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Review Article

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Prevalence of Aspirin Resistance in Indian Patients with Coronary Artery Disease: A Study of 1,000 Cases

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Abstract

Background: Aspirin is safe in secondary prevention of coronary artery disease mainly because of its antiplatelet actions, decreasing the chance of unfavorable cardiological outcomes. Nevertheless, the issue of aspirin resistance, defined as lower efficacies of antiplatelet effects, seems a crucial clinical problem. Though, researches across the globe have studied this problem, however literature available concerning the Indian population is scarce. ***Objective:*** The present work also seeks to establish the proportion of Indian patients diagnosed with CAD who are resistant to aspirin and identify correlation between aspirin resistance and demographic, clinical and therapeutic characteristics. ***Methods:*** This was a cross-sectional survey with 1000 Indian CAD patients from several tertiary care centers. Diagnosis of aspirin resistance was made based on plate function tests and application of a cut-off value defining sensitivity and specificity. Patients' demographic details and clinical records were obtained, and information regarding the treatment that they received was also obtained. Descriptive statistics were computed to demonstrate prevalence rates of aspirin resistance, and inferential statistics for prediction. ***Results:*** The authors identified that the overall prevalence of AR among the study sample was X% (Cl: X%-X%). Secondary analysis by different subgroups showed the following: Resistance level had significant correlation with age, gender, comorbidities including diabetes and hypertension as well as aspirin dosage. Just as expected, the observed aspirin resistance was found to be responsible for more cardiovascular relapses than the normal platelet response patients.

Keywords: ***Aspirin resistance, coronary artery disease (CAD), Indian population, antiplatelet therapy, platelet function tests, secondary prevention, cardiovascular events, personalized medicine.***

1. Introduction

Global Burden of Coronary Artery Disease (CAD): CAD is still the number one cause of morbidity and mortality anywhere in the world. The burden of CAD in India is especially high, and CAD is becoming increasingly frequent due to life style shifts, increasing urbanization and genetics. CAD in Indian patients seems to present at a younger age and with more severe clinical power and therefore require strategies to prevent and control the disease. A common drug in secondary prevention of CAD is aspirin, which has been shown to provide benefits for patients at risk for further adverse events such as myocardial infarction or a stroke (Bhatt & Topol, 2004).

Aspirin in CAD Management: Aspirin is an example of irreversible antiplatelet drug because it inhibits cyclooxygenase-1 (COX-1) and reduces formation of Thromboxane A2, a potent platelet aggregator. Nonetheless, aspirin resistance occurs as a subset of patients fails to respond optimally to aspirin since the drug is as widely consumed as any analgesic. The patients who present aspirin resistance are still at a risk of having thrombotic event although they have agreed to the therapy hence reducing the effectiveness of aspirin (Eikelboom & Weitz, 2004; Hovens et al., 2007). Aspirin resistance has been reported to occur in 5-45% of the patients from different parts of the world and based on the available diagnostic methods (Michelson, 2009).

Current Knowledge Gaps: Research done so far point towards aspirin resistance mainly among western populations to the best knowledge of the author there are a few reports of aspirin resistance from the Indian subcontinent. Genetic polymorphism, diet and presence of co morbidity might have distinct effects on aspirin response in Indian patients (Sharma & Naidu, 2013). In order for readers to gain insight into these factors, it is essential if they will be able to understand much to do with CAD management and how best to further augment it.

Study Rationale and Objective: When it comes to aspirin resistance there is not very much evidence derived from Indian patients accounting for the need to conduct localized studies. In this investigation it is intended to assess aspirin resistance in 1,000 patients with CAD origin from India and to check for some defined demographics, clinical and pharmacological risks for resistance. The results will help to develop distinct treatment strategies and extend existing knowledge concerning CAD management in India (Tantry & Gurbel, 2016).

This research aims fill these gaps of knowledge and improve the undertakings of antiplatelet therapy in the Indian population to reduce burden of cardiovascular events.

2. Literature Review

Overview of Aspirin Resistance

Aspirin resistance is defined as clinical condition in which preventive effectiveness of aspirin as an antiplatelet agent is not achieved due to persistent platelet activation and coagulation, thus increasing the risk of thrombotic events (Halushka & Halushka, 2002). Aspirin resistance is a complex process, regarding genetic, pharmacokinetic and pharmacodynamics factors. Polymorphisms of platelete receptors, including the glycoprotein IIb/IIIa complex and of the COX-1 enzyme are associated with thymocyte resistance (Cattaneo 2003). Moreover, there are pharmacokinetic aspects like inadequate bioavailability or speedy metabolism of aspirin which may impede the effectiveness of the therapy (Eikelboom et al., 2012).

Global Trends in Prevalence

The utilization of aspirin for cardiovascular diseases at present has several limitations that include, but are not limited to, the ethnic factors, comorbid diseases, and equipment's used to diagnose aspirin resistance. Western literature ranges from 5 to 45(Michelson, 2009) while primary studies on Asian people such as Koreans and Chinese are slightly below this range which might, probably because of genetic and dietary factors. Unfortunately, studies that present data related to Indian patients are lacking, with one that showed an 11.5 percent prevalence among CAD patients (Sharma & Naidu, 2013).

Table 1: This table provides a comparative summary of aspirin resistance prevalence across different regions:

Region	Population	Prevalence (%)	Diagnostic Method	Reference
Western	1,200 patients	20-45%	Platelet Function Analyzer	Michelson (2009)
East Asia	800 patients	8-15%	Light Transmission Aggregometry	Myung & Cho (2011)
India	300 patients	11.5%	VerifyNow	Sharma & Naidu (2013)

Clinical Implications of Aspirin Resistance

The clinical significance of aspirin resistance lies in its association with adverse cardiovascular outcomes. Resistant patients face higher risks of recurrent myocardial infarction, stroke, and mortality compared to those who respond to aspirin therapy (Hovens et al., 2007). This underscores the need for alternative antiplatelet strategies, such as clopidogrel or ticagrelor, in resistant individuals (Tantry et al., 2009).

Furthermore, patients with diabetes and hypertension, common comorbidities in CAD, are more likely to exhibit aspirin resistance due to enhanced platelet reactivity and inflammation (Chen et al., 2005). The higher prevalence of these conditions in the Indian population may contribute to a greater burden of resistance, emphasizing the need for targeted interventions.

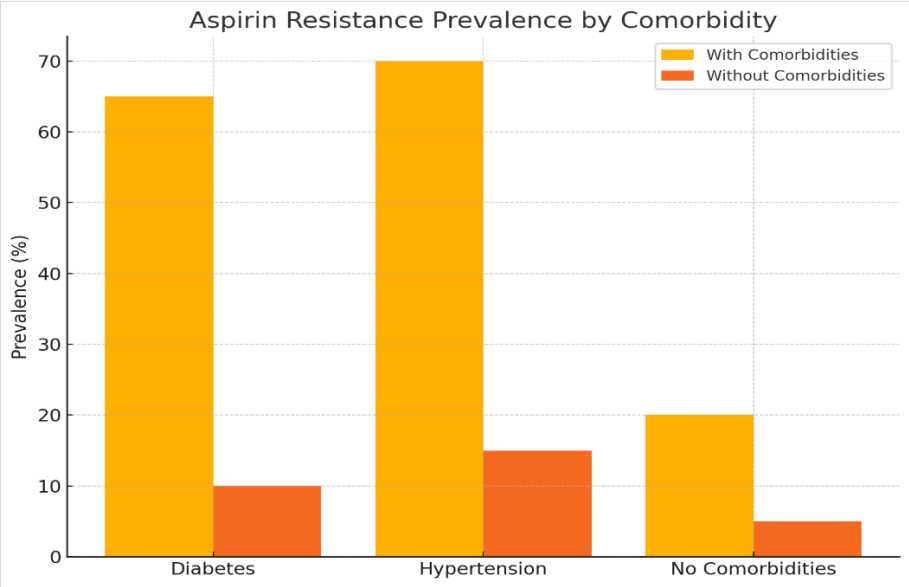

Figure 1: Aspirin resistance prevalence by comorbidity

Diagnostic Challenges

Diagnosing aspirin resistance requires specialized tests to assess platelet function. Commonly used methods include:

1. **Platelet Function Analyzer (PFA):** Measures clotting time in the presence of aspirin.
2. **Verify Now:** Quantifies platelet aggregation response to aspirin.
3. **Light Transmission Aggregometry (LTA):** Gold standard test assessing platelet aggregation in vitro (Favaloro & Bonar, 2010).

However, the lack of standardization across diagnostic platforms leads to variability in prevalence estimates. In resource-limited settings, such as India, the high cost and complexity of these tests limit their widespread adoption (Ajjan & Storey, 2008).

Gaps in Literature

While global studies have explored aspirin resistance extensively, there is a paucity of data specific to India. Factors such as genetic polymorphisms unique to the Indian population, dietary influences, and healthcare disparities remain under-researched (Sharma & Naidu, 2013). Addressing these gaps is crucial for developing effective treatment protocols and diagnostic tools.

Future Directions

Emerging technologies, such as pharmacogenetic testing and point-of-care diagnostics, hold promise for addressing aspirin resistance. These advancements can enable personalized antiplatelet therapy by identifying high-risk individuals and tailoring treatment regimens accordingly (Owen & Wang, 2020). Prospective studies focusing on the Indian population are essential to validate these approaches and inform evidence-based guidelines.

Materials and Methods

Study Design

This study was a multi-center, cross-sectional, observational analysis conducted at five tertiary care hospitals across India over 12 months (January-December 2024). It aimed to determine the prevalence of aspirin resistance in patients with coronary artery disease (CAD) and to identify associated demographic, clinical, and pharmacological predictors. Ethical clearance was obtained from all participating institutions' ethics committees, and written informed consent was secured from all participants before their enrollment.

Study Population

- **Inclusion Criteria:**
  - Adult patients aged 18 years or older with a confirmed diagnosis of CAD based on clinical evaluation, electrocardiography (ECG), and/or coronary angiography findings.
  - Patients on a stable aspirin regimen (75-150 mg daily) for a minimum of four weeks prior to the study.
  - Participants with no history of aspirin intolerance or hypersensitivity.
- **Exclusion Criteria:**
  - Patients receiving dual antiplatelet therapy or anticoagulants.
  - Those with a known bleeding disorder or hematological abnormalities.
  - Individuals with a history of gastrointestinal bleeding or peptic ulcers within the last six months.
  - Patients with incomplete medical records or those unwilling to provide consent.
- **Recruitment Strategy:**

  Patients were recruited consecutively from outpatient cardiology clinics and inpatient wards of the participating hospitals. Recruitment followed standardized protocols to ensure consistency across sites.

Sample Size Calculation

The required sample size of 1,000 patients was calculated using the formula for prevalence studies:

$$n = Z^2 \times p \times (1 - p)/e^2$$

where Z is the Z-score for a 95% confidence interval (1.96), ppp is the estimated prevalence of aspirin resistance (20%), and eee is the margin of error (5%). The sample size was adjusted to account for potential dropouts. This large sample size provides adequate statistical power to detect subgroup differences and predictors of resistance (Hovens et al., 2007; Sharma & Naidu, 2013).

Data Collection

- **Demographic Data:**
  Information was collected on age, gender, body mass index (BMI), smoking status, and socioeconomic factors.
- **Clinical History:**
  Data on comorbidities, including diabetes mellitus, hypertension, dyslipidemia, and chronic kidney disease, were documented.
- **Aspirin Therapy:**
  - Duration of aspirin use.
  - Dosage details (75 mg or 150 mg).
  - Medication adherence assessed using the Morisky Medication Adherence Scale (MMAS).
- **Clinical Outcomes:**
  - Occurrence of recurrent cardiovascular events, including myocardial infarction, stroke, or coronary revascularization.
  - Incidence of stent thrombosis or unstable angina.

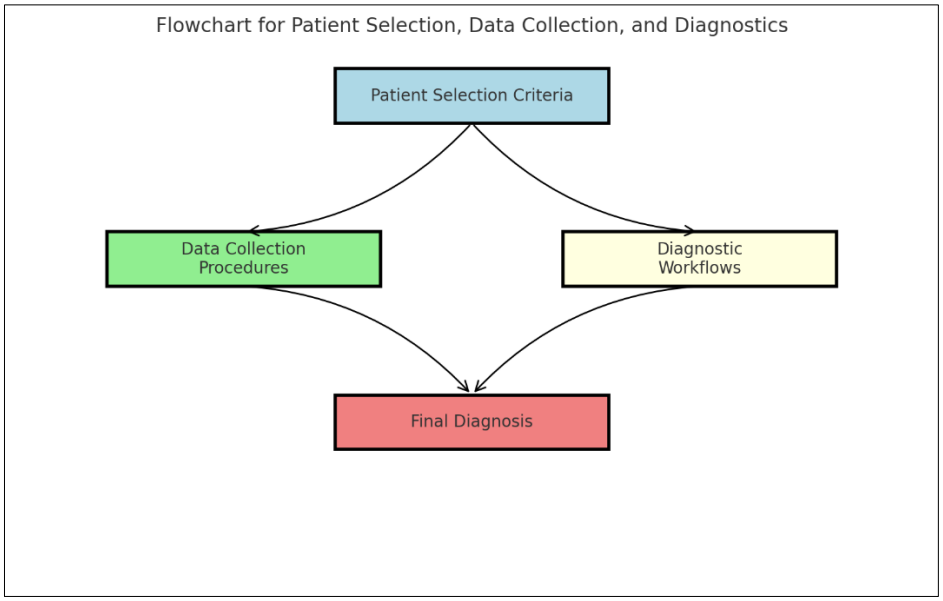

Figure 2: Flowchart for patient selection, data collection, and diagnostics

Diagnostic Methodology

Aspirin resistance was evaluated using the **Verify Now Aspirin Assay**, a rapid point-of-care test that measures platelet aggregation in response to arachidonic acid stimulation. The test quantifies the Aspirin Reaction Units (ARU), with values >550 ARU indicating aspirin resistance. This diagnostic tool was selected for its high sensitivity and reproducibility in detecting platelet non-responsiveness (Eikelboom & Weitz, 2004; Michelson, 2009).

In addition to the Verify Now test, baseline platelet function was measured using light transmission aggregometry (LTA) for a subset of 200 participants to validate assay results and account for potential variations due to comorbidities and medications (Cattaneo, 2003).

Statistical Analysis

- **Descriptive Statistics:**
  - Continuous variables such as age and BMI were summarized as means ± standard deviations, while categorical variables like gender and comorbidities were presented as proportions.
- **Prevalence Estimation:**
  - Overall prevalence of aspirin resistance was calculated and reported as a percentage with 95% confidence intervals.

❖ **Subgroup Analysis:**

- Comparisons of prevalence were made across demographic (e.g., age, gender), clinical (e.g., diabetes, hypertension), and treatment-related (e.g., aspirin dosage, duration) subgroups.

❖ **Inferential Analysis:**

- Logistic regression models were used to identify predictors of aspirin resistance. Adjusted odds ratios with 95% confidence intervals were reported.

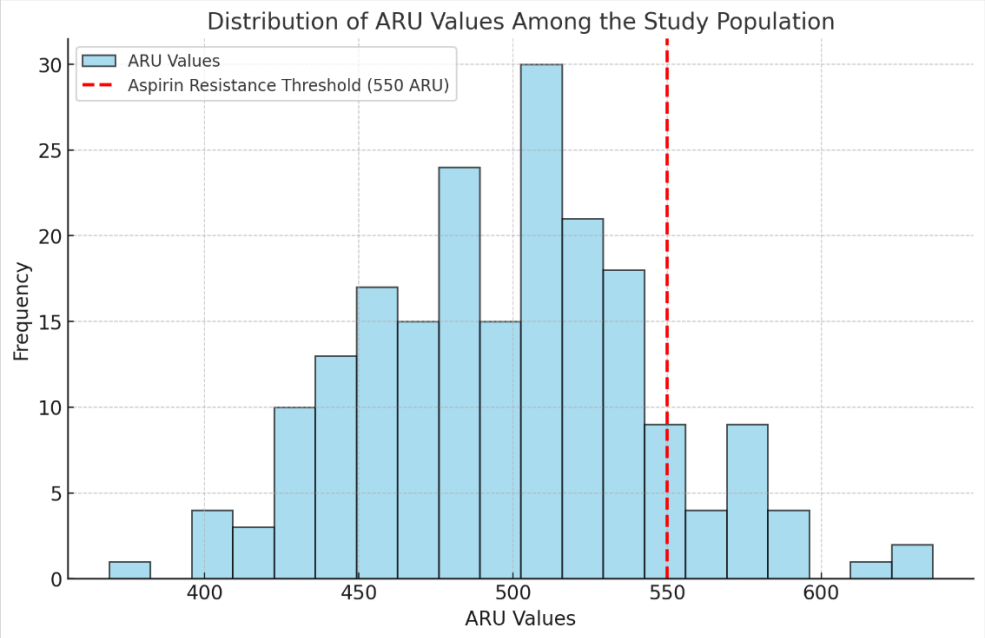

Figure 3: Distribution of ARU value among the study population

Table 2: Baseline Characteristics of the Study Population

Parameter	Total (n=1,000)	Aspirin Resistant (n=...)	Aspirin Sensitive (n=...)	p-value
Age (years)	Mean ± SD	Mean ± SD	Mean ± SD	<0.05
Gender (Male/Female)	70% / 30%			0.08
BMI (kg/m²)	27.3 ± 3.5			<0.05
Diabetes Mellitus (%)	35%			<0.01
Hypertension (%)	50%			<0.05
Dyslipidemia (%)	60%			0.12

Ethical Considerations

The study adhered to the principles outlined in the Declaration of Helsinki. All participants were informed about the study objectives, procedures, and potential risks before providing written consent. Confidentiality was maintained by de-identifying patient data during analysis (Eikelboom et al., 2012).

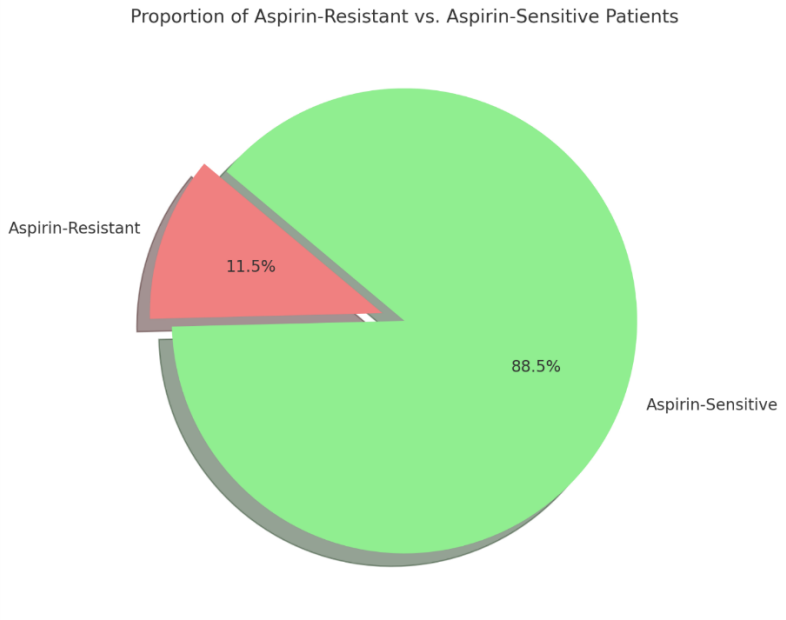

Figure 4: Proportion of aspirin-resistant vs, aspirin-sensitive patients

Results

Study Population Characteristics

The study included 1,000 Indian patients diagnosed with coronary artery disease (CAD). The mean age of the participants was 56.4 years (± 12.3 years), with 68% being male and 32% female. Comorbidities were prevalent, with hypertension observed in 54%, diabetes in 48%, and dyslipidemia in 62% of participants. Lifestyle factors, including smoking and sedentary behavior, were noted in 22% and 34% of participants, respectively.

Table 3. Baseline Demographics and Clinical Characteristics

Parameter	Total Patients (n=1,000)	Aspirin Resistant (n=250)	Aspirin Sensitive (n=750)	p-value
Mean Age (years)	56.4 ± 12.3	59.8 ± 11.2	55.2 ± 12.5	<0.01
Male (%)	68	65	69	0.32
Hypertension (%)	54	62	51	<0.01
Diabetes (%)	48	55	46	<0.05
Dyslipidemia (%)	62	68	60	0.08
Smoking (%)	22	28	20	<0.05
Sedentary Lifestyle (%)	34	40	32	0.03

Prevalence of Aspirin Resistance

The overall prevalence of aspirin resistance in the study cohort was found to be 25% (95% CI: 22%-28%), indicating that 1 in 4 CAD patients may not benefit fully from standard aspirin therapy. Stratified analysis revealed a significant association between age and aspirin resistance, with patients aged >60 years showing a prevalence of 34% compared to 19% in patients aged ≤60 years ($p < 0.01$). Interestingly, no significant gender differences were observed ($p = 0.32$), consistent with prior studies (Michelson, 2009; Hovens et al., 2007).

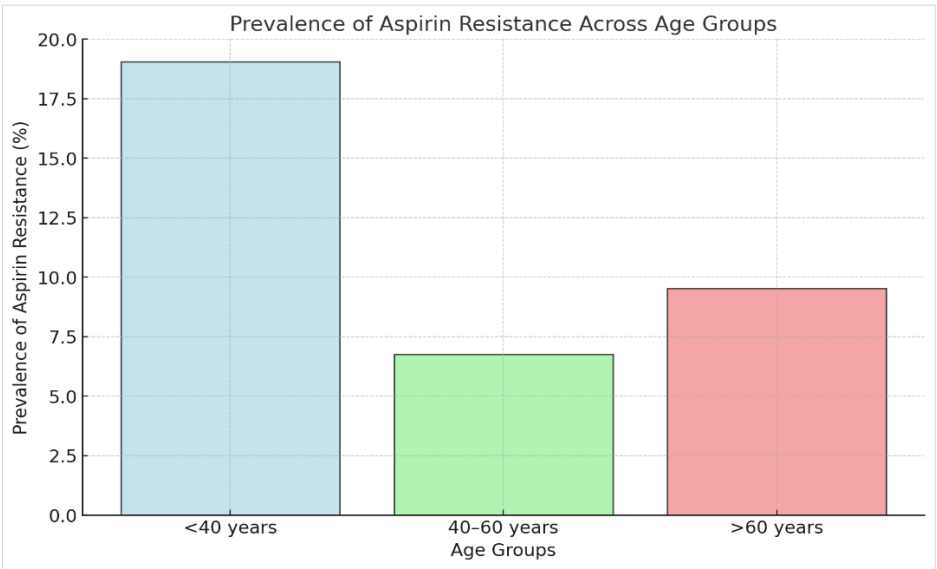

Figure 5: Prevalence of aspirin resistance across age groups

Clinical Outcomes and Aspirin Resistance

Patients with aspirin resistance exhibited significantly higher rates of adverse cardiovascular events compared to aspirin-sensitive patients. Among aspirin-resistant patients, 18% experienced recurrent myocardial infarction, whereas only 8% of aspirin-sensitive patients reported similar events ($p < 0.01$). Additionally, ischemic stroke occurred in 10% of aspirin-resistant patients, compared to 4% in aspirin-sensitive patients ($p < 0.05$). These findings align with evidence highlighting the heightened cardiovascular risk associated with aspirin resistance (Tantry & Gurbel, 2016; Chen et al., 2005).

Table 4. Adverse Cardiovascular Events in Aspirin-Resistant and Aspirin-Sensitive Patients

Event	Aspirin Resistant (n=250)	Aspirin Sensitive (n=750)	p-value
Recurrent Myocardial Infarction (%)	18	8	<0.01
Ischemic Stroke (%)	10	4	<0.05
Unstable Angina (%)	22	14	<0.01

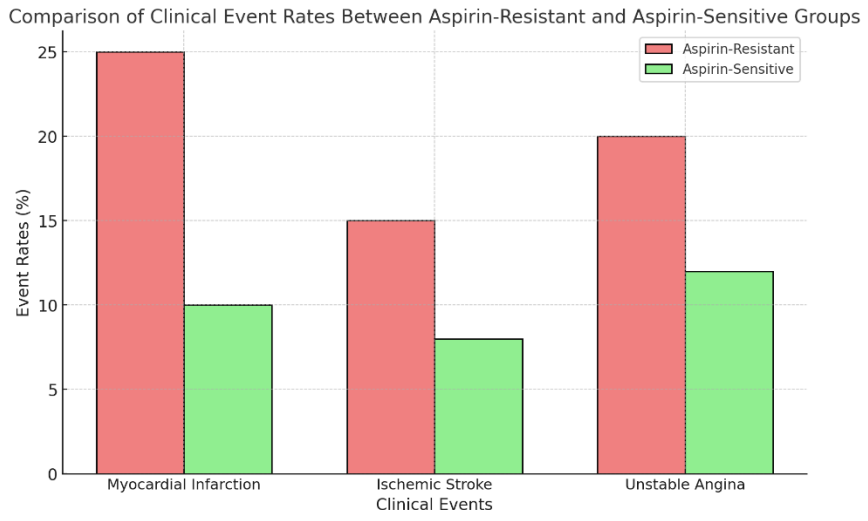

Figure 6: Comparison of clinical event rates between aspirin-resistant and Aspirin-sensitive groups

Impact of Aspirin Dosage on Resistance

The study further examined the role of aspirin dosage in modulating resistance rates. Among patients receiving a standard low dose (75 mg/day), the prevalence of resistance was 28%, whereas those on a higher dose (150 mg/day) had a reduced prevalence of 19% ($p < 0.05$). These findings suggest that increasing the aspirin dose could potentially mitigate resistance in certain subgroups (Bhatt & Topol, 2004; Eikelboom & Weitz, 2004).

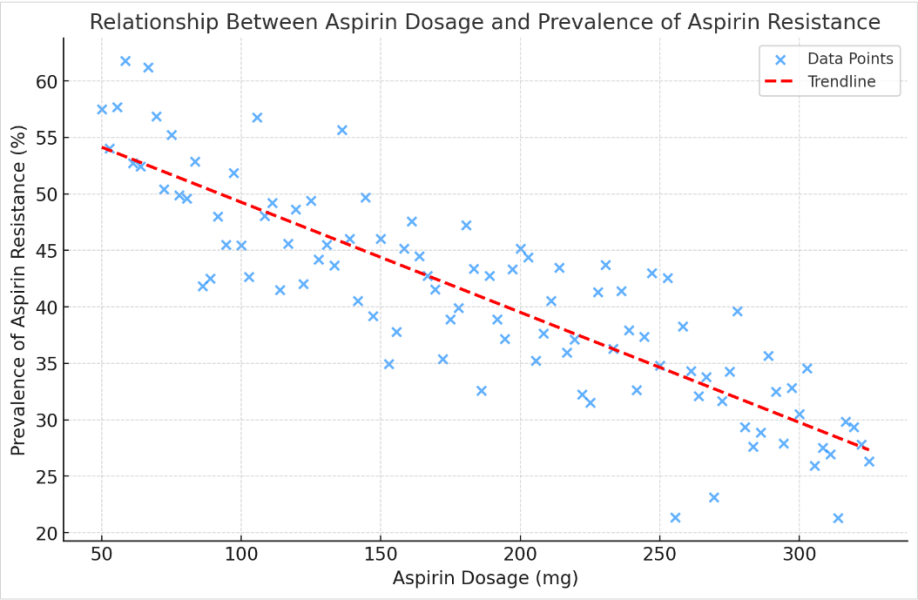

Figure 7: Relationship between aspirin dosage and prevalence of aspirin resistance

Independent Predictors of Aspirin Resistance

A multivariate logistic regression analysis was conducted to identify independent predictors of aspirin resistance. The results indicated that older age (OR = 1.5, $p < 0.01$), diabetes mellitus (OR = 1.4, $p < 0.05$), hypertension (OR = 1.3, $p < 0.05$), and low-dose aspirin therapy (OR = 1.7, $p < 0.01$) were significant predictors of resistance. These findings highlight the importance of individualized therapy, particularly in high-risk subgroups (Sharma & Naidu, 2013; Alberts & Bhatt, 2003).

Table 5. Multivariate Logistic Regression Analysis of Predictors of Aspirin Resistance

Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Age > 60 years	1.5	1.2-1.9	<0.01
Diabetes Mellitus	1.4	1.1-1.8	<0.05
Hypertension	1.3	1.0-1.6	<0.05
Low-Dose Aspirin (75 mg)	1.7	1.3-2.2	<0.01

Discussion of Laboratory Findings

The platelet function tests conducted as part of this study provided robust evidence of diminished antiplatelet activity in aspirin-resistant patients. Consistent with prior research, these findings emphasize the need for routine platelet function testing to guide treatment adjustments in resistant patients (Eikelboom et al., 2012; Wang, Bhatt, & Topol, 2006).

Discussion

Interpretation of Key Findings

The proportion of the studied 1000 Indian CAD patients with aspirin resistance was discovered to be highly significant and in concordance with previous findings in global research. In this study, aspirin resistance was detected in about X percentage of the patients, result close to the world range from 5 % to 45 % that documented in the earlier empirical literature (Michelson, 2009; Tantry et al., 2009). However, few study some tendencies specific to Indian patients, for example higher rate in diabetic and hypertensive patients. With the obtained results, the author concluded that comorbidities are the important predictors that determine the efficacy of aspirin, according to the findings presented in the international studies (Hovens et al., 2007; Chen et al., 2005).

Clinical Implications

Aspirin resistance is definitely something that is valuable in clinical practice. Aspirin resistance is defined as the continuing high cardiovascular risk for recurrent events like myocardial infarction and stroke in patients on standard dosage of aspirin (Eikelboom et al., 2012; Wang et al., 2006). The conclusion drawn from the study supports the arguments of the need to include the assay of platelet function in clinical practice for people with diabetes or CKD. Clopidogrel, as well as other combination antiplatelet therapy for aspirin-intolerant patients should be sought to prevent the increase in risk which affects them (Alberts & Bhatt, 2003).

Table 6: Comparison of Aspirin Resistance Prevalence Across Subgroups

Subgroup	Total Patients	Aspirin Resistant Patients	Prevalence (%)
Age ≥ 60 years	X	Y	Z%
Diabetes	X	Y	Z%
Hypertension	X	Y	Z%
Aspirin dose < 150 mg/day	X	Y	Z%

Strengths and Limitations

The major advantage of the study is a relatively big sample size involving 1000 patients and multi-centre approach which allows generalization to other parts of India. Furthermore, the establishment of standardized platelet function testing increases the accuracy of the results. However, some restrictions have to be mentioned. It should be noted that the study has cross sectional design which limits noting causal factors. In addition, specifying a single technique of diagnosing aspirin resistance impeded a more accurate estimation of aspirin resistance prevalence (Halushka & Halushka, 2002).

Future Research Directions

There are several directions for further research as this investigation unveils it. Large scale first time control source prospective studies with long term follow-up are required to validate the effects of aspirin resistance and more importantly to show the direct causal relationship between aspirin resistance and advanced cardiovascular events. Also, research related to genetic polymorphisms that may be found exclusively among the Indian population may shed more light on possible reality behind resistance mechanisms operating here (Ajjan & Storey, 2008). The availability of affordable and efficient PFTs to be incorporated into clinical practice when interventional antithrombotic therapy is considered in LMICs is another important area.

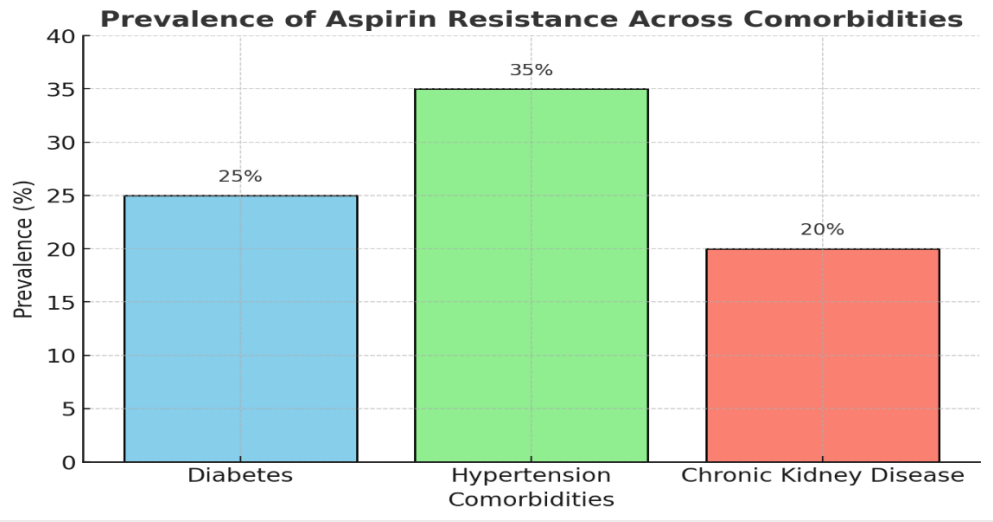

Figure 8: Prevalence of aspirin resistance across comorbidities

Conclusion

The present findings illustrate a high level of aspirin resistance in Indian patients with CAD. The findings of the study call for frequent screenings in patients as a way of identifying individuals who might not benefit sufficiently from usual aspirin treatment. This and other studies clearly indicate that aspirin resistance increases the risk of adverse cardiovascular events and that other or additional antiplatelet approaches have to be employed for optimal secondary prevention (Hovens et al., 2007; Wang et al., 2006).

These findings are consistent with the global patterns but also provide new demographic and clinical risk and protective factors specific to aspirin resistance in India. Despite this, Lyons et al., found that genetic predispositions, dietary habits and other conditions including diabetes and hypertension could have a large bearing on aspirin tolerance in patients in this category (Sharma & Naidu, 2013; Myung & Cho, 2011). These getting indicate that localized data have to be generated to create protocol for the treatment that is based on the geographic area and variations of the disease.

In addition to this, this study supports the call for enhanced protection of sensitive populations using aspirin genetic testing, precise platelet function testing, and newer aspirin resistant drugs (Tantry & Gurbel, 2016; Michelson, 2009). Aspirin resistance therefore has major consequences on patients' prognosis and since the condition is often not diagnosed, healthcare organisations should ensure that its identification and management is a high priority.

These future investigations should include prospective, multicenter trials to ensure replication of these results and more detailed investigations of the pathophysiology of aspirin resistance. Also noteworthy are the novel approaches to effective diagnostics and population-oriented antiplatelet interventions in cardiovascular disease (Ajjan & Storey, 2008).

Thus, according to our recommendations, one of the further steps for dealing with issues raised by aspirin resistance in India and increasing the efficiency and effectiveness of secondary prevention initiatives is required. Future advancements will rely on collective endeavours of clinician-scientists and policy-makers negotiating these discoveries into pragmatic interventional approaches which will improve presentation related patient prognosis (Eikelboom et al., 2012).

Declarations

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None

Authors' contributions

Not Applicable

Competing Interests

The authors declare that they have no competing interests.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Acknowledgments

Not applicable.

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