

A Pharmacoepidemiological Study Of Ticagrelor & Current Antiplatelet Agents In Acute Coronary Syndrome (ACS) & Percutaneous Transluminal Coronary Angioplasty (PTCA)

Authors

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Abstract

The incidence of ACS is rapidly increasing in India & causing high mortality. In the treatment pattern of ACS & PTCA, antiplatelet agents are prescribed as a part of maintenance & prophylactic therapy. Ticagrelor, a newer non-thienopyridine & first reversibly binding oral P2Y12 platelet inhibitor, provides faster, greater & more consistent platelet inhibition than clopidogrel. It is proved by the PLATO trials that it is more potent among anti platelet therapy used in ACS & PTCA patients. The utilization rate of various antiplatelet agents like Aspirin, Clopidogrel & Prasugrel compared to Ticagrelor in the common clinical practice was studied. The effect of contraindications, cost & Physician's preference related aspects play an important role in prescribing Ticagrelor in the ACS & PTCA patients, reasons for its poor usage in common clinical practice was studied.

Keywords: PLATO (Platelet Inhibition and Patient Outcome); Acute Coronary Syndrome (ACS); Percutaneous Transluminal Coronary Angioplasty (PTCA).

INTRODUCTION

Ticagrelor (Brilinta) was approved by the US Food and Drug Administration in July 2011 and is the first reversible oral P2Y receptor antagonist. Results from the platelet inhibition and patient outcomes (PLATO) trial showed ticagrelor provides faster, greater, and more consistent ADP-receptor inhibition than clopidogrel⁴

Ticagrelor is the first reversible P2Y₁₂ receptor antagonist to be available for clinical use. Compared with clopidogrel, ticagrelor elicits a faster and stronger antiplatelet effect and also displays greater clinical efficacy with a comparable rate of bleeding.

METHODOLOGY

Study Design:

A Prospective Observational unicentric study was carried out for studying the potential implementation of various antiplatelet agents & newer Anti platelet agent - Ticagrelor in ACS & PTCA patients.

Study Site:

The study was conducted in Department of Cardiology, Krishna Institute of Medical Sciences (KIMS) Hospital, (1-8-31/1, Minister Road, Secunderabad- 500 003, A.P, India), which is a 700 bedded multispeciality teaching hospital.

Study Period:

This study was conducted for six months, from Nov 2012 to April 2013.

Sample Size:

The sample size of the study was 150 .

Selection Criteria:

Inclusion Criteria:

1. All patients suffering with ACS in Inpatient wards & ICCU wards at KIMS hospital.
2. Adult Patients with ACS & PTCA

Exclusion Criteria

1. Outpatients of KIMS hospital.
2. Pediatric age group.
3. Pregnancy.

Tools used:

*Microsoft Excel 2010

*Graphpad Software – Quick Calcs.

Source of data:

*Patient data was collected prospectively from the case sheets in ICCU and Inpatient wards after taking consent from the patient to be included in the study.

Study Procedure

- A Prospective Observational study was carried out for studying the potential implementation of various antiplatelet agents & newer anti platelet agent - Ticagrelor in ACS & PTCA patients.
- Patient data collection form containing HAS BLED Score was designed to obtain the extent of usage of anti-platelet agents and the reasons for poor usage of Ticagrelor in common clinical practice.
- All patients dealing with the condition of ACS or undergoing PTCA in Inpatient wards & ICCU wards at KIMS hospital were identified and data including patient's demographic data, laboratory reports & medication chart was collected in patient data collection form, after taking the consent from the patients.
- Patients were checked out for the type of anti platelet agent being used & whether Ticagrelor is used or no was noted.
- ☐☐If Ticagrelor was not being used ,then the reasons for that like☐contraindications, cost related & Physician's preference related aspects were checked out.
- Finally the effect of contraindications, cost related & Physician's preference related aspects which play an important role in prescribing Ticagrelor in the Acute Coronary Syndrome (ACS) & Percutaneous Transluminal Coronary Angioplasty (PTCA) patients were analysed using statistical analysis.

PLAN OF WORK**The plan of work included**

Design of Patient data collection form

Design of Patient consent forms in English, Hindi, Telugu, Urdu

Approval from Institutional Ethics Committee

Identification of ACS & PTCA patients & enrolling for the study

Data including patient's demographic data, laboratory reports & medication chart was collected in patient data collection form

Type of anti platelet agent being used & Usage of Ticagrelor was noted

If Ticagrelor was not being used, then the reasons for that like contraindications, cost related & Physician's preference related aspects were checked out

Finally the effect of contraindications, cost related & Physician's preference related aspects which play an important role in not prescribing Ticagrelor in the Acute Coronary Syndrome (ACS) & Percutaneous Transluminal Coronary Angioplasty (PTCA) patients were analysed using statistical analysis

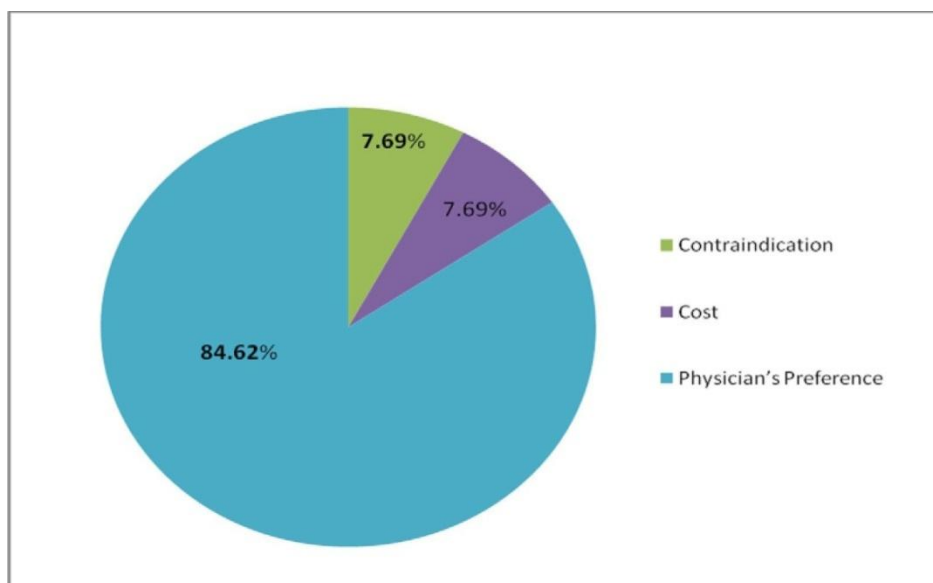
RESULTS & DISCUSSION

Reason for not prescribing the new antiplatelet drug – Ticagrelor was estimated among the patients of ACS- Medical therapy.

Table 1: Reason for not prescribing Ticagrelor in ACS - Medical therapy

Reason for not prescribing Ticagrelor in ACS - Medical therapy	No. of ACS - Medical therapy patients not prescribed with ticagrelor
Contraindication	7
Cost	7
Physician’s Preference	77
Total No. of ACS - Medical therapy patients not prescribed with ticagrelor	91

Figure 1 – Reason for not prescribing Ticagrelor in ACS - Medical therapy

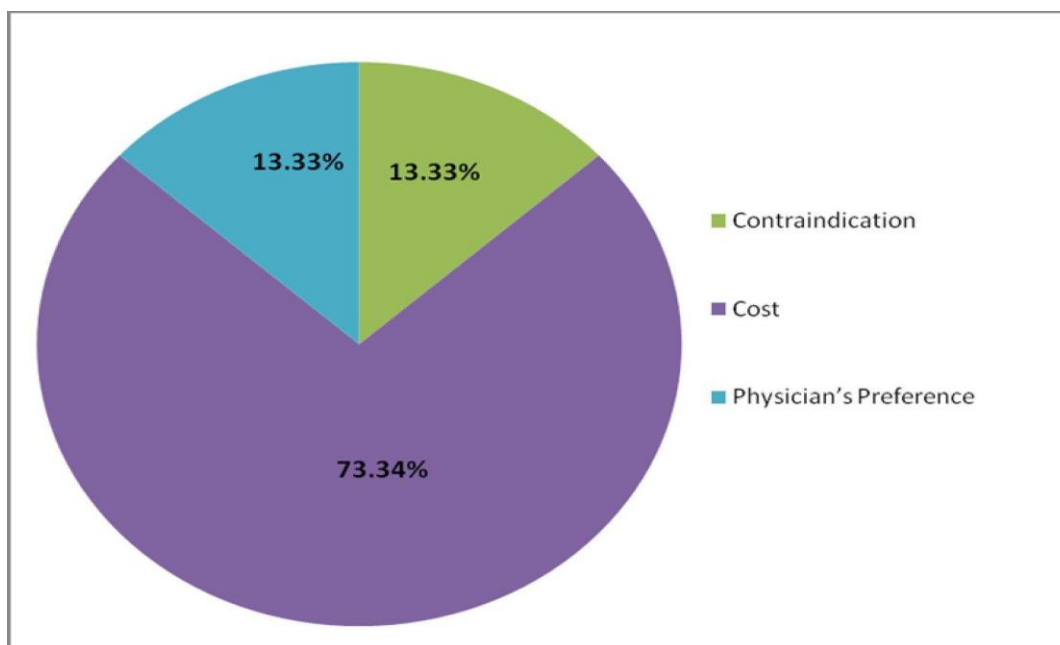


The main reason for not prescribing Ticagrelor in ACS - Medical therapy patients was found to be Physician’s Preference on prescribing the drugs.

Table 2: Reason for not prescribing Ticagrelor in PTCA –Stent (BMS)

Reason not prescribing Ticagrelor in PTCA –Stent (BMS)	No. of PTCA –Stent (BMS) patients not prescribed with ticagrelor
Contraindication	2
Cost	11
Physician’s Preference	2
Total No. of PTCA –Stent (BMS) patients not prescribed with ticagrelor	15

Figure 2- Reason for not prescribing Ticagrelor in PTCA –Stent (BMS)

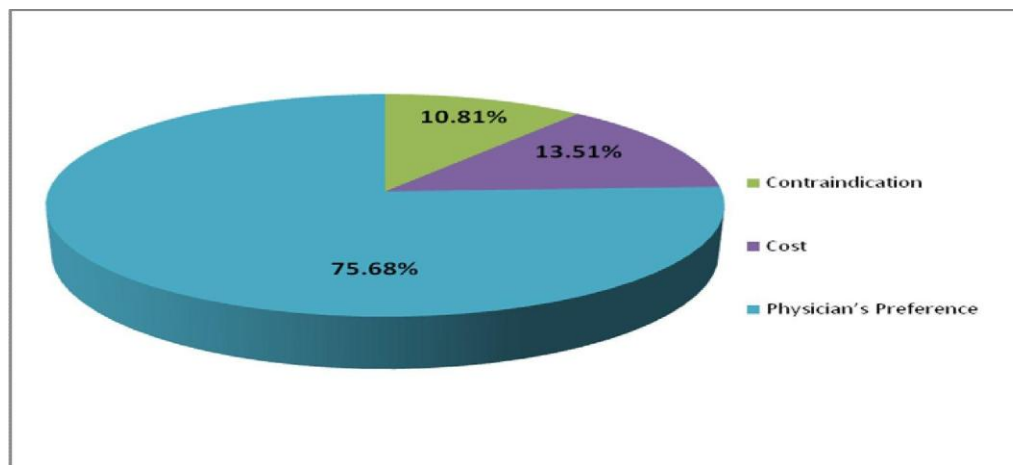


The main reason for not prescribing Ticagrelor in PTCA-Stent (BMS) patients was found to be the cost on prescribing the drugs Reason for not prescribing the new antiplatelet drug – Ticagrelor was estimated among the patients of PTCA – Stent (DES)

Table 3: Reason for not prescribing Ticagrelor in PTCA –Stent (DES)

Reason for not prescribing Ticagrelor in PTCA –Stent (DES)	No. of PTCA Stent (DES) patients not prescribed with ticagrelor
Contraindication	4
Cost	5
Physician’s Preference	28
Total No. of PTCA Stent (DES) patients not prescribed with ticagrelor	37

Figure 3 – Reason for not prescribing Ticagrelor in PTCA –Stent (DES)



The main reason for not prescribing Ticagrelor in PTCA-Stent (DES) patients was found to be the Physician’s Preference on prescribing the drugs

Table 4 : Reason for not prescribing Ticagrelor in ACS medical therapy , PTCA – Stent BMS & DES

Reason for not prescribing Ticagrelor	Patients of Medical therapy	Patients of PTCA–Stent (BMS)	Patients of PTCA–Stent (DES)	Total
Contraindication	7	2	4	13
Cost	7	11	5	23
Physician's Preference	77	2	28	107
Total	91	15	37	143

Table 4 a : Chi- square test to analyze the reason for not prescribing Ticagrelor in ACS - Medical therapy , PTCA –Stent BMS & DES

Observed value (O)	Expected value (E)	Observed value -Expected value (O-E)	(Observed value -Expected value) ² (O-E) ²	(Observed value -Expected value) ² / Expected value (O-E) ² / E
7	8.272727273	-1.272727273	1.619834711	0.195804196
7	14.63636364	-7.636363636	58.31404959	3.984189723
77	68.09090909	8.909090909	79.37190083	1.165675446
2	1.363636364	0.636363636	0.404958678	0.296969697
11	2.412587413	8.587412587	73.74365495	30.5662106
2	11.22377622	-9.223776224	85.07804783	7.580162517
4	3.363636364	0.636363636	0.404958678	0.12039312
5	5.951048951	-0.951048951	0.904494107	0.151989022
28	27.68531469	0.314685315	0.099026847	0.003576873
Chi- square value (χ^2) = 44.06497119				

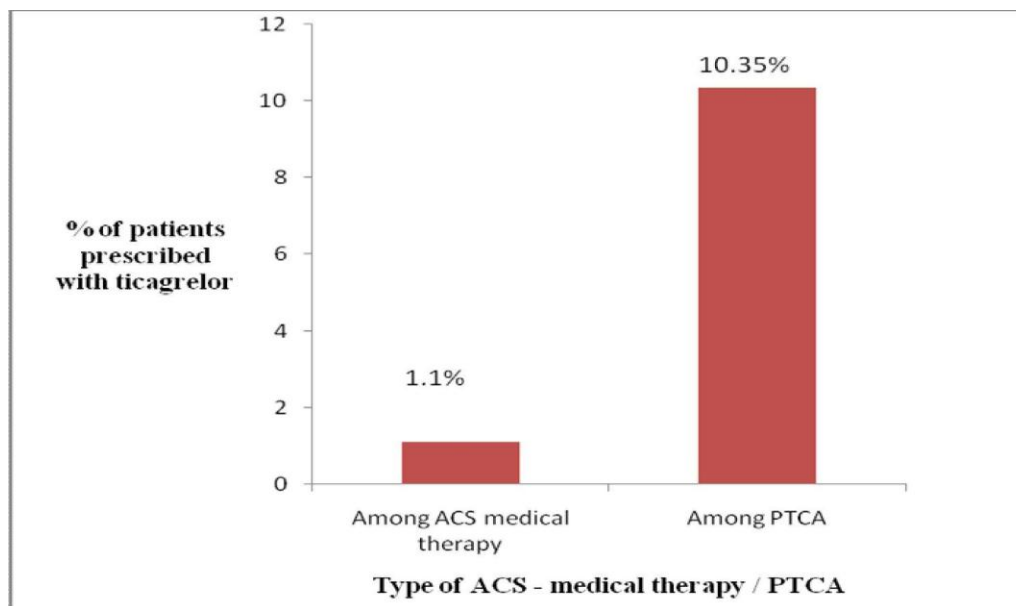
Chi- square value (χ^2) is 44.06497119 ; df (degrees of freedom) is 4 . The two-tailed P value is less than 0.0001.By conventional criteria, this difference is considered to be extremely statistically significant.

Thus the relation between reason for not prescribing the new antiplatelet drug – Ticagrelor among the patients of ACS- medical therapy , PTCA – stent BMS & DES was considered to be extremely statistically significant . The Prescribing rate of the drug Ticagrelor in ACS & PTCA patients were analysed

Table 5: Prescribing Rate of Ticagrelor in ACS & PTCA

Prescribing Rate of Ticagrelor in ACS & PTCA	No. of patients prescribed with ticagrelor	Total no. of patients treated with medical therapy & PTCA
Among ACS medical therapy	1	92
Among PTCA	6	58
Total No. of patients prescribed with ticagrelor in ACS & PTCA	7	150

Figure 5– Prescribing Rate of Ticagrelor in ACS & PTCA



The Prescribing Rate of Ticagrelor in PTCA patients was more (10.35%) compared to that of ACS -Medical therapy patients.

SUMMARY:

- In ACS & PTCA patients, Antiplatelet agents were prescribed as a part of the therapy.
- Aspirin, Clopidogrel & Prasugrel were prescribed more in the common clinical practice compared to the newer non thienopyridine drug, Ticagrelor.
- Among the enrolled patients for the study, patients of age group 66-70 were found to be more (18%).
- In the study population, male patients were found to be more (76.67%) compared to the female patients (23.33%).
- Among the Male patients, more were treated with medical therapy (78.26%) & among the Female patients more have undergone PTCA (25.86%).
- Comparing the PTCA with BMS stent & DES stent, it was observed that many of the male patients undergone PTCA with DES stent & many of the Female patients have undergone PTCA with BMS Stent (33.33%).
- Monotherapy was widely used in Females at the rate of (35.72 %), whereas Dual Anti Platelet therapy (combination therapy) was widely used in males at the rate of (80.76 %).
- Among the Medical therapy patients who were treated with Dual Anti Platelet therapy, most of them were given a combination of Aspirin + Clopidogrel (93.5%).
- Among the patients who have undergone PTCA with BMS Stent & treated with Dual Anti Platelet therapy, most of them were given a combination of Aspirin + Clopidogrel (80%).
- Among the patients who have undergone PTCA with DES Stent & treated with Dual Anti Platelet therapy, most of them were given a combination of Aspirin + Prasugrel (58.14%).
- The main reason for not prescribing Ticagrelor in ACS - Medical therapy patients was Physician's Preference (84.62%).
- The main reason for not prescribing Ticagrelor in PTCA –Stent (BMS) patients was Cost (73.34%) & in PTCA –Stent (DES) patients was Physician's Preference (75.68%) .
- The Prescribing rate of Ticagrelor in PTCA patients was more (10.35%) compared to that of ACS - Medical therapy patients.

CONCLUSION:

- Though **Ticagrelor**, is more potent among the anti platelet therapy used in the Acute Coronary Syndrome (ACS) & Percutaneous Transluminal Coronary Angioplasty (PTCA) it was underutilized mainly due to high cost and thus Physician's non preference.
- **Aspirin + Clopidogrel** combination was used more among the dual anti
- Platelet therapy (combination therapy) in patients treated with **Medical therapy** and **PTCA with BMS Stent**.
- **Aspirin + Prasugrel** combination was prescribed more among the dual anti Platelet therapy (combination therapy) in patients who have undergone PTCA **with Stent DES**.

FUTURE PROSPECTS FOR THIS STUDY:

This study can be further extended by evaluating the events or outcome of the study subjects by a follow up after 12 months of treatment with Ticagrelor & other anti platelet agents and shall be evaluated for its comparative reduction of total events like cardiovascular death , stroke, myocardial infarction .

LIST OF ABBREVIATIONS

- ACS : Acute Coronary Syndrome
- BMS : Bare Metal Stent
- COX-1 :Cyclo oxygenase -1 enzyme
- DES : Drug-Eluting Stent
- HAS BLED Score : Hypertension, Abnormal liver and kidney function test, Stroke, Bleeding, Labile INR, Elderly, Drugs
- NSTEMI :Non-ST segment elevation myocardial infarction
- PLATO : Platelet Inhibition and Patient Outcomes
- PTCA : Percutaneous transluminal coronary angioplasty
- STEMI : ST segment elevation myocardial infarction

ACKNOWLEDGEMENT

It is by the blessings of the **God Almighty** that we were able to complete our investigational studies successfully and present this work for which we are eternally indebted. We take the privilege to acknowledge

all those who have helped us in completion of this work. It is our proud privilege to express our heartfelt gratitude to our institutional guide **Dr. Lakshmi Sivasubramanian, M.Pharm, Ph.D., Bharat Institute of Technology (Pharmacy) & hospital guide Dr. Dayasagar Rao.V, Cardiologist, KIMS Hospital, Hyderabad** for their valuable guidance, cooperation, help and moral support throughout our project. We accolade our highest respect to **our parents** for their moral support and dedicated efforts to educate us to this level.

Lastly, we express our sincere thanks to one and all who have contributed directly and indirectly for completion of our research work.

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