. Palappallil Sasidharan Dhanya ,Chooriyil Nidheesh , Kudakkachira Mathew Kuriakose ,Narayanan Puthiyaveetil. Pattern of oral anticoagulant use following prosthetic heart valve replacement: a prospective observational study , Indian J Thorac Cardiovasc Surg (july-september 2011) Vol 27 (3):119-124

[8]. Ignacio Mosquera Perez, Javier Muniz Garcia. Use of Anticoagulation at the Time of Discharge in Patients with Heart Failure and Atrial Fibrillation, Heart Failure, 22 August 2002 – 14 April 2003

[9]. Gerald R. Fortuna, MD, Eric W. Mueller, PharmD. The impact of preinjury antiplatelet and anticoagulant pharmacotherapy on outcomes in elderly patients with hemorrhagic brain injury, Surgery Vol 144 Number 04 October 2008

[10]. Mengistu G, Lemma B, Molla M. Utilization patterns of anticoagulants at medical ward of HiwotFana Specialized University Hospital, Harar, Ethiopia. J Basic ClinPharma 2017;8:235-238

[11]. Sultan Alghadeer, Lori Hornsby. Assessment of novel oral anticoagulant use within a community teaching hospital, Saudi Pharmaceutical Journal (2017) 25, Page no. 93 – 98.

[12]. Hossein Khalili, PharmD, SiminDashti-Khavidaki, PharmD. Anticoagulant Utilization Evaluation in a Teaching Hospital : A Prospective Study. Journal of Pharmacy Practice, November 23, 2010

[13]. Muneeshwar Reddy T, Durga Prasad TS. A study on Antiplatelet and Anticoagulant Utilization in a Tertiary care Hospital, International Journal of Pharmaceutical and Clinical Research, 2018 ; 10 (5) : 155- 161.

[14]. VineelaChadalavada, GangulaVenkata Naga Mounika. Drug Utilization Evaluation and Assessment of Economic Burden of Anticoagulant in a Tertiary care Hospital in South India, Journal of Pharmaceutical and Scientific Innovation, 2008; 7 (5)

[15]. Vinod Kumar, M., Ravishankar. Drug Utilization Evaluation of Cardiovascular Drugs in Outpatient Department in Tertiary care Hospital : A Descriptive Observational Study. International Journal of Current Research, Volume 7 Issue 09, September 2015.

[16]. Jesso George, Padmini Devi. Patterns and Determinants of Cardiovascular Drugs

Utilization in Coronary care Unit Patients of Tertiary care Hospital. Journal of Cardiovascular Disease Research 4(2013) 214- 221.

[17]. Arun Kumar Haridas, Bharathi Shridhar Bhat. Systematic Education about Anticoagulant Drugs : For Better Patient Compliance and to Extenuate Complications in Post Cardiovascular Surgery Patients. Journal of the Practice of Cardiovascular Sciences, March 15 2020IP : 223. 237.177.112

[18]. Mohammad Mehdi Shahpouri, SeyedMousavi, Role of heparin and LMWH in Acute Ischemic Stroke, Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences, accepted 2012 Jan 5

[19]. NafaaAlzubaidi, Manju Sharma. Drugs Utilization Study and Adverse Drug Reaction Reporting among Patients Using Anticoagulant in a Tertiary care Teaching Hospital. Journal of Drug Delivery and Therapeutics 2019, 9(3-s) : 181-185

[20]. Eric A Secemsky, MD, Msc. Use of Chronic Oral Anticoagulant and Associated Outcomes among Patients Undergoing Percutaneous Coronary Intervention. Journal of American Heart Association, August 22 2016.

[21]. Anakwue RC, Ocheni S, Madu AJ. Utilization of oral Anticoagulant in a Teaching Hospital In Nigeria, Annals of Medical and Health Science Research/ Sep-Oct 2014 Volume 4/ Special Issue 3.

[22]. Subrahmanya Prasad Pandiri, Grishma Jalemu. Quality and Superiority of Anticoagulant Therapy in Neurological Patients in a Tertiary care Hospital, International Archives of Integrated Medicine, Vol 6, Issue 7, July 2019

[23]. J. Lodder, P. J.M. Van Der Lugt. Evaluation of the Risk Of Immediate Anticoagulant Treatment In Patient with Embolic Stroke of Cardiac Origin, Stroke Vol 14 No. 1 Jan – Feb 1983

[24]. Willem J. M Dewilde, Tom Oribans. Use of Clopidogrel with or Without Aspirin In patient Taking Oral Anticoagulant Therapy and Undergoing Percutaneous Coronary Intervention.www. thelancet.com Vol 381 March 30 2013

[25]. Sonia Anand, M. D, Ph.D., Oral Anticoagulant and Antiplatelet Therapy and Peripheral Arterial Disease. The New England Journal Of Medicine, July 19, 2007 Vol 357 No. 3

[26]. Alex N. Isasc, Pharm.D., BCPS. Medication Utilization Evaluation of Dabigatran and Rivaroxaban within a Large, Multi Centre Health System, JHPR.orgVol 2, Issue 3.