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A Prospective Observational Study on Appropriateness of Oral Anticoagulant Therapy: Role of Clinical Pharmacist in Anticoagulation Clinic

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ABSTRACT

BACKGROUND: Anticoagulants work by interrupting the process involved in the formation of blood clots. They are sometimes called blood thinning medicines, although they don't actually make the blood thinner. Venous thromboembolism incidence ranges between 1 and 1.8 per 1000 person-years and is associated with substantial mortality. The rate of major extra cranialhaemorrhage on oral anticoagulant therapy ranges from 0.4 to 2% per year. Different definitions of major haemorrhage, International Normalised Ratio target ranges, age distribution, burden of comorbid illness, and type of coumarin challenge comparability of studies. Direct oral anticoagulants like dabigatran, apixaban, edoxaban are the drugs used for the prevention of thrombosis in several cardiovascular contexts. There is no Food and Drug Administration approved method to monitor the anticoagulant effect of direct oral anticoagulants. Qualitative coagulation assays such as activated partial thromboplastin time, thrombin time, and prothrombin time can be used as first line tests if evaluation for medication compliance is clinically important.

AIM: The main aim of the study is to evaluate the appropriateness of anticoagulants in patients by using various scales.

METHOD: This is a Prospective Observational study which was carried out in and around Guntur over a period of 6 months i.e. October 2020 to march 2020. About 150 study participants were analyzed for appropriateness of oral anticoagulants. To determine incidence and prevalence of different types of diseases (using anticoagulants) in different age groups, genders, a sample size of 1000 subjects were included.

RESULTS: At least one inappropriate criteria was detected from a total of 150 patients during the study period. Based on the CHA2DS2-VAScore the patients included in the study comes under low risk (n=85,56.6%) followed by intermediate risk(n=58,38.6%).most of the subjects included in this study had intermediate TTR (n=73,48.6%) followed by good TTR (n=56,37.3%). 24 (16%)patients included in the study had tyuly no risk ,their HAS-BLED score is 0 followed by 91(60.6%)patients included in the study has low risk. The Epidemiological results of this study revealed that there was a higher use of direct oral anticoagulants among people with age of 71-80 years and males were highly affected when compared to females.

CONCLUSION: Inappropriate use of direct oral anticoagulants pose additional worse outcomes in patients treated with anticoagulation therapy since they have a negative impact on the patient's Quality of life and in addition escalates cost of therapy. So, to ensure the preventability of bleeding risk in many cases, and effective assessment of appropriate use of direct oral anticoagulants could be the need of hour with the involvement of health care professionals and clinical pharmacists.

KEYWORDS: Anticoagulation therapy, HAS-BLED score, Medication appropriateness index, Drug utilization evaluation.

I. INTRODUCTION

DEFINITION: Anticoagulants are medicines that prevent the blood from clotting as quickly or as effectively as normal. Some people call anticoagulants blood thinners. However, the blood is not actually made any thinner - it just does not clot so easily whilst you take an anticoagulant. Anticoagulants are used to treat and prevent blood clots that may occur in blood vessels.

International Journal of Pharmaceutical Research and Applications
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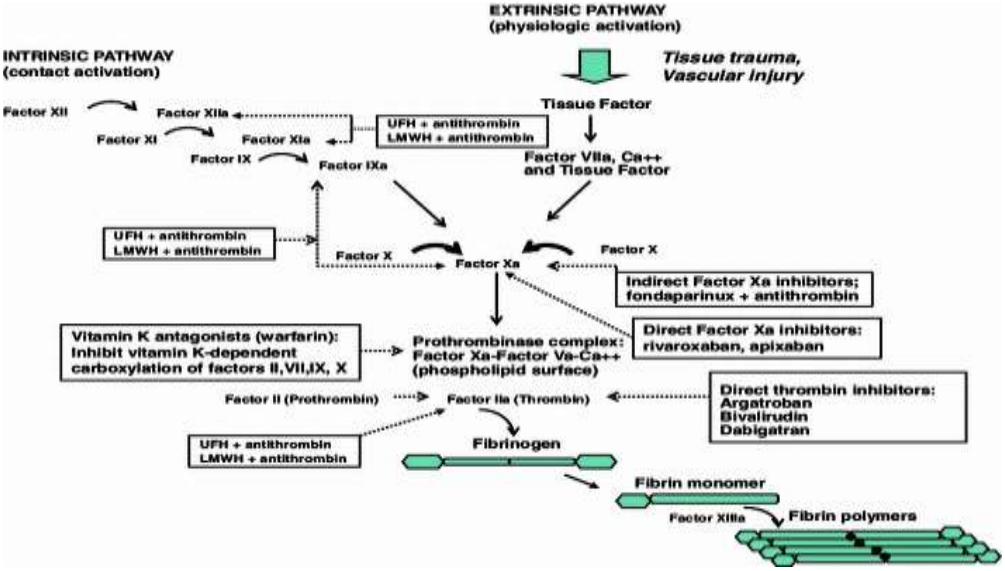
CLOTTING MECHANISM:



CLASSIFICATION: There are three main types of anticoagulant medications:

- Vitamin K antagonists
- Direct Oral Anticoagulants (DOACs)
- Low molecular weight heparins (LMWH)

Each type works in a different way to prevent unneeded blood clots.

DRUG PROFILES

APIXABAN

SYNONYM: Eliquis

CATEGORY: Factor Xa inhibitors

INDICATIONS: Apixaban is indicated for reducing the risk of stroke and systemic embolism in patients who have nonvalvular atrial fibrillation, prophylaxis of deep vein thrombosis (DVT) leading to pulmonary embolism (PE) in patients after a hip or knee replacement surgery, and treatment of DVT and PE to reduce the risk of recurrence.

DOSE: Dose adjustments considered if serum Cr > 1.5, weight is < 60 kg, or patient is taking other medications known to be strong inhibitors of CYP3A4 and P-glycoprotein.

ADVERSE EFFECTS:

- Bleeding gums, nosebleeds, heavy vaginal bleeding, red, pink, or brown urine, red or black, tarry stools, coughing up or vomiting blood or material that looks like coffee grounds, swelling or joint pain, headache.

PHARMACOKINECTICS:

Absorption: The maximum plasma concentration (C_{max}) of apixaban occurs 3-4 hrs after oral administration. Compared with oral administration, the bioavailability of 2.5mg of apixaban solution was approximately 60% and 84%lower than released in the distal small bowel and ascending colon, respectively.

Distribution: The volume of distribution is approximately 21L, suggesting distribution mainly into extracellular fluid, which comprises vascular and interstitial fluid. The blood to plasma ratio of apixaban is 0.9:1 in humans, suggesting that apixaban is uniformly distributed between plasma and red blood cells.

Metabolism and elimination: mainly metabolised by CYP3A4 with minor contributions from CYP1A2, 2CB, 2C9, 2C19 and 2J2. 56% of apixaban dose is excreted through feces. 24.5% dose is excreted through urine. Apparent elimination half-life is 12hrs.

PHARMACODYNAMICS: As a result of FXa inhibition, apixaban prolongs clotting tests such as prothrombin time (PT), INR, and activated partial thromboplastin time (aPTT). Changes observed in these clotting tests at the expected therapeutic dose, however, are small, subject to a high degree of variability, and not useful in monitoring the anticoagulation effect of apixaban.

MECHANISM OF ACTION: Apixaban is a highly selective, orally bioavailable, and reversible direct inhibitor of free and clot-bound factor Xa. Factor Xa catalyzes the conversion of prothrombin to thrombin, the final enzyme in the coagulation cascade that is responsible for fibrin clot formation. It selectively inhibits the activated factor Xa in a reversible manner. It inhibits both free factor Xa

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and also clot bound factor Xa. Inhibition of factor Xa also leads to reduced formation of factor II (thrombin).

CONTRAINDICATIONS:

Apixaban is contraindicated for use by patients with severe hypersensitivity to the drug.

RIVAROXABAN

SYNONYM: Xarelto

CATEGORY: Factor Xa inhibitor

INDICATIONS:

- Reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation
- Treatment of deep vein thrombosis (DVT)and pulmonary embolism (PE)
- Prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery.

DOSE:

- **General Notes:**
- 15 mg and 20 mg tablets should be taken with food whereas 10 mg tablets can be taken with or without food.
- **Reduction of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation**:
- 20 mg daily with evening meal
- **Prophylaxis of DVT Following Surgery:**
- 10 mg daily. Give initial dose 6-10 hours after surgery provided that hemostasis has been established
- **Treatment of DVT and PE:**
- 15 mg twice daily with food for the first 21 days; then 20 mg daily with food, at approximately the same time each day
- Reduction in risk of recurrence following initial 6 months of treatment: 20 mg daily with food at approximately the same time each day

ADVERSE EFFECTS: Back pain, Bleeding gums, Bloody stools, Bowel or bladder dysfunction, Burning, crawling, itching, numbness, prickling, "pins and needles", or tingling feelings, Coughing up blood, Difficulty with breathing or swallowing, Dizziness, Headache

PHARMACOKINETICS:

Absorption: The absolute bioavailability of rivaroxaban is dose-dependent. For the 10 mg dose, it is estimated to be 80% to 100% and is not affected by food. Rivaroxaban 10 mg tablets can be taken with or without food. For the 20 mg dose in the fasted state the absolute bioavailability is approximately 66%.

Distribution: Plasma protein binding of rivaroxaban in human plasma is approximately 92% to 95%, with albumin being the main binding component. The steady-state volume of distribution in healthy subjects is approximately 50 L.

Metabolism: Approximately 51% of an orally administered [14C]-rivaroxaban dose was recovered as inactive metabolites in urine (30%) and feces (21%). Oxidative degradation catalyzed by CYP3A4/5 and CYP2J2 and hydrolysis are the major sites of biotransformation.

Elimination: Following oral administration, approximately one-third of the absorbed dose is excreted unchanged in the urine, with the remaining two-thirds excreted as inactive metabolites in both the urine and feces.

PHARMACODYNAMICS: Dose-dependent inhibition of FXa activity was observed in humans and the neoplastin prothrombin time (PT), activated partial thromboplastin time (aPTT) and HepTest are prolonged dose-dependently. Anti-factor Xa activity is also influenced by rivaroxaban.

MECHANISM OF ACTION: Rivaroxaban competitively inhibits free and clot bound factor Xa. Factor Xa is needed to activate prothrombin (factor II) to thrombin (factor IIa). Thrombin is a serine protease that is required to activate fibrinogen to fibrin, which is the loose meshwork that completes the clotting process. The action of rivaroxaban is irreversible.

DABIGATRAN

SYNONYM: Pradaxa

CATEGORY: Direct thrombin inhibitor

INDICATIONS:

- Deep vein thrombosis (DVT) and pulmonary embolism (PE)
- Reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation.

DOSE:

- **DVT & PE:**
- Treat with parenteral anticoagulant for first 5-10 days, then start dabigatran
- If CrCl> 30 mL/min: 150 mg orally twice daily
- If CrCl 15-30 mL/min: 75 mg orally twice a day
- **Stroke Prevention in Non-valvular Atrial Fibrillation:**
- 150 mg orally twice a day
- If CrCl> 30 mL/min: 150 mg orally twice daily
- If CrCl 15-30 mL/min: 75 mg orally twice a day
- **If switching from parenteral anticoagulant to dabigatran:**

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 1774-1787 www.ijprajournal.com ISSN: 2456-4494

- Start dabigatran within 2 hrs of next dose of parenteral agent
- **If switching from dabigatran to a parenteral anticoagulation:**
- Start the parenteral anticoagulant 12 hrs (if CrCl> 30 mL/min) or 24 (if CrCl< 30 mL/min) after the last dose of dabigatran
- **If switching from warfarin to dabigatran:**
- Stop warfarin and when INR < 2, start dabigatran

ADVERSE EFFECTS:

- Bleeding, Stomach or intestinal ulcer, A type of stomach irritation called gastritis, Bleeding of the stomach or intestines, Nosebleed, Bruising

PHARMACOKINETICS:

Absorption: The absolute bioavailability following oral administration is ~ 3 to 7%. Dabigatran etexilate is a substrate of the efflux cell membrane transporter P-gp. After oral administration in healthy volunteers, the Cmax occurs at 1hour post-administration in the fasted state.

Distribution: Dabigatran is approximately 35% bound to human plasma proteins. The red blood cell to plasma partitioning of dabigatran measured as total radioactivity is less than 0.3. The volume of distribution of dabigatran is 50 to 70 L.

Metabolism: After oral administration, dabigatran etexilate is converted to dabigatran. The cleavage of the dabigatran etexilate by esterase-catalyzed hydrolysis to the active principal dabigatran is the predominant metabolic reaction. Dabigatran is not a substrate, inhibitor, or inducer of CYP450 enzymes.

Elimination: Dabigatran is eliminated primarily in the urine. Renal clearance of dabigatran is 80% of total clearance after intravenous administration. After oral administration of radiolabelled dabigatran, 7% of radioactivity is recovered in urine and 86% in feces.

PHARMACODYNAMICS: At recommended therapeutic doses, dabigatran etexilate prolongs the coagulation markers such as aPTT, ECT, and TT. INR is relatively insensitive to the exposure to dabigatran and cannot be interpreted the same way as used for warfarin monitoring. The aPTT test provides an approximation of PRADAXA's anticoagulant effect.

MECHANISM OF ACTION: Dabigatran and its acylglucuronides are competitive, direct thrombin inhibitors (DTI). Because thrombin (serine protease) enables the conversion of fibrinogen into fibrin during the coagulation cascade, its inhibition prevents the development of a thrombus. Both free and clot-bound thrombin, and thrombin-induced platelet aggregation are inhibited by the active components of dabigatran.

DRUG INTERACTIONS:

Amikacin: Amikacin may decrease the excretion rate of Dabigatran etexilate which could result in a higher serum level.

Amantadine: Amantadine may decrease the excretion rate of Dabigatran etexilate which could result in a higher serum level.

PATIENT COUNSELLING:

- Inform patients that they may bleed more easily, may bleed longer, and should call their health care provider for any signs or symptoms of bleeding.
- Do not put dabigatran in pill boxes or pill organizers.
- When more than one bottle is dispensed to the patient, instruct them to open only one bottle at a time.
- Instruct patient to remove only one capsule from the opened bottle at the time of use. The bottle should be immediately and tightly closed.
- Advise patients not to chew or break the capsules before swallowing them and not to open the capsules and take the pellets alone.

DRUG UTILIZATION AND EVALUATION: An ongoing, systematic, criteria-based program of medicine evaluations that will help ensure appropriate medicine use. If therapy is determined to be inappropriate, interventions with providers or patients will be necessary to optimize pharmaceutical therapy. This terminology is similar to that drug use review (DUR) and medication use review (MUR)

CLASSIFICATION:

DUR is typically classified in three different categories: prospective, concurrent and retrospective.

1. Prospective DUR
2. Concurrent DUR
3. Retrospective DUR

NEED FOR DUE: Irrational medicine use has occurred for as long as medicines have been available. In treating patients with modern medicines, several choices of therapy are available—rather than just one that all providers

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must follow. This increased number of medicines and treatment options serves to increase the number of irrational medicine treatment encounters and, ultimately, poor patient outcomes. Casual observation, as well as more systematic study of prescribing practices, frequently reveals a pattern of diversity among prescribers in the treatment of even the most common conditions.

Polypharmacy is one problem. Other common medicine use problems are choosing incorrect medicines, prescribing the incorrect dose, prescribing medicines that cause adverse drug reactions (ADRs) or medicine interactions, and using more expensive medicines when less expensive medicines would be equally or more effective. Other medicine use problems that suggest a need for DUE include the following—

- Problems indicated from World Health Organization (WHO)/Management Sciences for Health (MSH) indicator studies
- High number of ADRs
- Signs of treatment failures
- Excessive number of nonformulary medications used
- Use of high-cost medicines where less expensive alternatives exist
- Excessive number of medicines within a therapeutic category

MEDICATION APPROPRIATENESS INDEX:

The Medication Appropriateness Index (MAI) measures the appropriateness of prescribing for elderly patients, using 10 criteria for each medication prescribed. For each criterion, the evaluator rates whether the medication is appropriate, marginally appropriate, or inappropriate. Support is provided through explicit definitions and instructions. Potentially inappropriate prescribing for older adults is a major public health concern. While there are multiple measures of potentially inappropriate prescribing, the Medication Appropriateness Index (MAI) is one of the most common implicit approaches published in the scientific literature. The objective of this narrative review is to describe findings regarding the MAI's reliability, comparison of the MAI with other quality measures of potentially inappropriate prescribing.We conclude that the MAI may serve as a valuable tool for measuring potentially inappropriate prescribing in older adults.

CHA_2DS_2VASc – score:

The CHA_2DS_2-VASc Score is the most commonly utilized method to predict thromboembolic risk in atrial fibrillation. This is excellent information for clinicians to use in educating patients about annual stroke risk. Many patients are hesitant to begin anticoagulation due to the expense and inconvenience. After understanding that a 4% annual risk for stroke (if the CHA_2DS_2-VASc Score is 4) equates to 40% risk over 10 years, patients are more willing to comply. However, with this scoring system, the basis for decisions on antithrombotic therapy was poorly defined in a large proportion of patients with intermediate thromboembolic risk, since antiplatelet and anticoagulation therapy are considered equally valid options.

HAS-BLED Score:

Bleeding is a significant complication when patients are on anticoagulant therapy. The risk of bleeding overall when anticoagulant therapy is used is 3.8%. A number of risk factors are associated with increased bleeding when patients are on anticoagulants. A practical risk score HASBLED score was developed to estimate 1year risk for major bleeding in patients with atrial fibrillation. HAS-BLED score provides a practical tool to assess the individual risk of bleeding in AF patients potentially supporting clinical decision making regarding anti thrombotic therapy.

METHODOLOGY

Study design : A prospective observational study

Study site : **C**ardiology Hospitals, Narasaraopeta and Guntur.

Study period : A Period of 6 months.

Sample size : By using statistical tools sample size will be calculated

Study criteria:

Inclusion criteria:

- The patients who are on oral anticoagulation therapy were included.
- Patients with other co-morbid conditions were also includedin the study.
- Male and female patients of age 18years and above were included in the study.

Exclusion criteria:

- Patients who are not willing to participate in our study were excluded.
- Pregnant patients were excluded from the study.
- Patients who are on therapy with heparin and low molecular weight heparin were excluded.

Study method:

- Study is conducted in and around Narasaraopet and Guntur.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 1774-1787 www.ijprajournal.com ISSN: 2456-4494

- A data collection form will be developed in which all the details of the patients are noted.
- Consent form will be taken from subjects who wish to participate in our study.
- Patients will be given adequate knowledge on anticoagulants- its early screening measures and also on Dietary changes, lifestyle modifications have to be followed.
- Subjects who are not willing to participate in the study will also be counselled with the help of information leaflets.
- After collection of data from the patients who had developed atleast one inappropriate criteria due to inappropriate use of anticoagulation therapy will be assessed by using MAI scale,CHA2DS2-VAScore and HAS-BLED score.
- Patients who understood that they were at risk of bleeding were advised for to attend for regular follow-up and counselled about the importance of medication adherence, ADR's severity & life style modifications which helps to reduce hospitalization.
- The data will be analyzed by using descriptive analysis, and suitable scales.

II. RESULTS

CATEGORIZATION OF SUBJECTS BASED ON COMORBIDITIES

S.No.	COMORBIDITIES	Total number of subjects(n=1000)	PERCENTAGE (%)
1.	CAD	510	51
2.	COVID	190	19
3.	IHD	70	7.0
4.	MI	65	6.5
5.	DVT	50	5.0
6.	CHF	34	3.4
7.	PLEURAL EFFUSION	25	2.5
8.	CARDIAC MYOPATHY	18	1.8
9.	ISCHEMIC STROKE	16	1.6
10.	CARDIAC FAILURE	12	1.2
11.0	PULMONARY EMBOLISM	10	1.0

Table 01: CATEGORIZATION OF SUBJECTS BASED ON COMORBIDITIES

Table 01 shows that the patients who are included in the study,most of them had CAD (n=510,51%) followed by COVID(n=190,19.0%), IHD (n=70,7.0%).

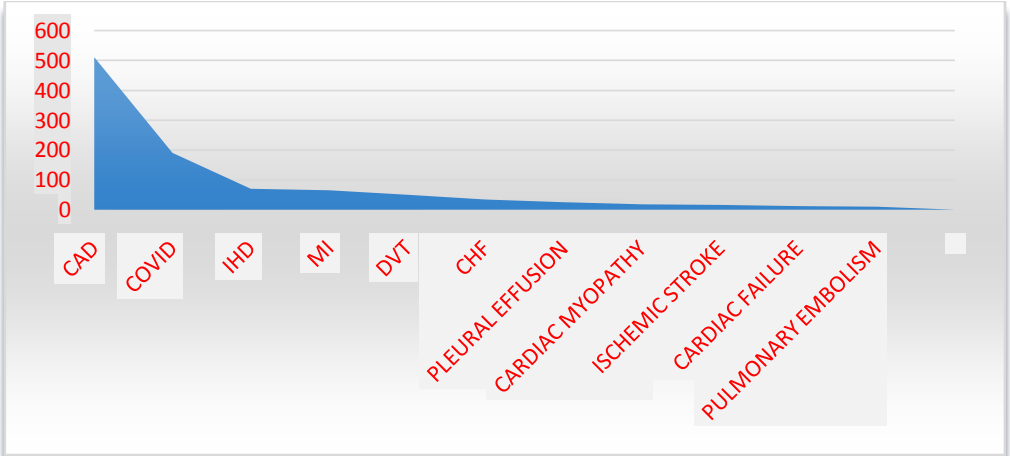

Figure 01: shows categorization of subjects based on comorbidities

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 1774-1787 www.ijprajournal.com ISSN: 2456-4494

TABLE 02: AGE WISE DISTRIBUTION OF STUDY POPULATION

S.No.	AGE IN YEARS	NO OF PATIENTS	FREQUENCY%
1	31-40	09	6
2	41-50	30	20
3	51-60	43	28.6
4	61-70	35	23.3
5	71-80	23	15.3
6	81-90	10	6.66

TABLE 02: out of 150 patients, majority of the patients fall between the age group 51-60(n=43,28.6%) followed by 61-70 (n=35,23.3%)

FIG 02:FREQUENCY DISTRIBUTION OF PATIENTS BASED ON AGE

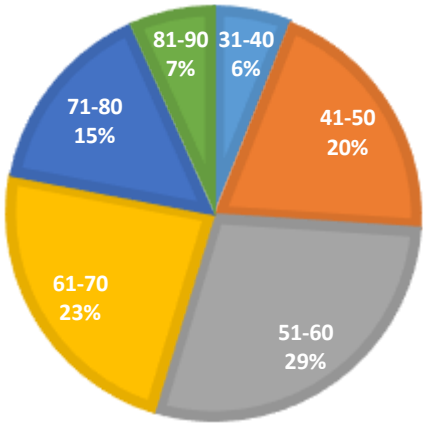

TABLE 03: DISTRIBUTION OF STUDY POPULATION BASED ON GENDER

S.NO	GENDER	NO. OF CASES	PERCENTAGE (%)
1	MALE	98	65.3%
2	FEMALE	52	34.6%
	Total	150	100%

TABLE 03: Among the study population, total number of patients enrolled are males (n=98, 65.3%**)** and females (n=52, 34.6%).

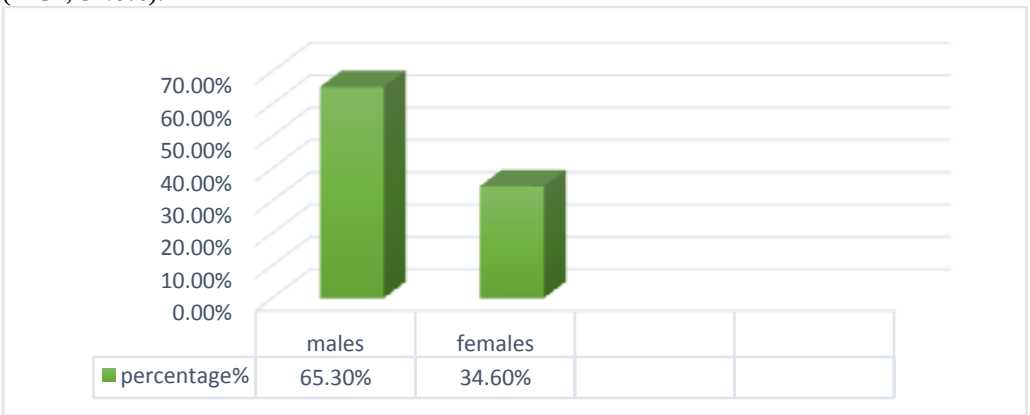

FIG 03: GENDER WISE DISTRIBUTION

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 1774-1787 www.ijprajournal.com ISSN: 2456-4494

DIRECT ORAL ANTICOAGULANTS USAGE (150)

S.NO	TYPE OF DOAC'S	NO OF CASES (n=150)	PERCENTAGE (%)
1	APIXABAN	65	43.3
2	RIVAROXABAN	59	39.3
3	DABIGATRAN	26	17.3

Table 04: Direct oral anticoagulants usage

Table 04shows that most of the patients incuded in this study was treated with apixaban(n=65,43.3%)followed by rivaroxaban(n=59,39.3%) .

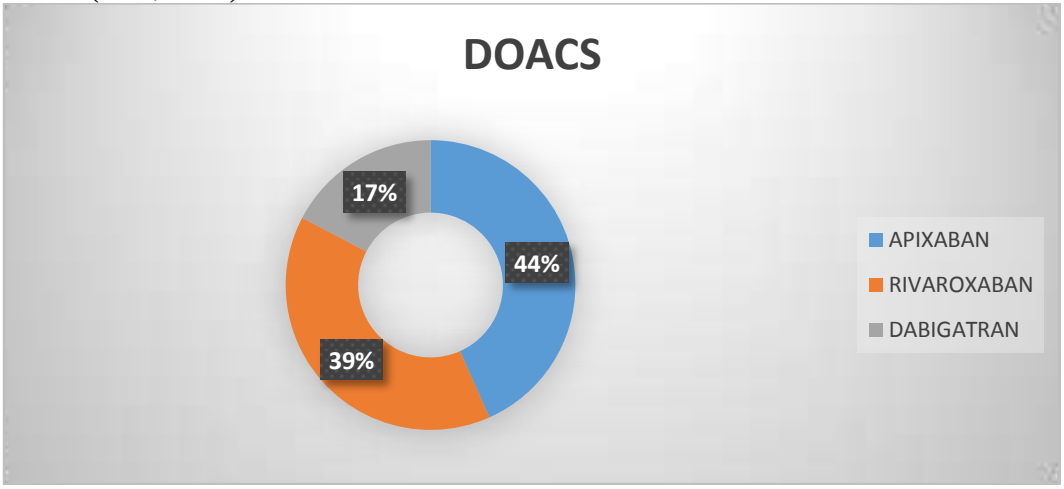

Figure 04: shows direct oral anticoagulants usage

POSSIBLE DRUG INTERACTIONS

S.No.	DRUGS	TYPE OF INTERACTION	DRUG INTERACTION
1	STREPTOKINASE<->APIXABAN	MAJOR	RISK OF BLEEDING
2	STREPTOKINASE<->RIVAROXABAN	MAJOR	RISK OF BLEEDING
3	STREPTOKINASE<->DABIGATRAN	MAJOR	RISK OF BLEEDING

TABLE 05 : Possible Drug interactions

Table 05 shows that the major drug interaction(streptokinase<->DOACS) was risk of bleeding.

CHA2DS2-VASc

S.NO	RISK	NO OF CASES(n)	PERCENTAGE(%)
1	Low risk (CHA2DS2-VASc=0)	85	56.6
2	Intermediate risk (CHA2DS2-VASc=1)	58	38.6
3	High risk(CHA2DS2-VASc>2)	07	4.66

TABLE 06: CHA2DS2-VAScore

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 1774-1787 www.ijprajournal.com ISSN: 2456-4494

Table 06 shows that most of the patients included in the study comes under low risk (n=85,56.6%) followed by intermediate risk(n=58,38.6%)

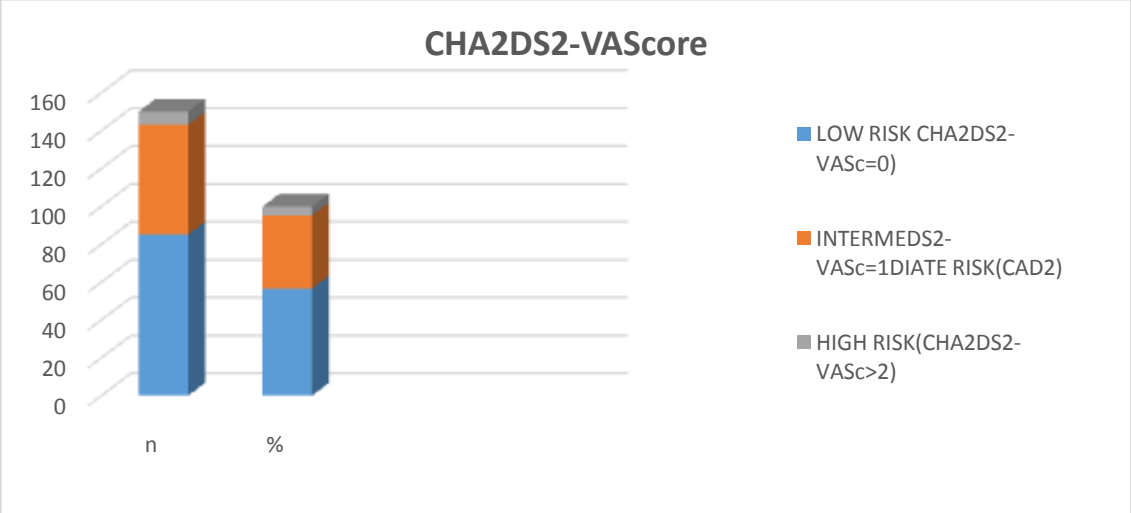

Figure 06: shows CHA2DS2-VAScore

TIME IN THERAPEUTIC RANGE

S.NO	TTR RANGE	NO OF SUBJECTS(n)	PERCENTAGE (%)
1	GOOD (>70%)	56	37.3
2	INTERMEDIATE (50%-70%)	73	48.6
3	POOR (<50%)	21	14.0

TABLE 07:TIME IN THERAPEUTIC RANGE

Table 07 shows that most of the subjects included in this study had intermediate TTR (n=73,48.6%) followed by good TTR (n=56,37.3%)

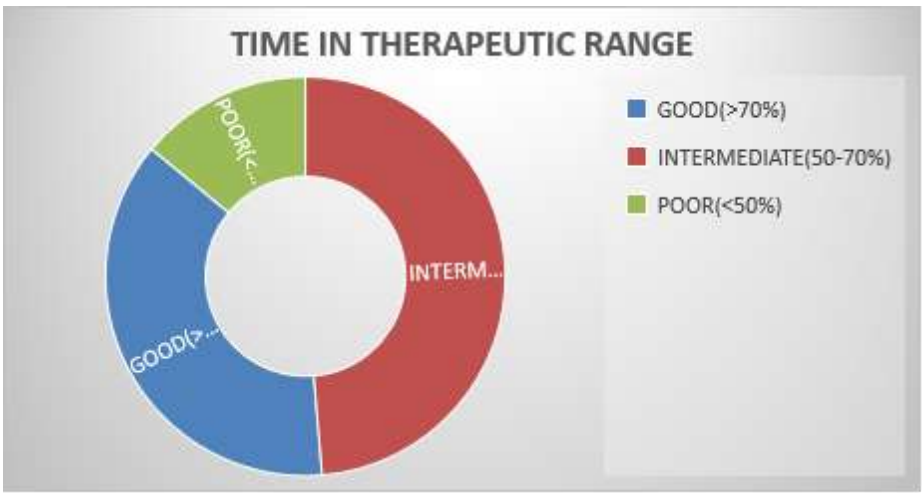

Figure 07: shows time in therapeutic range

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 1774-1787 www.ijprajournal.com ISSN: 2456-4494

INTERNATIONAL NORMALIZED RATIO

S.NO	INR RANGE	NO OF CASES(n)	PERCENTAGE(%)
1	<1.5	68	45.3
2	1.5-2.0	50	33.3
3	>2.0	32	21.3

TABLE 08: INTERNATIONAL NORMALIZED RATIO

Table 08 shows that most of the people included in this study,the INR is <1.5 (n=68,45.3%) and the least number of peoples INR is>2.0(n=32,21.3%)

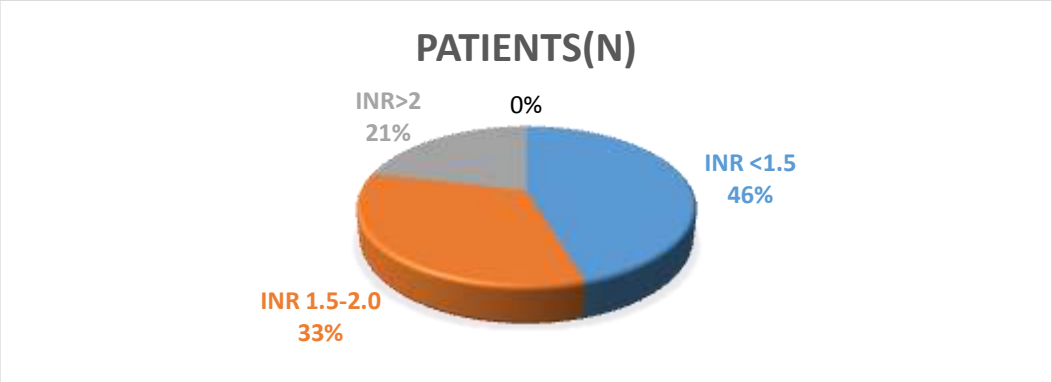

Figure 08 : shows international normalized ratio

HAS-BLED SCORE

S.NO	HAS-BLED RANGE	NO OF CASES(150)	PERCENTAGE (%)
1	TRULY NO RISK(0)	24	16
2	LOW RISK OF BLEEDING(0-2)	91	60.6
3	HIGH RISK(>3)	35	23.3

TABLE 09: HAS-BLED SCORE

Table 09 shows that 24 (16%)patients included in the study had truly no risk ,their HAS-BLED score is 0 followed by 91(60.6%)patients included in the study has low risk .

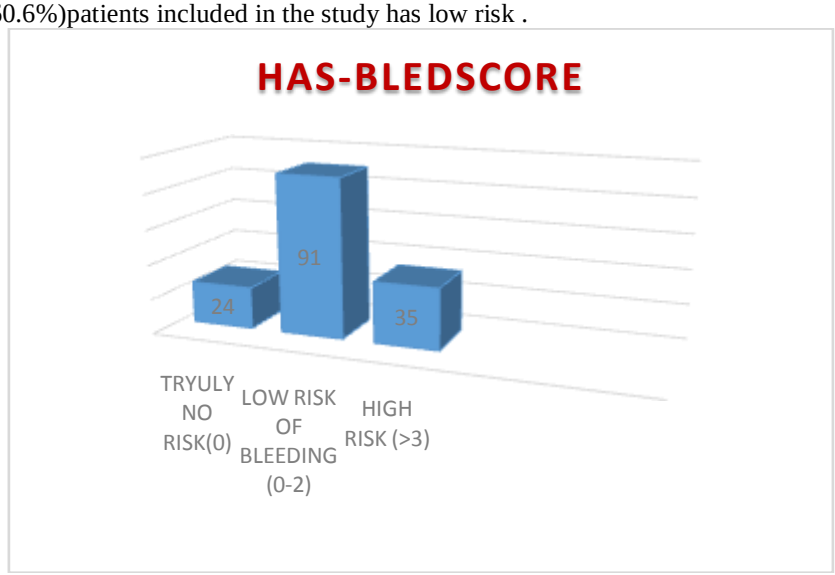

Figure 09: shows HAS-BLED score

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 1774-1787 www.ijprajournal.com ISSN: 2456-4494

MEDICATION APPROPRIATENESS INDEX

S.NO	CRITERION	A	B	C
1	INDICATION	124	20	6
2	CHOICE	140	6	4
3	DOSAGE	148	-	2
4	ADMINISTRATION,CORRECT	132	14	4
5	ADMINISTRATION,PRACTICAL	148	-	2
6	DRUG-DRUG INTERACTION	117	32	1
7	DRUG-DISESE INTERACTION	133	16	1
8	DUPLICATION	146	4	0
9	DURATION OF THERAPY	145	-	5

TABLE 10 : MEDICATION APPROPRIATENESS INDEX

Table 10 shows that most of the patients incided in the study had better medication appropriateness index . A=appropriate, B=inappropriate with limited clinical importance and C= inappropriate

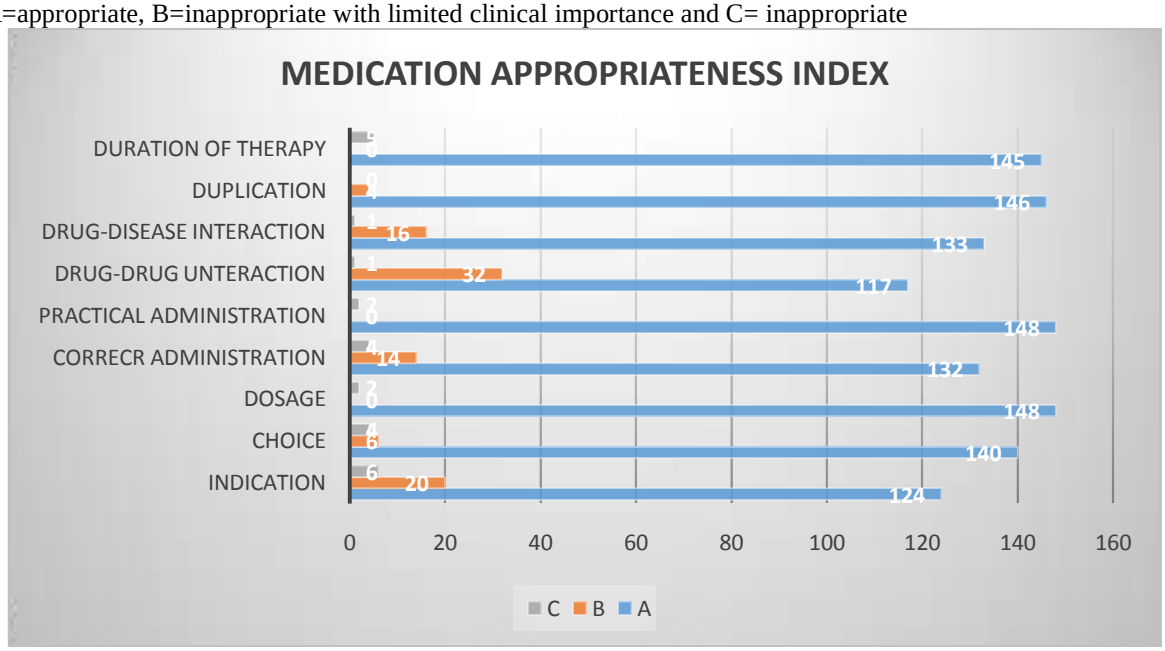

Figure 10: shows medication appropriateness index

III. DISCUSSION

In our study, we educated patients regarding medications, Dietary and Lifestyle modifications by using PILs. A total of 1000 study population were reviewed and quantified the proportion of inappropriate use of anticoagulants in different age groups, Genders and subjects whose BMI is more than the normal ranges over a period of 6 months.Regarding the epidemiology survey, (Table.1; fig.1)shows categorization of subjects based on type of disease. most of them are diagnosed as CAD (n=510,51.0%), COVID (n=190,19.0%), IHD (n=70,7.0%), MI(n=65,6.5%), and less population had ischemic stroke(n=16,1.6%), cardiac failure(n=12,1.2%).

Age wise distribution of study population, (Table.2; fig.2) out of 150 patients, majority of the patients fall between the age group 51-60(n=43,28.6%) followed by 61-70 (n=35,23.3%) & 71-80 (n=15.3%).

Distribution of study population based on gender, (Table.3; fig.3) Among the study population, total number of patients enrolled are males (n=98, 65.3%**)** and females (n=52, 34.6%).

Based on the direct oral anticoagulant's usage that (Table.4; fig.4) most of the patients were treated with apixaban (n=65, 43.3%), followed by rivaroxaban (n=59,39.3%), and dabigatran (n=26,17.3%).

Possible drug interactions (Table.5; fig.5) are observed that the major drug interaction(streptokinase<->DOACS) was risk of bleeding.

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That the CHA2DS2-VAScore reveals (n=85,56.6%) patients with low risk , (n=58,38.6%) intermediate risk and (n=7,4.66%) high risk.(Table.6;fig.6)

In the study population,regarding bleeding risk , HAS-BLED score conclude that most of the patients have low risk of bleeding having a score 0-2(n=91,60.6%),(n=24,16%) patients had no risk of bleeding that the score is 0 and ppatients have high risk of bleeding had a score greater than 3(n=35,23.3%) (Table.7; fig.7).

International normalized ratio, (Table.8; fig.8) shows that most of the people included in this study,the INR is <1.5 (n=68,45.3%) and the least number of peoples INR is>2.0(n=32,21.3%)

HAS-BLED score (Table.9; fig.9) shows that 24 (16%)patients included in the study had truly no risk ,their HAS-BLED score is 0 followed by 91(60.6%)patients included in the study has low risk .

(Table.10; fig.10) provides that each patient has at least one inappropriate criteria. Most of the patients met inappropriate indication, followed by choice. In MAI A = appropriate, B = inappropriate with clinical importance and C = inappropriate.

IV. CONCLUSION

DOACS are indisputably an important step in the field of anticoagulation.Anticoagulant drugs have Narrow Therapeutic Index and have a high propensity to cause risk of bleeding.Hence, early detection of risk of bleeding and appropriate use may minimize the harm either by modifying the dose or changing the offending drug with a suitable alternative.With the aim of improving patient's QOL and to reduce Hospitalization, we educated patients about medications usage and its side effects, Dietary modifications, Lifestyle changes which plays a major role in reducing the progression of symptoms occurred due to inappropriate use of anticoagulants. Appropriate use of anticoagulant therapy and any deviation from the guidelines to a larger extent also depend on patients characteristics and concomitant therapy patient is receiving. By using the different scales like HAS-BLED score,CHA2DS2-VAScore have to minimize the risk bleeding.This study has highlighted the appropriateness of DOACS and identified the priorities for strengthening the education of pharmacists,HCPS and patients with regard to choice of anticoagulant,dose adjustment and modalities of administration.

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