



CODEN [USA]: IAJ PBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.1439050>Available online at: <http://www.iajps.com>

Research Article

**A STUDY ON RESISTANCE OF CLOPIDOGREL: INCIDENCE
OF CONFLICT OF DUAL ANTIPLATELET THERAPY AFTER
CORONARY INTERVENTION**¹Dr. Shumaila Malik, ²Dr. Huma Hafeez, ³Naureena Munawer¹Holy Family Hospital, Rawalpindi. PMDC No. 82598-P²Women Medical Officer, BHU Misrial, Rawalpindi. PMDC No. 81549-P³Nishter Medical College**Abstract:**

Background: The basic of managing coronary artery ailment in coronary interference is dual antiplatelet therapy (APD). In our influenza the pattern of resistance in contradiction of clopidogrel is unidentified.

Objective: Assessment of the occurrence of hypoactivation / resistance to Clopidogrel in people of Pakistan after percutaneous coronary intervention (PCI) is the main purpose of this study.

Place and duration of study: Present research paper was completed in the period of one year from April 2017 to March 2018 at the venue of Jinnah hospital, Lahore.

Material and Methods: Patients reported one month earlier before they undergo from PCI after informed consonance. In addition to their routine medications each and every patient was medicated with Clopidogrel 75 mg and Aspirin 75 mg in the intervals of 12 hours in a day and also 5 to 6 hours earlier to PCI medicated them with clopidogrel 600 mg. Blocking analysis test was performed as P2Y12 and samples of blood were also collected from all selected patients. Time for the test was calculated in integers of seconds known as "Closing Time". On the basis of time patients were distributed in time categories and named them as receiver (closing time > 225 seconds), resistant (closing time < 106 seconds) and hypo-receiver (closing time between 106 and 224 seconds). Amongst the all patients carried out the analysis of coronary hazard aspects and demographical information.

Results: Examined the total numbers of patients (50) amongst them 12 were female and rests 38 were male. The results as to time categories were 60 percent (30) in closing time criteria, 30 percent (15) patients responded completely to Clopidogrel-resistant and only ten percent (5) were hypertensive. After the PCI patients were kept under observation for one month and found no clinically noteworthy coronary incident in them.

CONCLUSION: The quantity of hypoactive or resistant to clopidogrel patients was more than one third (>1/3) of the post-PCI patients.

Keywords: platelet anti-aggregation, Acute Coronary Syndrome (ACS), Clopidogrel resistance, P2Y12.

Corresponding author:**Dr. Shumaila Malik,**

Holy Family Hospital, Rawalpindi.

PMDC No. 82598-P

QR code



Please cite this article in press Shumaila Malik et al., A Study on Resistance of Clopidogrel: Incidence of Dual Antiplatelet Therapy after Coronary Intervention., Indo Am. J. P. Sci., 2018; 05(09):

INTRODUCTION:

When an acute coronary syndrome (ACS) symptom appears than usually coronary angioplasty is very necessary. Nowadays, after an ACS, extra care is necessary for every patient therefore they are advised for DAP and medicines prescribed to them are normally clopidogrel and aspirin only when there is no anti symbol appears. This is essential for antithrombotic therapy, which contributes a major role in care of acute coronary syndrome (ACS). After studying different books and materials it was found that the patients who were resistant to clopidogrel are nearly thirty percent (30%).

Currently, we are unaware of this thing that atherothrombotic events will be prevented after induced level of platelet inhibition due to clopidogrel. Amongst low response to thrombotic events and clopidogrel found no describable affiliation. In the view of these details, it is necessary to suggest more effective atherothrombotic medicines for example Prasugrel but it is being discussed because it is at raised hazard of stroke. Generally, for thienopyridine prescribed antiplatelet agent is Clopidogrel, nevertheless, on resistance in our patients there is no sufficient native statistics available.

Present research study was held to describe about the hypoactivation or resistance to clopidogrel. In the area of plaque, the von Willebrand factor rupture and upon adherence to collagen platelets formulate a monolayer. Consequences of this are the thrombin produced by the clotting cascade activates additional thrombocytes from the atherothrombosis and work, activation and release of side agonists, adenosine diphosphate (ADP) and thromboxane A₂. This is the main reason which makes importance of antiplatelet therapy after PCI and to take care of ACS.

MATERIALS AND METHODS:

Present research study was accomplished in the period of 12 months from April 2017 to March 2018 and conducted in Cardiology Department Jinnah hospital, Lahore, Pakistan. Patients were received one month earlier before they undergo from PCI informed

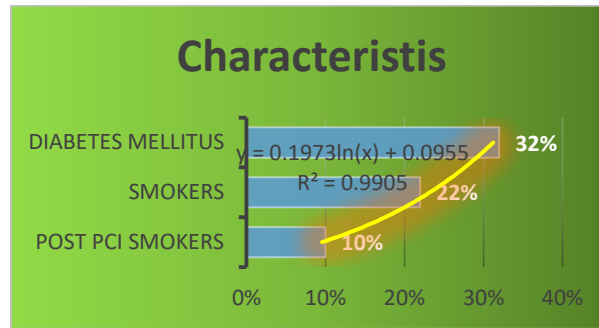
consent was taken from them and their families. In addition to their routine medications each and every patient was medicated with Clopidogrel 75 mg and Aspirin 75 mg in the intervals of 12 hours in a day and also 5 to 6 hours earlier to PCI medicated them with clopidogrel 600 mg. Selection criteria was based on patient's previous history of medication, all those were eliminated who were found in usage of irregular medication or other drugs that react to clopidogrel as like omeprazole. Collected the samples of venous blood from all selected patients with 3.20 % buffered sodium citrate and then these samples were amalgamated and tested for P2Y₁₂ blockade with PFA, Innovance 200 Siemens. With a single-use cartridge specific for test clopidogrel, analysis was carried out to access P2Y₁₂ blockade. Calculated the time for the test in integers of seconds known as "Closing Time". Distributed the patients in categories as resistant (ending time <106 seconds), receiver (ending time > 225 seconds) and hiporeactivos (ending time in the middle of 106 and 224 seconds) based on time. Amongst the all patients deeply observed the coronary hazard aspects and demographical information. With the help of SPSS version 25 (64 bit), statistical analysis was carried out. Categorical variables such as clopidogrel resistance, diabetes, smoking and gender were taken as percentages and counts. In relation to gender, for the observation of clopidogrel resistance performed fisher exact test (Chi-square test). The test was administered as two tails and a value of P <0.05 was considered considerable.

RESULTS:

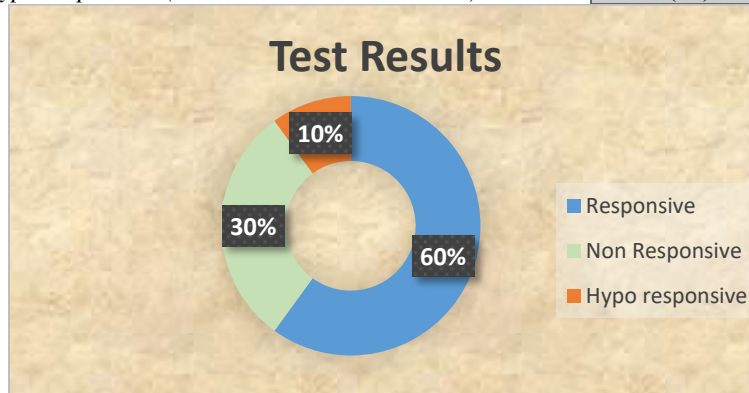
Overall participants of this study was 50 and their age was from 35 to 70 amongst which quantity of women were 12 and 38 were men. Calculated ratios of these were as 22 percent (11) smokers, 10 percent (5) patients after PCI continued to smoke and 32 percent (16) patients had diabetes mellitus. The ratio of patients in accordance with value of closing time was as 60 percent (30) were completely recipients, 30 percent (15) patients were resistant to clopidogrel and 10 percent (05) were hypo responsive. The said figures are shown in table below.

Table No 1: Important Clinical Characteristics

Characteristic		Result n = (50) N = %
Gender	Male	76 % (38)
	Female	24 % (12)
Smokers		22 % (11)
Post PCI Smokers		10 % (05)
Diabetes Mellitus		32 % (16)

**Table No 2: Test Results**

<i>Clopidogrel Responsiveness (Closure Time in seconds)</i>	Result n = (50) N = %
<i>Responsive (Closure Time \geq 225 sec)</i>	60 % (30)
<i>Non Responsive (Closure Time \leq 106 sec)</i>	30 % (15)
<i>Hypo responsive (Closure Time 106 - 224 sec)</i>	10 % (05)

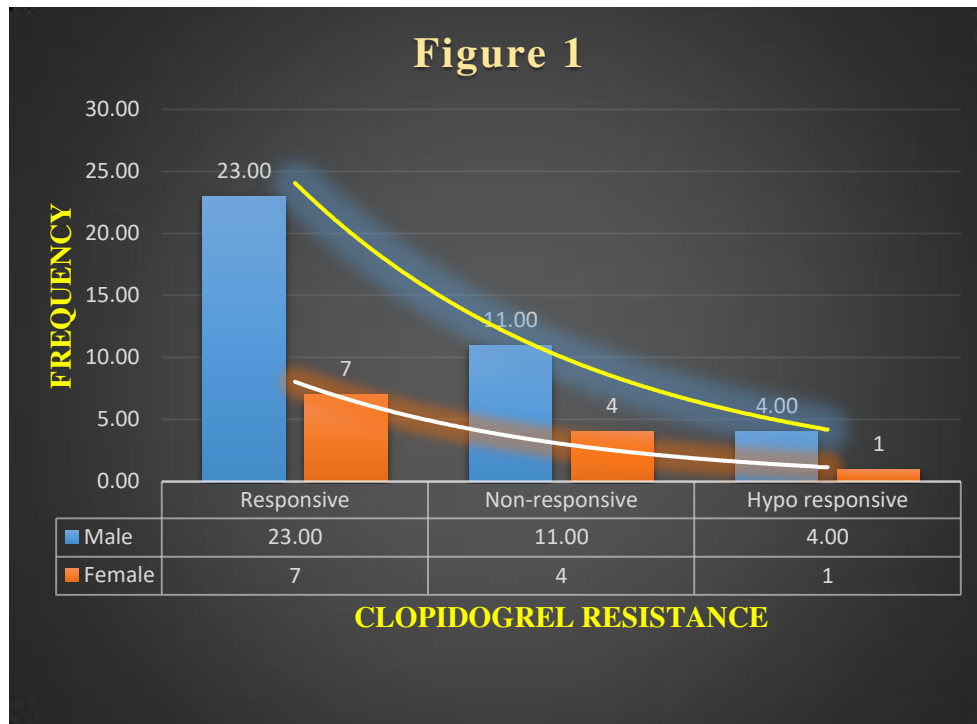


It was found that non-diabetic males had greater result rate than female in the same group to clopidogrel.

Table No3: Association of Diabetes mellitus and clopidogrel resistance with respect to gender

		Female N=% (n=12)	Male N=% (n=38)	P-value
Diabetes Mellitus	Non-responsive	16.67% (2)	10.52% (4)	0.9254
	Hypo responsive	08.33% (1)	07.89% (03)	
	Responsive	08.33% (1)	13.15% (05)	
Non Diabetes Mellitus	Non-responsive	16.67% (2)	18.42% (07)	0.0409
	Hypo responsive	16.67% (2)	02.63% (01)	
	Responsive	33.33% (4)	47.36% (18)	

However, on the response of Clopidogrel alone there was no effect observed. No results suggesting ischemia were narrated 4 weeks after PCI despite the high in ratio resistance to clopidogrel in any of our patients. Results are shown in figure 1 below.



DISCUSSION:

This has been observed through this study that frequency of resistance to clopidogrel is very high in the people of Pakistan. Medicine is always advised after PCI to prevent the patients from atherothrombosis. Out of 50 patients only 60% responded, 10% patients were hypertensive and 30% were resistive. Throughout the duration of study found no indication of ischemia in 40% patients. All these patients were medically fit with twice platelet anti-aggregation (DAPT). After studying the results, it was found that by examining the P2Y12 blocking (an in vitro evaluation) provide no guidance about the medical condition of the patients. With optical platelet aggregation, in one study, Gurbel et al assessed platelet roles in response to ADP. Out of 96 patients, after 24 hours of treatment those patients were at higher risk for being more responsive who have very high reactivities before treatment. In another study by Soffer D et al it was found that after medicating clopidogrel dose 450mg those patients who have less platelet inhibitors have a greater angina category. There was less follow-up time and small sample scope, due to this such results were not achieved in the present study. Except for the change in response to clopidogrel, anti-thrombotic drugs have limitations. Present study in terms of its effectiveness, do not cover the prolonged future of the medical treatment. Less clinical events, very short follow-up time and small sample sizes were the main limitations of the current study.

CONCLUSION:

Carried out observation on the total 50 patients amongst them as per gender classification, 38 were men and rest 12 were women. Hypoactive or resistant antiplatelet agents were observed in 40% of patients who were undergone the process of PCI and were using clopidogrel. After the PCI patients were kept under clinical observation for 4 weeks and found that there was no adverse cardiac events or ischemic symptoms.

REFERENCES:

- Verdoia, M., Pergolini, P., Barbieri, L., Rolla, R., Nardin, M., Negro, F., Suryapranata, H. and De Luca, G., 2018. Impact of pre-procedural dual antiplatelet therapy on periprocedural myocardial infarction in patients undergoing percutaneous coronary interventions with adjunctive tirofiban. *Thrombosis research*, 164, pp.17-23.
- Han SW, Park JH, Cheon KY, Lee KY. Abstract WP395: Verifynow P2Y12 Assay with regard to Cytochrome P450 2C19 Polymorphisms and Stroke Recurrence.
- Yang, A., Pon, Q., Lavoie, A., Crawford, J.J., Harenberg, S., Zimmermann, R.H., Booker, J., Kelly, S., Lavi, S., Cantor, W.J. and Mehta, S.R., 2018. Long-term pharmacodynamic effects of Ticagrelor versus Clopidogrel in fibrinolytic

- treated STEMI patients undergoing early PCI. *Journal of thrombosis and thrombolysis*, 45(2), pp.225-233.
4. Bath PM, May J, Heptinstall S. Clinical utility of remote platelet function measurement using P selectin: assessment of aspirin, clopidogrel, and prasugrel and bleeding disorders. *Platelets*. 2018 Apr 18:1-6.
 5. Narata AP, Amelot A, Bibi R, Herbreteau D, Angoulvant D, Gruel Y, Janot K. Dual Antiplatelet Therapy Combining Aspirin and Ticagrelor for Intracranial Stenting Procedures: A Retrospective Single Center Study of 154 Consecutive Patients with Unruptured Aneurysms. *Neurosurgery*. 2018 Feb 26.
 6. Wang Y, Yan BP, Liew D, Lee VW. Cost-effectiveness of cytochrome P450 2C19* 2 genotype-guided selection of clopidogrel or ticagrelor in Chinese patients with acute coronary syndrome. *The pharmacogenomics journal*. 2018 Jan;18(1):113.
 7. Lee, J.M., Kim, H.K., Lim, K.S., Park, J.K., Choi, K.H., Park, J., Hwang, D., Rhee, T.M., Yang, J.H., Shin, E.S. and Nam, C.W., 2018. Influence of Local Myocardial Damage on Index of Microcirculatory Resistance and Fractional Flow Reserve in Target and Nontarget Vascular Territories in a Porcine Microvascular Injury Model. *JACC: Cardiovascular Interventions*.
 8. Hassan AE, Shariff U, Qureshi A. Abstract TP84: Safety and Effectiveness of Ticagrelor in Patients with Clopidogrel Resistance Undergoing Angioplasty, Stent or Flow Diverter Placement.
 9. Zhang L, Li Y, Yang BS, Li L, Wang XZ, Ge ML, Jing QM, Ma YY, Wang G, Liu HW, Zhao X. A Multicenter, Randomized, Double-Blind, and Placebo-Controlled Study of the Effects of Tongxinluo Capsules in Acute Coronary Syndrome Patients with High On-Treatment Platelet Reactivity. *Chinese medical journal*. 2018 Mar 5;131(5):508.
 10. Tsujimoto, M., Enomoto, Y., Miyai, M., Egashira, Y. and Iwama, T., 2018. Optimal platelet function test for in-stent tissue protrusion following carotid artery stenting. *Journal of International Medical Research*, p.0300060518762949.
 11. Harima, Ayako, Akinori Sairaku, Ichiro Inoue, Kenji Nishioka, Toshiharu Oka, Yasuharu-Nakama, Kazuoki Dai, - Kuniomi Ohi, Haruki Hashimoto, and Yasuki Kihara. "Real life experience- of a stent less revascularization strategy using a combination of excimer laser and drug coated balloon for patients with acute coronary syndrome." *Journal of interventional cardiology* (2018).