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## Case Study Article

# Pharmacogenomic Variability in Bangladeshi Patients – A Case Study on CYP2C19 Polymorphism and Clopidogrel Resistance

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### ABSTRACT

The CYP2C19 gene is one of the polymorphisms that affects the effectiveness of Clopidogrel, this critical antiplatelet medication used in managing cardiovascular diseases (CVD). Such genetic variations can make patients resistant to clopidogrel, that is, they do not effectively respond to the medication and thus increase the risk of cardiovascular adverse events. In this case report, we emphasise the need for pharmacogenomic testing in personalizing treatment strategies for patients in Bangladesh, where such testing is not routinely done. The CYP2C19 gene is highly polymorphic and variants such as CYP2C19\*2 and CYP2C19\*3 responsible for reduced enzyme activity impairing conversion of clopidogrel to a pharmacologically active form are associated with reduced activity. These loss of function alleles have been shown to be associated with clopidogrel resistance and therefore less optimal therapeutic outcomes, as have been reported in studies Su et al. Due to lack of routine genetic testing, Bangladeshi patients face two potentially catastrophic problems regarding BMPT; some are poor metabolizers and yet remain undiagnosed, while other patients remain undiagnosed despite their biology making clopidogrel without benefit, which leads to treatment failure and increasing risk for cardiovascular events. The findings from this case report advocate for the integration of pharmacogenomic testing into clinical practice in Bangladesh. Defining patients with a genetic propensity to clopidogrel resistance enables healthcare providers to select other antiplatelet therapy for some, including ticagrelor or prasugrel that do not require CYP2C19 for activation. Such a personalized approach would greatly improve patient outcomes and reduce major adverse cardiovascular events in the Bangladeshi population.

## INTRODUCTION

Clopidogrel is a prodrug that is activated mainly to its therapeutic level by metabolic conversion to its

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active form mostly by cytochrome P450 enzyme CYP2C19. This mechanism is essential to avoid thrombotic events in patients with cardiovascular diseases such as Myocardial infarct and stroke [1]. CYP2C19 polymorphisms play an important role in defining the different phenotypic metabolizers – poor, intermediate, extensive, and ultra rapid respectively. Reduced conversion of clopidogrel to its active product CDP-BEI occurs in poor metabolizers with single loss of function alleles such as CYP2C19\*2 and CYP2C19\*3, and it is associated with reduced platelet inhibition and increased cardiovascular adverse events. [2, 3]. Current clinical landscape demonstrates the failure of genetic testing for patients going through treatment for cardiovascular conditions in Bangladesh. Routine pharmacogenomic assessments are lacking, and thus finding clopidogrel resistant patients is hampered by the inability to assess corresponding patients who are at risk for the condition, preventing both treatment efficacy and patient safety [1]. The purpose of this case study is to demonstrate the clinical implications of CYP2C19 polymorphism on the treatment of clopidogrel therapy in a Bangladeshi patient where pharmacogenomic testing needs to be incorporated into clinical practice.

### **Case Presentation**

In this case study the patient is a 62 year old male with, among other things, a history of hypertension and hyperlipidemia, and has suffered recurrent cardiovascular events even when on clopidogrel therapy. On the other hand, the family history was present in terms of cardiovascular disease, as his parents had suffered from myocardial infarctions at roughly young ages. In the case of clopidogrel, the patient had recurrent strokes and myocardial infarction, with doubts on the effectiveness of his treatment regimen [4, 5]. Laboratory tests showed elevated lipid levels and abnormal platelet aggregation responses upon clinical evaluation, which suggested resistance to clopidogrel. Further

investigation into the patient's CYP2C19 genotype is then needed to help understand why he failed treatment, as these findings prompted further investigation [5]. However, the patient's history of therapy failure coupled with the clinical symptoms adds to the importance of a comprehensive pharmacological strategy for the patient.

### **Molecular and Genetic Analysis**

Blood samples were collected to there is genotyping for presence of CYP2C19 polymorphisms for the molecular analysis. To determine accurately the genetic variants linked to clopidogrel metabolism, the PCR and NGS methodologies were used for testing [6, 7]. Categorizing the patient as a poor metabolizer was found by the results; patient was homozygous for the CYP2C19\*2 allele. The clinical observation of treatment resistance corroborates this association with significantly reduced clopidogrel activation to this genetic profile. Loss of function alleles such as CYP2C19\*2 and CYP2C19\*3 identified are examples of genetic factors influencing therapeutic outcomes and drug metabolism. In this case, the identity of the patient's poor metabolizer status directly led to insufficient platelet inhibition, despite clopidogrel therapy, despite adherence to clopidogrel therapy [6, 3]. This finding underscores the need for personalized medicine in which genetic testing can aid in making treatment decisions and providing better outcomes for patients.

### **Pharmacological Management & Treatment Outcome**

A revised treatment plan was then put in place having determined the CYP2C19 polymorphism. To overcome this drawback of genetic variability in drug metabolism, the patient was switched from clopidogrel to a non-prodrug ticagrelor, which does not need to undergo metabolism by CYP2C19 [9, 10]. It has been demonstrated that ticagrelor supplies more consistent platelet



inhibition, and affords lower risk of CV events, than does clopidogrel, especially in patients with known genetic polymorphisms affecting drug metabolism [9, 10]. First, regular platelet aggregation tests were used to monitor the patient's response to the new therapy. This resulted in significant improvement in platelet inhibition that was associated with a correspondingly lower incidence of subsequent recurring cardiac events. This outcome emphasizes the effectiveness of pharmacotherapy that is tailored to the patient when the patient has a genetic predisposition related to drug metabolism [6, 9]. This case demonstrates the possibility of obtaining improved clinical outcomes by integration of pharmacogenomic testing in routine clinical practice.

## **DISCUSSION**

This case study provides the findings of several critical issues related to pharmacogenomics in Bangladesh. Healthcare providers such as cardiologists and pharmacists are unaware of the clinical implications of genetic variability to drug response, including antiplatelet drugs like clopidogrel [1, 3]. Moreover, the shortage of genetic testing facilities constitutes one of the major hindrances of adapting the personalized medicine within the region [1, 3]. Other populations show a high prevalence of CYP2C19 polymorphisms among South Asians and indicate that the same genetic factors likely play a role in clopidogrel resistance in Bangladeshi patients [2, 11]. These findings are also clinically important because they emphasize the importance of routine genetic testing, before prescribing clopidogrel, especially in those with a history of cardiovascular events [6, 3]. Setting guidelines for the pharmacogenomic testing may facilitate more precise treatment strategies and improve patient outcomes.

## **CONCLUSION & RECOMMENDATIONS**

It presents the clopidogrel resistance in Bangladeshi patients, which is about CYP2C19 polymorphism a big factor and recommends pharmacogenomic testing in clinical practice. Currently, integration of pharmacogenomic screening programs in hospitals is necessary to identify patients who may not adequately respond to standard clopidogrel therapy. In addition, genetic testing may also be used to add to the national cardiovascular treatment protocol that can help with personalized medicine practice and give better patient care and outcomes. Also from the government side, it is important to subsidize genetic screening for patients who are high risk. These policies will close the gap to individualize the treatment option and also to make the real option available to general patients and the chance of getting the maximum number of real therapy types from the genome. This further also aims to both better the therapeutic potency and avoid pharmacological actions due to errors of treatment formulation that can be associated with genetic heterogeneity. Such programs and policies could initiate a significant alteration in the control of cardiovascular diseases in Bangladesh. This paves way for healthcare providers to personalize treatment strategies according to diverse genetic makeups of patients, improve overall health outcomes, decrease the chronicity of recurrent CVD, and improve the lives of patients with CVD. This calls for the advancement of pharmacogenomic initiatives in Bangladesh to be on par with international trends in the healthcare industry with the aim of allowing personalized medicine by taking into consideration the genetic insights to ensure individualized treatment.

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