

Usage pattern and rationality of Antiplatelet, Anticoagulant, and Fibrinolytic use in the Cardiac Care Unit of a tertiary care teaching hospital of rural Bengal

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Abstract

Introduction: There is widespread use of antiplatelet agents, fibrinolytics and anticoagulants among patients admitted with cardiac emergencies in the Cardiac care unit (CCU) of this tertiary care teaching hospital. However there are no studies that give an in depth understanding of the extent and rationality of such use. **Objective:** The objective of this study was to outline the extent and rationality of use of these agents among the patients admitted to the CCU. **Design:** Record based Cross sectional study. **Methods:** We assessed the prescriptions and management given to patients admitted to our hospital with cardiac emergencies between three months from the month of February to month of April in the year 2018. The magnitude of use of antiplatelet agents, anticoagulants and fibrinolytics was assessed and rationality of such use was evaluated on a case-to-case basis. **Results:** Total 47 patients admitted in the CCU with cardiac emergencies, an age range of 18 to 72 years, 48.9% were male. Acute coronary syndrome (including unstable angina, NSTEMI, and STEMI) made up for 59.57% of the diagnosis. Of the 47 patients 4 died and rest were discharged. All patients with ACS were given loading dose of 300mg or 325 mg Aspirin and by chewing and 300mg of Clopidogrel and maintenance dose of either 75mg or 150mg Aspirin orally. All ACS patients got 75 mg clopidogrel as maintenance dose. Another 8.51% patient got Warfarin with Clopidogrel combination for stroke prevention in Atrial fibrillation. Nearly half (48.93%) patients received LMWH and 8.51% got only Warfarin 2 mg orally. Around a quarter of the patients (21.27%) received Streptokinase 1.5 IU by infusion as fibrinolytic therapy. On basis of Harrison's Text Book 19th edition and ACC/AHA Practical guidelines shows that use of Warfarin due to Atrial fibrillation in 8.51% patient was rational because warfarin is superior than antiplatelet for stroke prevention. Use of Aspirin and Clopidogrel as antiplatelet was rational. All fibrinolytics were also used rationally. **Conclusion:** To conclude, in most of the patients studied antiplatelets, fibrinolytics and anticoagulant were used rationally and in all the patients.

Key Word : Antiplatelet, Fibrinolytic, Anticoagulant, CCU

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Introduction

Cardiovascular diseases (CVD) consist of diseases of

both heart and blood vessels. So we can categorize it into coronary heart disease (CHD), coronary artery disease (CAD), and acute coronary syndrome (ACS) broadly [1]. CHD is a major cause of death and disability in developed countries [2]. Although the mortality for this condition has gradually declined over the last decades in western countries, it still causes about one-third of all deaths in people older than 35

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years [3]. Of the 56.9 million deaths worldwide in 2016, more than half (54%) were due to Ischaemic heart disease and stroke and was accounting for a combined 15.2 million deaths in 2016. These diseases have remained the leading causes of death globally in the last 15 years [4]. Nearly two-thirds of the burden of NCD mortality in India is currently contributed by CVD-related conditions [5]. The office of the Registrar General of India (RGI) has periodically reported data on cardiovascular mortality rates in India [6]. These data have been summarized as circulatory system deaths in the Medical Certification of Cause of Deaths reports, and in 1980s and 1990s it was reported that CVD led to 15%-20% of deaths in the country[7]. An increasing trend in proportionate CVD mortality has been reported, with 20.6% deaths in 1990, 21.4% in 1995, 24.3% in 2000, 27.5% in 2005, and 29.0% in 2013[8]. Deaths from heart-related disease among rural Indians have surpassed those among urban Indians. A combination of poverty, ignorance, lack of access to quality care and smoking may be driving heart disease-related deaths in India. Anticoagulant, Thrombolytic, and Anti-Platelet Drugs are used in CCU to treat strokes, myocardial infarctions, pulmonary embolisms, disseminated intravascular coagulation (DIC) and deep vein thrombosis (DVT) --- all potentially life-threatening conditions. Non-ST elevation ACS comprises unstable angina (UA) and NSTEMI segment elevated myocardial infarction (NSTEMI). All patients presenting with ACS/NSTEMI should receive aspirin plus any one of these three (Clopidogrel/Prasugrel/Ticagrelor) agents. Anticoagulation is recommended for all patients in addition to antiplatelet agents[9,10]. An increasing number of anticoagulants (previously referred to as antithrombins) are available and include unfractionated heparin (UFH), low molecular weight heparin (LMWH), fondaparinux and bivalirudin. The choice of anticoagulation depends on the risk of ischemic and bleeding events and choice of the initial management strategy (e.g. urgent invasive, early invasive or conservative)[9]. Reperfusion therapy is the cornerstone of STEMI management and should be instituted in all patients presenting within 12 hours of onset of symptoms[9-11]. The most efficacious reperfusion therapy available is timely primary PCI, but it may not be the most effective in the Indian context, given the relative paucity of PCI-capable centers[9]. Moreover, since most of these centres are located in urban areas, the distances involved in transporting patients from rural areas become prohibitive. Fibrinolytic therapy therefore remains the most practicable reperfusion strategy for India. Nearly

60% of patients receive fibrinolysis with streptokinase as initial treatment[12]. For patients with AF and an elevated CHA2DS2-VASc score of 2 or greater in men and 3 or greater in women, oral anticoagulants are recommended including Warfarin, Dabigatran, Rivaroxaban, Apixaban, Edoxaban. For patients with AF who have mechanical heart valves, warfarin is recommended. Selection of anticoagulant therapy should be based on the risk of thromboembolism, irrespective of whether the AF pattern is paroxysmal, persistent, or permanent[13].

Methodology

It was a record based and cross-sectional study. The study was done in Bankura Sammilani Medical College & Hospital, Bankura, West Bengal in rural Bengal for the patients admitted in the period of three months from the month of February to month of April in the year 2018. The BHT of the patient admitted in CCU with any kind of health problem was studied for the use of anti-platelet, anti-coagulant and fibrinolytic drug.

Inclusion criteria

We have included all patients who were given the study drugs in CCU in that time period, discharged or died or shifted to the step down unit.

Exclusion criteria-

- Sick patients those were discharged within 24 hours of CCU admission.
- The patients were given other treatment except the study drugs.

Objective-

- To outline the extent of use of Anti platelet, Anti-coagulant and Fibrinolytic among the patients admitted to the CCU
- To assess the rationality of each of these drug according to the ACC/AHA, American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

The BHT of the patients met our inclusion and exclusion criteria were studied thoroughly and the data for demographic character, diagnosis and given drug was collected in a XL sheet. Then analysis was done by using Graph Pad Prism Version 5 software. Arithmetic mean and standard deviation were measured. Same time we have measured the use of the study drugs in accordance to the guidelines, like-

- 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction
- 2018 AHA/ASA Stroke Early Management Guidelines

- 2019 AHA/ACC/HRS Focused Update of the 2014 Guideline for Management of Patients with Atrial Fibrillation
- 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes

Then we have studied the rationality of usage pattern of anti-platelet, anti-coagulant and fibrinolytic in reference with the guidelines for their appropriateness. Ethics committee approval taken and the results analysed.

Result

In our study we found all age group of people admitted to the CCU with a various type of problems who were given the study drugs. Gender distribution is almost equal. Age ranges from 18-72 year. Mean of age was 54.89 with a Standard Deviation of 15.8. 48.9% patient population were male in the study. We found arrhythmia and ischaemic heart disease for the causation of admission in CCU those who were given anti-platelet, anti-coagulant and fibrinolytic agent. Unstable angina comprised of 11%, ST segment elevated MI was 30%, Non ST segment elevated MI was 19% of admission rate in CCU in that time period. In case of arrhythmia, Atrial fibrillation, Complete heart block and Paroxysmal supraventricular tachycardia was associated with admission rate of 8%, 21% and 11% respectively (Fig-1). Aspirin and Clopidogrel were used as antiplatelet agents. Loading dose was 300 mg and maintenance dose was 75 mg in case of both the drug. Both Aspirin and Clopidogrel were used in 59.57% patient as loading dose. Clopidogrel was used as maintenance dose slightly higher than Aspirin (68.09%

vs 59.57%) (Fig-2). Anti-coagulant used was limited to oral Warfarin 2 mg and parenteral Low molecular weight heparin (LMWH) 60 Unit and 40 Unit. 80.84% LMWH and 8.51% Warfarin were used in case of anti-coagulant therapy. Only fibrinolytic was used Streptokinase. Only in case of treatment of STEMI standard dose was given in 21.27% of study population (Fig-3). All the patients of STEMI got fibrinolytic who reached the hospital within first 3 hours. Those who came with STEMI to CCU after 6 hour, they either did not get Fibrinolytic or got it outside from where they were referred. 4.25% got Streptokinase within 1st hour and 21.27% within 3 hours and with STEMI & 8.51% patient did not get any fibrinolytic (Fig-4). Among other drug in the aforesaid patient, Pantoprazole was used highest (78.72%) followed by Metoprolol (61.7%), and Ranitidine (59.57%). Atorvastatin, Sorbitrate, Glyceryl-tri-nitrate, Ondansetron, Furosemide and Alprazolam, Morphine, Tramadol, Verapamil, Nicorandil, Amiodarone, Promethazine, Aldactone and Linezolid was also used frequently (Fig-5). LMWH was used for STEMI, NSTEMI, Unstable angina and DVT prophylaxis for the patients prepared for Permanent Pace Making. Oral anticoagulant Warfarin was used for Stroke prevention in patients of AF only. As the dual antiplatelet agent, Aspirin and Clopidogrel loading dose was used for STEMI, NSTEMI and Unstable angina. Maintenance dose was used for these drugs for the same purpose. As oral anticoagulant, only Warfarin was used and all the patients maintained INR between 2-2.5. Antiplatelet and anticoagulant drugs did not show any recorded adverse events. 21.27% among all patients received Streptokinase as fibrinolytic (20% developed hypersensitivity reaction).

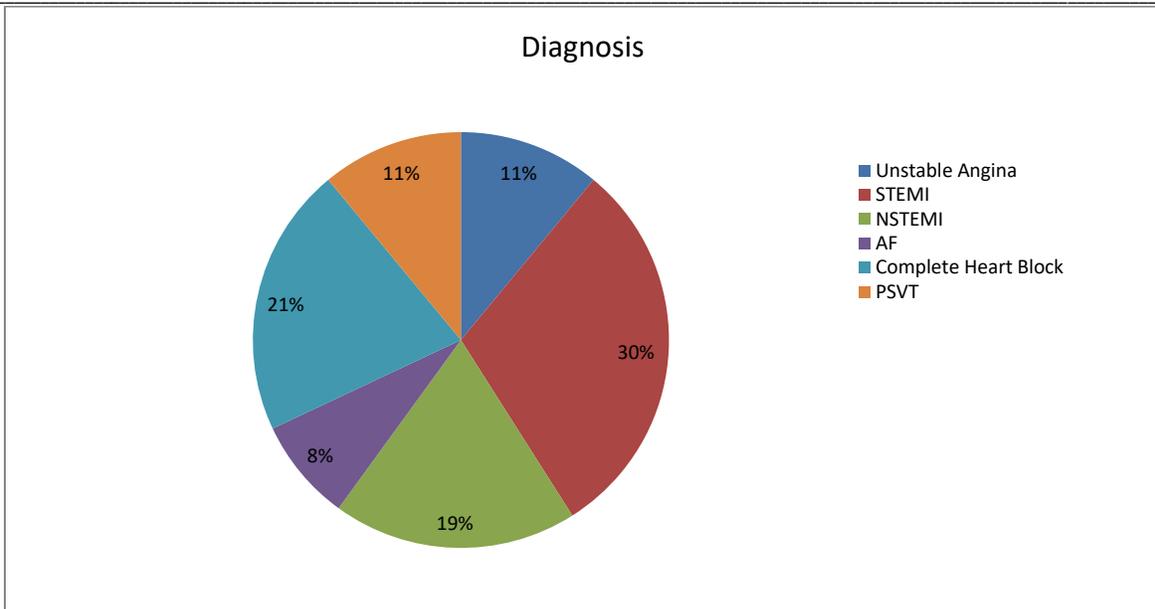


Fig 1:Diagnosis

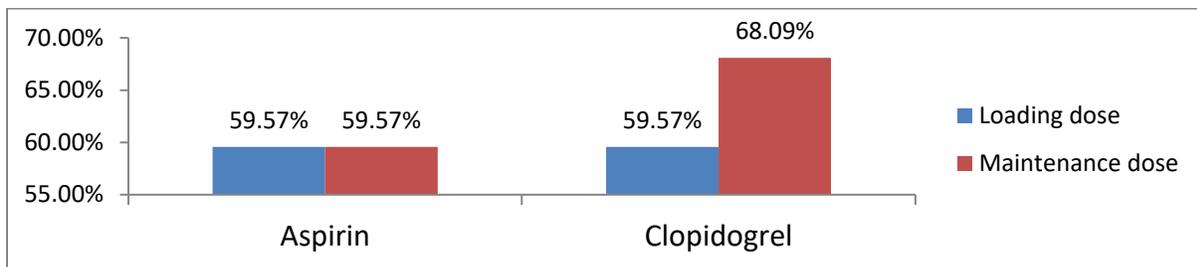


Fig 2:Anti-platelet therapy

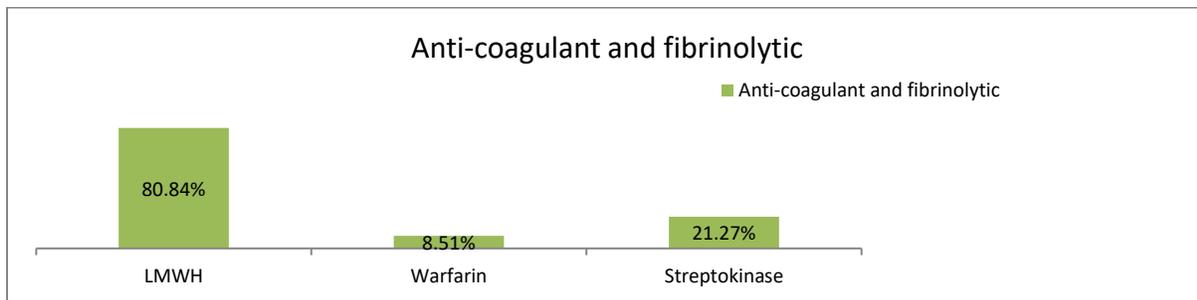


Fig 3:Anti-coagulant and fibrinolytic

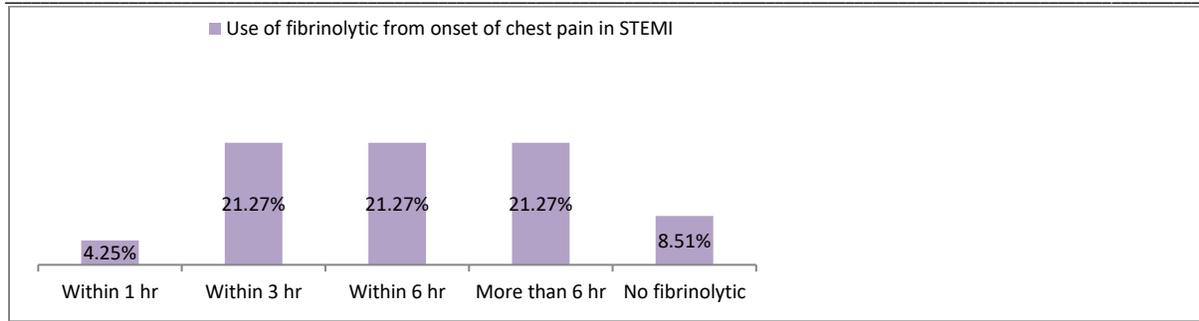


Fig4: Use of fibrinolytic from onset of chest pain in STEMI

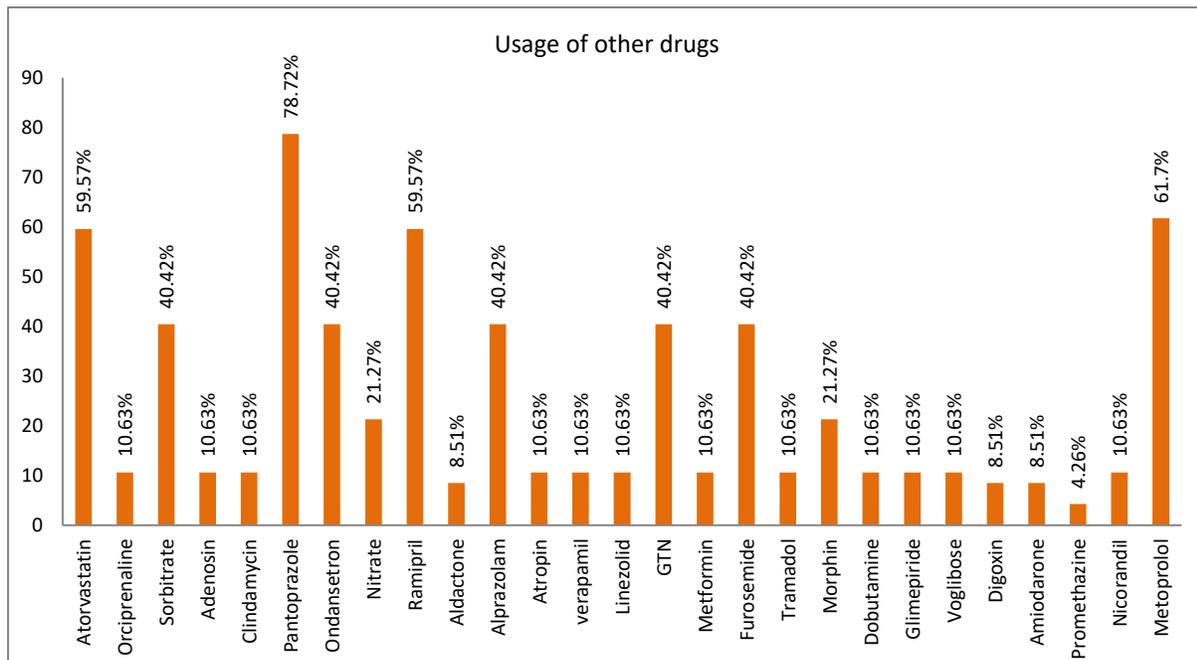


Fig 5:Usage of other drugs

Discussion

Data from 12,665 patients with ACS were analyzed through the use of data from the Global Registry of Acute Coronary Events (GRACE).The timing of use of antithrombotic and antiplatelet agents in patients with ACS varied among therapies. An increase in the use of LMWHs, oral anticoagulants, and thienopyridines after the first 24 hours was revealed, whereas the use of UFH, aspirin, and GP IIb/ IIIa inhibitors declined. During hospitalization, 25% of patients were given three, 13% four, and 4% five antithrombotic and/or antiplatelet agents. At discharge, aspirin was used in 87.2% of patients and thienopyridines in 28.6%. Approximately 91% of patients received aspirin,

ticlopidine, or clopidogrel or a combination of aspirin and a thienopyridine. Combined therapy of aspirin and ticlopidine or clopidogrel was used in 21.0% of all patients with ACS[14].In our study Anti-coagulant used was limited to oral Warfarin 2 mg and parenteral Low molecular weight heparin (LMWH) 60 Unit and 40 Unit. 80.84% LMWH and 8.51% Warfarin were used in case of anti-coagulant therapy. The reason behind this is that only hospital supplied medicine were used. Both Aspirin and Clopidogrel were used in 59.57% patient as loading dose. Clopidogrel was used as maintenance dose slightly higher than Aspirin (68.09% vs 59.57%). The use of anti-coagulant and antiplatelet was in accordance to the guideline of ACC/AHA in the patient of ACS other than STEMI

and arrhythmia [8,9]. Oral anticoagulant Warfarin was used for Stroke prevention in patients of AF only. As the dual antiplatelet agent, Aspirin and Clopidogrel loading dose was used for STEMI, NSTEMI and Unstable angina. Maintenance dose was used for these drugs for the same purpose. As single antiplatelet agent only Clopidogrel was used in 8.51% patients along with Warfarin for Stroke prevention is also rational as for stroke prevention it is better choice than Aspirin [15]. In a study at Department of Medicine, Rajah Muthaiah Medical College and Hospital, Annamalai University, Chidambaram, Tamil Nadu, India out of 100 patient 92 were given Streptokinase, 4, 2 and 2 patients got Reteplase, Tenecteplase and Reteplase respectively [16]. In a study conducted in Iran [17], the mean time interval between arrival at the hospital and electrocardiogram (ECG) assessment was 6.30 min, taking ECG and patient's admission was 21.6 min and transferring the patient from admission to CCU ward was 31.9 min. The time between transferring the patients to CCU ward and fibrinolytic administration order and the time between its ordering and infusion was 31.2 min and 14.0 min respectively. In our study among 30% of STEMI patients, 4.25% got Streptokinase within 1st hour and 21.27% within 3 hours and with STEMI 8.51% patient did not get any fibrinolytic. Surprisingly no patient attended the hospital between 3-6 hours from onset of chest pain. Probably they were treated at primary referral centre or referred elsewhere as our study place had no facility for cathlab. Other 8.51% patient did not get any fibrinolytic as they attended Hospital beyond the recommended Door to Needle time. It was as per ACC/AHA guideline [18]. It was a short duration. Most importantly PTCA was not done till the study was conducted at BSMC & H. Only Government supply drugs were used. Investigation reports of all patients were not available.

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References

1. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. *Ann Transl Med.* 2016;4(13):256.
2. Roger VL. Epidemiology of myocardial infarction. *Med Clin North Am.* 2007;91(4):537-ix.
3. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe: epidemiological update. *Eur Heart J.* 2013 ;34(39):3028-34.
4. <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death>. Accessed on April 20, 2018.
5. Patel V, Chatterji S, Chisholm D et al. Chronic diseases and injuries in India. *Lancet.* 2011;377:413-28.
6. Registrar General of India, **Report on Medical Certification of Cause of Death 2013**, Office of the Registrar General, New Delhi, India (2015). Available at: www.censusindia.gov.in/2011-document/mccd_2013.pdf. Accessed April 21, 2018
7. Gupta R, Misra A, Pais P, Rastogi P, Gupta VP. Correlation of regional cardiovascular disease mortality in India with lifestyle and nutritional factors. *Int J Cardiol.* 2006 ;108(3):291-300.
8. Task Force for Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of European Society of Cardiology, Bassand JP, Hamm CW et al. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. *Eur Heart J.* 2007; 28(13) :1598-1660
9. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, Jaffe AS, Jneid H, Kelly RF, Kontos MC, Levine GN, Liebson PR, Mukherjee D, Peterson ED, Sabatine MS, Smalling RW, Zieman SJ; ACC/AHA Task Force Members; Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014 ;130(25):2354-94.
10. Von Beckerath N, Taubert D, Pogatsa-Murray G, Schömig E, Kastrati A, Schömig A. Absorption, metabolization, and antiplatelet effects of 300-, 600-, and 900-mg loading doses of clopidogrel: results of the ISAR-CHOICE (Intracoronary Stenting and Antithrombotic Regimen: Choose Between 3 High Oral Doses for Immediate Clopidogrel Effect) Trial. *Circulation.* 2005 Nov 8;112(19):2946-50.

11. Gislason GH, Jacobsen S, Rasmussen JN, Rasmussen S, Buch P, Friberg J, Schramm TK, Abildstrom SZ, Køber L, Madsen M, Torp-Pedersen C. Risk of death or reinfarction associated with the use of selective cyclooxygenase-2 inhibitors and nonselective nonsteroidal antiinflammatory drugs after acute myocardial infarction. *Circulation*. 2006;113(25):2906-13
12. GUIDELINES FOR THE MANAGEMENT OF CARDIOVASCULAR DISEASES IN INDIA .Part 1 .Ministry of Health & Family Welfare.Govt. of India, New Delhi. <http://clinical.establishments.gov.in/WriteReadData/149.pdf>. Accessed on April22,2018
13. January CT, Wann LS, Calkins H et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2019 ;74(1):104-132.
14. Budaj A , Brieger D, Steg, Ph G ,et al. Global patterns of use of antithrombotic and antiplatelet therapies in patients with acute coronary syndromes: insights from the Global Registry of Acute Coronary Events (GRACE).*American Heart Journal*.2003;146(6): 999 – 1006.
15. Kasper, Fauci, Hauser, Longo, Jameson, Loscalzo. *Harrison's Principles of Internal Medicine* ,19th edition,2015,McGraw Hill;1603.
16. Abraham MM, Reddi sudheer V, Periyasamy S, Gopalakrishnan G. Prescribing patterns of thrombolytics in acute MI and their outcome. *International Journal of Medical and Health Research*.2018;4(7):49-51.
17. Zeraati F, Homayounfar S, Esna-Ashari F, Khalili M. Fibrinolytic Therapy in CCU Instead of Emergency Ward: How It Affects Door to Needle Time?. *Int J Prev Med*. 2014;5(3):308-12.
18. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, Hochman JS, Krumholz HM, Kushner FG, Lamas GA, Mullany CJ, Ornato JP, Pearle DL, Sloan MA, Smith SC Jr; American College of Cardiology; American Heart Association; Canadian Cardiovascular Society. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction--executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction). *J Am Coll Cardiol*. 2004;44(3):671-719.

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