



## EVALUATION AND UTILIZATION OF ANTIPLATELET AND ANTICOAGULANT DRUGS IN THE PREVENTION OF CARDIOVASCULAR EVENTS AND STROKE

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### ABSTRACT

**Introduction:** Cardio vascular disease is the most common cause in elderly people worldwide reaching 17- million annually. Stroke has been used to include episodes of focal brain dysfunction due to focal ischemia or hemorrhage as well as sub-arachanoid hemorrhages. Stroke ranking 3rd in mortality behind heart disease and cancer. Most popular drugs used worldwide for the prevention of cardiovascular incidents and stroke are antiplatelets and anticoagulants.

**Materials & Methods:** The present prospective observational study was carried out in the department of General Medicine (IP) of Rajiv Gandhi Institute of Medical Sciences (RIMS), Kadapa, AP, A total of 864 subjects were studied in 1yr (October 2012- October 2013) & the patients are enrolled to the study according to the inclusion & exclusion criteria.

**Results:** In the present study antiplatelets use in the treatment of Myocardial infraction (MI) and Heart failure (HF), as a combination of aspirin + clopidogrel (14.46%) & (6.48%) respectively and aspirin alone was less compared to combination therapy i.e., 6.8% & 6.13%. The usage of antiplatelets + anticoagulants (Aspirin + Clopidogrel + LMWH) was observed in the regular practice for treatment of Angina (12.03%) and DVT (10.76%). The anti-coagulant alone was used in Atrial fibrillation and DVT.

**Conclusion:** Our results demonstrated that use of antiplatelets is the most common or frequent 1st line agent for cardiovascular events & Stroke. And also we found that the combination therapy may be more superior to monotherapy with respect to specific patients groups.

Quality improvement measures to educate physicians of the evidence regarding antiplatelets & anticoagulant drugs for cardiovascular events and stroke.

**Keywords:** Antiplatelets, Anticoagulants, Stroke, Cardiovascular diseases, Aspirin

### INTRODUCTION

A cardiovascular disease is defined as any serious abnormal condition of the heart or blood vessel. It includes coronary heart diseases, peripheral vascular diseases, congenital heart diseases and many other conditions.

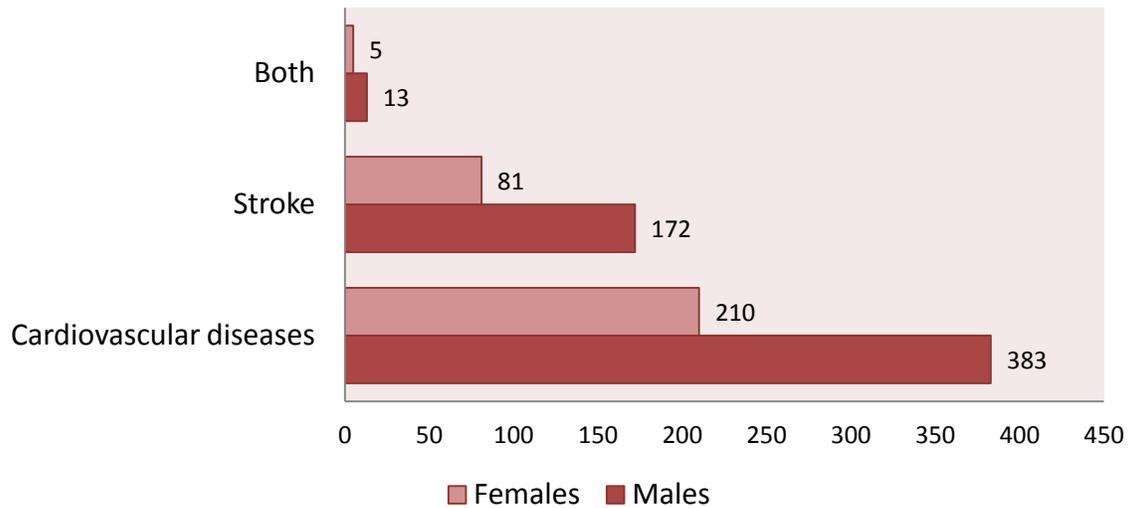
Cardio vascular disease is the most common cause in elderly people worldwide reaching 17-million annually.<sup>1</sup> Approximately 43 million Americans have BP >140/90mmHg. Incidence increases with the age i.e., 60%-71%. People > 60yrs of age have hypertension, according to the data obtained from the 3<sup>rd</sup> national health and nutrition examination survey.<sup>2</sup> Heart failure is a common medical condition that affects almost 5 million people in the US with > 5,00,000 new cases diagnosed each year. The incidence increases to 6%-10% in patients older than age 65 years.<sup>2</sup> Ischemic heart diseases(IHD) continues to be the leading single cause of death in the US (231.1 to 297.9 deaths/1,00,000) each year more than 5 million patients present to emergency rooms with chest discomfort and related symptoms. Approximately 1.5 million are

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hospitalized for acute coronary syndromes.<sup>2</sup>

Stroke has been used to include episodes of focal brain dysfunction due to focal ischemia or hemorrhage as well as sub-arachnoid hemorrhages.<sup>3</sup>

adoption of less healthy lifestyles. About 1/5<sup>th</sup> of the patients with an acute stroke will die within a month of the event and atleast 1/2 of those who survive will be left with physical disability. Among the stroke patients 2/3<sup>rd</sup> patients are aged over 60 years. Older patients with stroke are more likely to have other

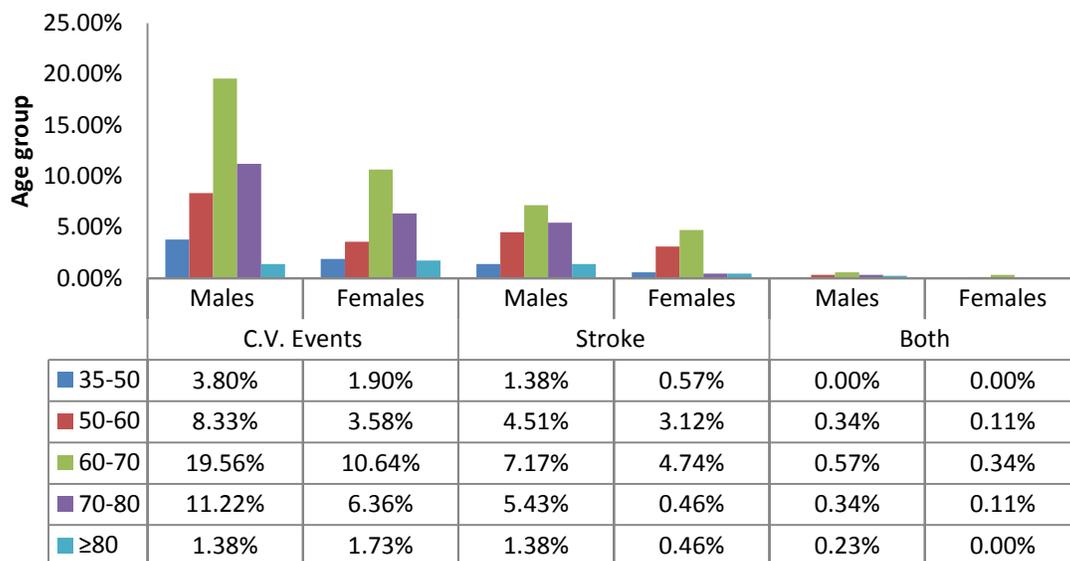


**Figure1: Gender wise distribution of Cardiovascular events & Stroke types**

Stroke ranking 3<sup>rd</sup> in mortality behind heart disease and cancer. It is the most frequent clinical manifestation of cerebral blood vessel disease particularly in elderly. The incidence of stroke rises gradually with age and in many developing countries, the incidence is rising because of the

pathology such as IHD, cardiac failure, COPD, osteoarthritis and visual impairment.<sup>3</sup>

Development of cardiovascular events and stroke directly related to the non- modifiable risk factors such as age, gender, family history and modifiable



**Figure: 2 Age wise distribution of Cardiovascular events and Stroke types**

**Table1: Frequency of risk factors for Cardiovascular events and Stroke types in the whole study group**

Risk factors	C.V.Events		Stroke	
	Males	Females	Males	Females
Family history	92	71	37	18
Cigarette smoking	313	0	126	0
Tobacco usage	142	163	32	35
Alcohol consumption	165	0	93	0
HTN	396	215	185	86
Dyslipidemia	204	137	91	36
Diabetes	287	188	127	52
Obesity	306	495	163	71

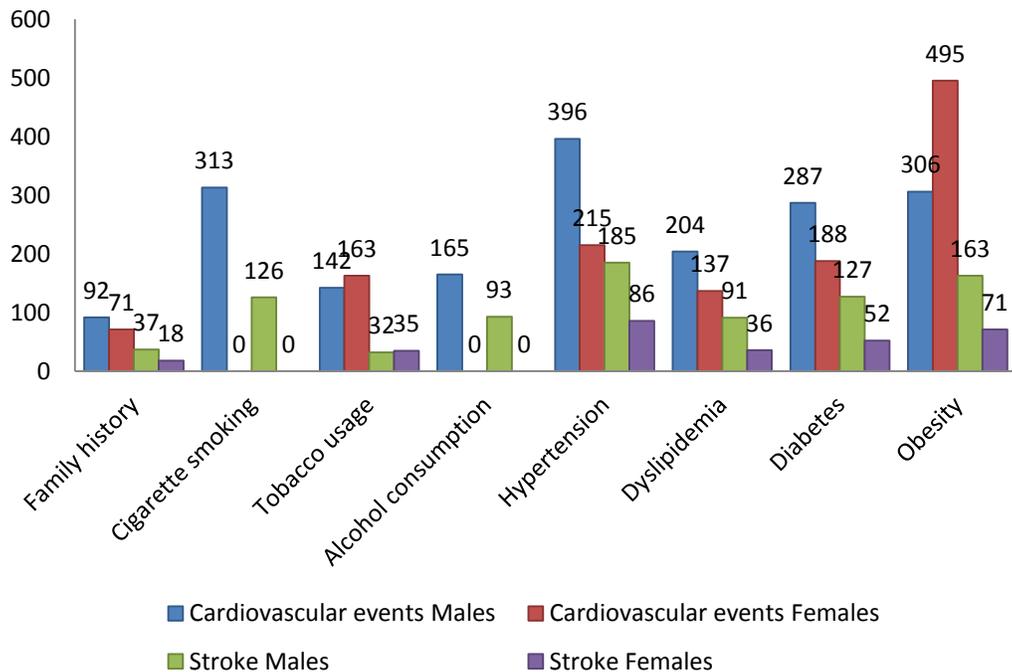
risk factors such as cigarette smoking , hypertension, congestive heart failure, dyslipidemia, diabetes, obesity, tobacco usage , alcohol consumption, physical inactivity and unhealthy diet.<sup>4</sup>

Drugs that interfere with plate let function can be classified into 3 categories: Those that prevent cardiovascular disease (Primary prevention), those that treat an acute disease, and those that treat a chronic disease (Secondary prevention).There are both oral (taken by mouth) and intravenous (given through a vein) drugs that inhibit platelet function and are used to treat patients with cardiac and cerebrovascular diseases.<sup>5</sup> Most popular drugs used worldwide for the prevention of cardiovascular incidents and stroke are antiplatelets an d

anticoagulants. Antiplatelets drugs such as Aspirin, Clopidogrel, Ticlopidine, Dipyridamole, and anticoagulants such as Heparin, Low Molecular Weight Heparin (LMWH), Warfarin, & Vitamin k.

In high-risk patients, Aspirin decreases the risk of 1<sup>st</sup> time heart attack by more sthan 20%. After a heart attack, aspirin can reduce the risk of a recurrent heart attack by about 30%. Similarly, an antiplatelets agent can reduce the risk of recurrent stroke or transient ischemic attack (TIA) and help to prevent the blockage (occlusion) of vessels that have previously been opened (Patency) with a stent.<sup>6</sup>

In the most recent meta-analysis<sup>7</sup> of the Antithrombotic trialists collaboration, allocation of high-risk patients to a prolonged course of



**Figure3: Frequency of risk factors for Cardiovascular events and Stroke types in the whole study group**

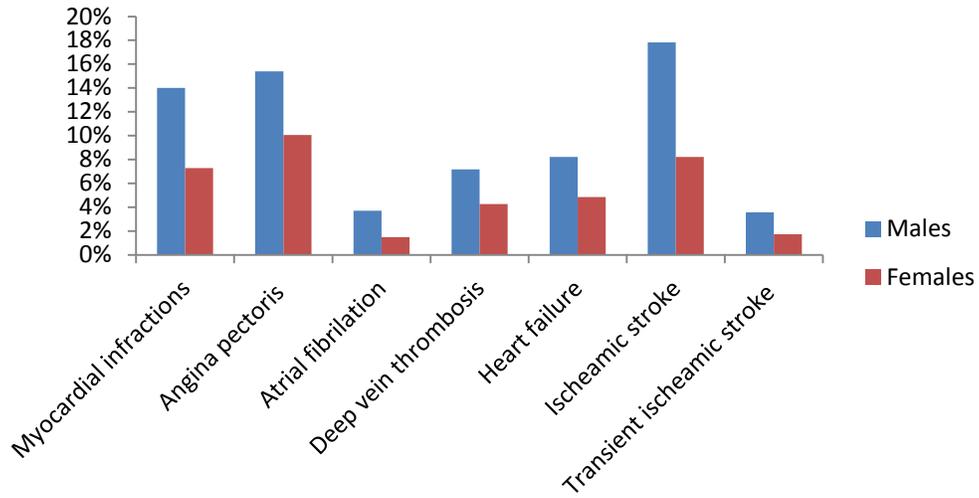


Figure4: Frequency of Cardiovascular events and Stroke types in the whole study group

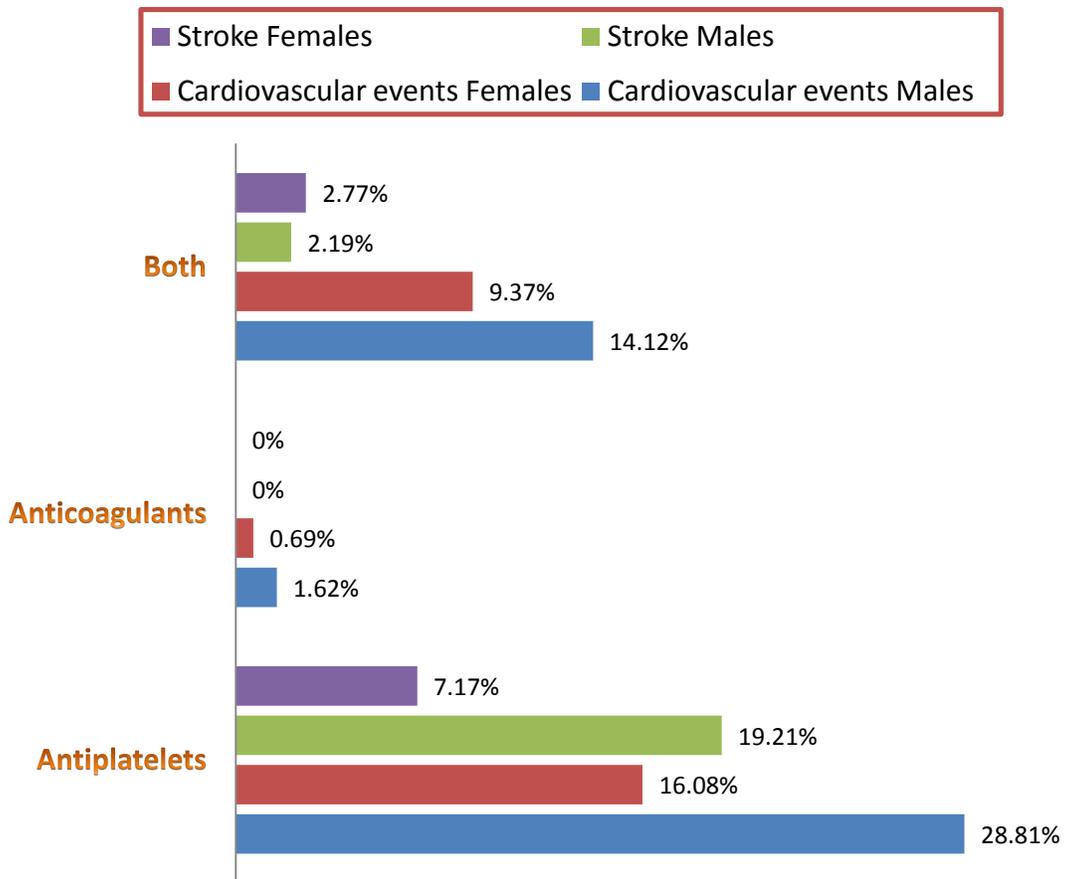


Figure5: Frequency of use of Antiplatelets and Anticoagulants in Cardiovascular events and Stroke

antiplatelet therapy reduced the combined outcome of nonfatal myocardial infarction, non-fatal stroke or

vascular death ('serious vascular events') by about 25%. Non-fatal myocardial infarction was reduced by

1/3<sup>rd</sup>, non-fatal stroke by 1/4<sup>th</sup> and vascular mortality by 1/6<sup>th</sup>. Absolute reductions in the risk of having a serious vascular event were 36 per 1000 treated for 2 years, among patients with previous myocardial infarction; 38 per 1000 patients treated for 1 month among patients with acute myocardial infarction; 36 per 1000 treated for 2 years among those with previous stroke or TIA; 9 per 1000 treated for 1 month among those with acute ischaemic stroke and 22 per 1000 treated for 2 years among other high-risk patients, including those with stable angina, peripheral arterial disease and atrial fibrillation.

### **AIM & OBJECTIVE OF THE STUDY**

The present study aimed that to evaluate the utilization of antiplatelets & anticoagulants drugs in the prevention of cardiovascular events & stroke types in elderly patients.

- To study the prescribing pattern of antiplatelets and anticoagulants drugs in cardiovascular events & stroke types.
- To study the risk factors for cardiovascular events and stroke types in elderly patients.

### **MATERIALS & METHODS**

The present prospective observation study was carried out in the department of general medicine IP of Rajiv Gandhi institute of medical sciences (RIMS), kadapa, AP, A 800 bedded multidisciplinary tertiary care teaching hospital. A total of 864 subjects were studied in 1yr (October 2012- October 2013) of study duration & the patients are enrolled to the study according to the inclusion & exclusion criteria.

### **INCLUSION CRITERIA**

Patients who were diagnosed as cardiovascular events and/or stroke types with the prescription orders.

### **EXCLUSION CRITERIA**

Patients who are not under treatment of antiplatelets & anticoagulants drugs irrespective of age and gender. Pregnant & lactating women

### **STUDY MATERIALS**

A well-structured specially designed patient data collection proforma was used to collect all the necessary & relevant baseline information of patients which includes demographic details, present /past medical & medication history etc., the

drugs given on SOS basis was also taken into consideration.

### **STATISTICAL ANALYSIS**

Results were expressed in percentage and drugs prescribed for cardiovascular events & stroke types were also observed based on column statistics.(p-value< 0.05 was considered as statistically significant.

### **RESULTS**

A total of 864 patients were recruited under inclusion criteria & were followed for the present study those are prescribed with antiplatelets and anticoagulants drugs.

### **DISCUSSION**

The growth of heart diseases is dependent on a number of interlinked factors such as aging, changing lifestyles and food habits, and other rapidly evolving socioeconomic determinants across developing nations. All these factors together create a domino effect, resulting in increased incidence of cardiovascular diseases. Socioeconomic determinants like improved access to healthcare, higher income levels and globalization, and urbanization drive increases in CVD risk factors. Improved healthcare in India has increased the average life expectancy from 48.8 years in 1970 to 64.1 years in 2009, resulting in a growing aging population which faces an increased risk of heart diseases. Higher income levels and globalization have induced a nutritional shift resulting in the rise of unhealthy food and decreased intake of fruits and vegetables. India's rapid urbanization, with 31.8% of Indians living in urban areas and the decadal growth rate for urban areas almost three times the rate in rural areas,<sup>8</sup> has led to a number of issues like reduced physical activity, unhygienic and overcrowded living conditions, growing levels of stress, and higher exposure to pollution. These socioeconomic determinants have fuelled the growth of risk factors – both modifiable and non-modifiable. Modifiable risk factors are those that can easily be changed to reduce the risk of the occurrence of the disease, while non-modifiable risk factors like age and genetic makeup can't be controlled. For example, the nutritional shift has moved a number of people to unhealthy eating habits. Between 1983 and 2004, while the per capita consumption of protein went down, the amount of fats intake increased by more than 25%, both in

**Table2: Frequency of use of Antiplatelets and Anticoagulants in Cardiovascular events**

Cv events	Antiplatelets (n=408)				Anticoagulants n=20)		Antiplatelets+Anticoagulants (n=232)	
	Aspirin (n=112)		Aspirin + Clopidrogel (n=296)		LMWH (n=20)		Aspirin + clopidrogel+low molecular weight heparin (n= 232)	
	Male (n=78)	Female (n=34)	Male (n= 183)	Female (n= 113)	Male (n= 14)	Female (n= 6)	Male (n= 143)	Female (n= 89)
Myocardial infraction (MI)	41 (4.74%)	18 (2.08%)	80 (9.25%)	45 (5.2%)	---	---	---	---
Angina pectoris (AP)	---	---	72 (8.33%)	43 (4.97%)	---	---	60 (6.94%)	44 (5.09%)
Atrial Fibrillation (AF)	---	---	---	---	10 (1.15%)	4 (0.46%)	22 (2.54%)	9 (1.04%)
Deep vein thrombosis (DVT)	---	---	---	---	4 (0.46%)	2 (0.23%)	58 (6.7%)	35 (4.05%)
Heart failure (HF)	37 (4.28%)	16 (1.85%)	31 (3.58%)	25 (2.89%)	---	---	3 (0.34%)	1 (0.11%)
Total	78 (9.02%)	34 (3.93%)	183 (21.18%)	113 (13.07)	14 (1.6%)	6 (0.69%)	143 (16.55%)	89 (10.3%)

urban and rural areas.<sup>9</sup> This, coupled with reduced physical activity, gives rise to intermediate risk factors such as hypertension and obesity. Smoking, another key risk factor, has also increased significantly. Around 14% of Indians smoke daily, and increasingly younger people are taking up smoking. Smoking is a major cause of atherosclerosis, and doubles the chances of mortality from heart diseases. The result is an increasing number of cases with intermediate risk factors and comorbidities – diabetes, hypertension, dyslipidaemia, and obesity. India is not just the diabetes capital of the world with more than 50 million patients, it also has the highest prevalence of metabolic syndrome and obesity - 20 million Indians are obese today with 70 million projected by 2025; 20% of Indians suffer from hypertension.<sup>11</sup> These factors together have accelerated the growth of cardiovascular diseases in India as well as the mortality levels from these diseases.<sup>12</sup>

- Globalization
- Urbanization
- Improved healthcare
- Unhealthy diet
- Reduced physical activity
- Stress

- Ageing population
- Diabetes
- Dyslipidaemia
- Hypertension
- Obesity
- Smoking
- Increase in the number of CVD cases
- Earlier onset of disease
- Higher mortality

In the present study the incidence of stroke and cardiovascular events was found to be more in male patients when compared to the female patients. The occurrence of CV diseases and stroke were more in the age group of 60-70 years (43.05%) followed by 50-60years (23.9%). The major risk group was found in the male patients with a habit of cigarette smoking and none of the female patients were smokers in the study. Smoking is followed by the associated co-morbid conditions such as HTN, Obesity and Diabetes respectively. And there is 15.39% of male patients were with Angina, 14% were with M.I and 17.82% males were with Ischemic stroke. The frequencies in females were 10.06%, 7.29% and 8.21% respectively. The usage of antiplatelets was more when compared to the usage of anticoagulants in both CVD and Stroke.

For secondary prevention (in patients with previous MI, Stroke or unstable angina) , aspirin definitely reduces subsequent MI, Stroke and cardiovascular death and in 1985 , the US food & drug administration approved the prescription labeling of aspirin for the treatment of patients with a previous MI or unstable angina.<sup>13</sup>

alone in preventing ischemic stroke, MI, vascular death or rehospitalization for ischemic events.<sup>15</sup>

Among eligible ischemic stroke patients 85+ years of age only 11% received pharmacological DVT prophylaxis, 78% received antiplatelets medications, 76% received anticoagulants for atrial fibrillations & 70% received antithrombotic at discharge.<sup>16</sup>

**Table3: Frequency of use of Antiplatelets and Anticoagulants in Stroke**

	Antiplatelets (n=228)				Anticoagulants (n=0)		Antiplatelets+Anticoagulants (n=43)	
	Aspirin( n=50)		Aspirin+ clopidogrel (n=178)		LMWH (n=0)		Aspirin + Clopidogrel+ LMWH (n=43)	
Stroke	Male (n=39)	Female (n=11)	Male (n=127)	Female (n=51)	Male	Female	Males (n=19)	Female (n=24)
Ischeamic stroke	39 (4.51%)	11 (1.27%)	103 (11.92%)	42 (4.86%)	-----	-----	12 (1.38%)	18 (2.08%)
TIA	-----	-----	24 (2.77%)	9 (1.04%)	-----	-----	7 (0.81%)	6 (0.69%)
Total	39 (4.51%)	11 (1.27%)	127 (14.6%)	51(5.9%)	0	0	19 (2.1%)	24 (2.77%)

In the pre sent study among antiplatelets the usage of combination of Aspirin + Clopidogrel (14.46%) was more compared to Aspirin (6.8%) alone in M.I. And in Heart failure that Aspirin + Clopidogrel (6.48%) was more compared to aspirin (6.13%). The usage of antiplatelets + anticoagulants (Aspirin + Clopidogrel + LMWH) was observed in the regular practice for treatment of Angina(12.03%) and DVT(10.76%). The anti-coagulant alone was used in Atrial fibrillation and DVT. The use of Aspirin + Clopidogrel combination was found to be frequent in case of Ischeamic stroke (20.6%).

However, the Taiwanese patients in the REACH registry received antiplatelets therapy more frequently than the patients from other geographical regions (84.7% vs 78.6%) – prescribed in 85.28% of patients with cerebrovascular diseases of these, 55% received aspirin and the remaining patients received other antiplatelet agents.<sup>14</sup>

In a recent trial, more than 7,000 patients with a previous stroke received clopidogrel and aspirin or clopidogrel alone for 18months. Combination therapy was not more effective than Clopidogrel

## CONCLUSION

Our study shows that the total % of treated patients with an indication for antiplatelets and/or anticoagulant therapy.

Our results demonstrated that antiplatelets use may beneficial to the 2<sup>o</sup> prevention of ischemic stroke in the patients with IHD history , especially in those with risk of cardiovascular diseases, DM, HTN, AF & MI etc.,

Our study findings suggest that combination therapy may be more beneficial than monotherapy in the prescribing of clopidogrel- aspirin combination may increased substantially during the study period.

OAC drugs are prescribed less frequently with the combination of antiplatelets and rarely among older people with AF & TIA.

So it is necessary to develop Quality improvement measures to educate physicians of the evidence regarding antiplatelets & anticoagulant drugs for cardiovascular events and stroke. It is necessary to develop educational programs among general practitioners concerning current

recommendations for pharmacological cardiovascular and stroke prevention.

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