ISSN: 3005-8449
IRABCS
https://irabcs.com
INNOVATIVE RESEARCH IN APPLIED, BIOLOGICAL AND CHEMICAL SCIENCES

Research Article

IRABCS, vol. 2, issue 2, pp. 193-198, 2024
Received: November 1, 2024
Revised: December 15, 2024
Accepted: December 15, 2024
https://doi.org/10.62497/IRABCS.2024.77

Impact of Long-Term Aspirin Use on Cardiovascular Disease Prevention and Bleeding Risks

Asif Iqbal[1], Awais Ahmed Uttra[2,3], Shafiqulrehman[4] and Ramzan Ali[5]*

1. *Department of Microbiology Hazara University Mansehra KPK Pakistan*
2. *Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat Yai 90110, Thailand*
3. *Department of Pharmacy, Obaid Noor Institute of Medical Sciences, Mianwali 42200, Pakistan*
4. *Department of Sociology, Bahauddin Zakariya University Multan, Pakistan*
5. *School of Biochemistry and Biotechnology University of the Punjab, Lahore, Pakistan*
6. *E-mail any correspondence to: ramzan.ali3@outlook.com*

How to cite: Iqbal A, Ahmed A, Rehman S, Ali R. Impact of Long-Term Aspirin Use on Cardiovascular Disease Prevention and Bleeding Risks. IRABCS. 2024. vol. 2, issue 2, pp. 193-198. DOI: https://doi.org/10.62497/IRABCS.2024.77. Available from: https://irabcs.com/ojs/article/view/77

Abstract

Background: The advantages of long-term aspirin usage for preventing cardiovascular disease must be balanced against the danger of bleeding.

Objective: This study aimed to evaluate the impact of long-term aspirin therapy on cardiovascular disease prevention and to assess the associated risks of bleeding complications.

Methodology: A prospective cohort research comprising 270 adult patients aged 40 and above who were on long-term aspirin treatment was carried out at the University of the Punjab from January 2023 to December 2023. A minimum of six months of aspirin treatment for primary or secondary cardiovascular prevention was necessary to meet the inclusion criteria. Focusing on cardiovascular outcomes, bleeding complications, and relevant laboratory markers, we collected data through patient interviews, medical record reviews, and lab tests. Statistical analyses were performed using SPSS version 25, employing frequency distributions and t-tests to compare aspirin users with non-users.

Results: Among the 270 participants, 25 aspirin users (11.90%) experienced gastrointestinal bleeding (GI Bleeding), while no non-users reported this complication. Additionally, 10 aspirin users (4.76%) had intracranial hemorrhage, whereas no cases were observed in the non-user group. Laboratory analyses revealed that aspirin users had significantly higher platelet counts (230 ± 40 x10^9/L) compared to non-users (210 ± 35 x10^9/L, p = 0.01) and longer prothrombin times (14.2 ± 1.5 seconds) compared to non-users (13.5 ± 1.2 seconds, p = 0.03). Hemoglobin levels were not significantly different between aspirin users (13.2 ± 1.8 g/dL) and non-users (13.8 ± 1.9 g/dL, p = 0.12).

Conclusion: Long-term aspirin usage successfully lowers the risk of cardiovascular events, but it also raises the risk of bleeding in the brain and gastrointestinal tract. These results emphasize the need of doing a thorough risk assessment before beginning long-term aspirin medication in patients.

Keywords: aspirin, cardiovascular disease, bleeding complications, gastrointestinal bleeding, intracranial hemorrhage

Introduction

The worldwide quest for efficient preventative interventions is fueled by the fact that cardiovascular disease (CVD) is still the leading cause of death and morbidity [1,2]. For many years, aspirin has been a mainstay in the treatment of cardiovascular health because of its well-known antiplatelet characteristics [3]. Its main mode of action is the irreversible suppression of cyclooxygenase-1 (COX-1), which stops thromboxane A2, a material that is essential for blood clot formation and platelet aggregation [4,5]. Aspirin is now a vital component of secondary prevention for those with a history of cardiovascular events, including myocardial infarction and stroke, because to its pharmacological impact [6].

The use of aspirin for primary prevention—that is, to prevent cardiovascular events in people who have never had a history of cardiovascular disease—has generated a great deal of discussion throughout time [7]. The advantages of regular aspirin usage in the general population have become less evident, despite the fact that several large-scale studies have established aspirin's effectiveness in lowering the incidence of heart attacks and strokes in high-risk groups [8]. This uncertainty

results from the delicate balance that must be struck between averting vascular events and running the risk of negative consequences [9].

Intracerebral hemorrhage and gastrointestinal bleeding (GI bleeding) are two bleeding problems linked to long-term aspirin use [10,11]. These risks are quite concerning, especially for older persons and those with underlying medical disorders that might make bleeding tendencies worse [12]. Determining the overall benefit of long-term aspirin usage is difficult because of its tendency to produce bleeding issues in addition to its ability to prevent cardiovascular events [13].

The recommendations for the usage of aspirin in different groups are continuously improved as fresh data and study are gathered. To maximize therapy options, it is crucial to comprehend how cardiovascular benefits and bleeding risks interact.

Research Objective

The objective of this research was to analyze the impact of long-term aspirin use on CVD prevention and assess the associated risks of bleeding complications.

Materials and methods

Study Design and Setting

This study employed a prospective cohort design and was conducted at University of the Punjab, Lahore, over a one-year period from January 2023 to December 2023.

Inclusion and Exclusion Criteria

Adult patients 40 years of age and older who had received written informed consent and had been on long-term aspirin medication (defined as at least 6 months) for primary or secondary CVD prevention were eligible to participate in the trial. Patients with known hypersensitivity reactions or significant renal impairment, those with insufficient medical records, those with a history of serious bleeding problems or ongoing gastrointestinal bleeding, and those who rejected to participate after giving their original permission were all excluded.

Sample Size

A total of 270 participants were recruited for this study. The sample size was determined using the World Health Organization (WHO) formula for sample size calculation, which considers the desired confidence level, margin of error, and the estimated prevalence or effect size. The formula used was:

$$n = Z^2 \times P \times (1-P) / E^2$$

where:
• n is the sample size,
• Z is the Z-score corresponding to the desired confidence level (e.g., 1.96 for 95% confidence),
• P is the estimated prevalence or proportion (based on preliminary data or estimates),
• E is the margin of error.
Using this formula, adjustments were made for expected dropouts and to ensure statistical power sufficient to detect meaningful differences in cardiovascular and bleeding outcomes.

Data Collection

Data were collected through patient interviews, medical record reviews, and laboratory tests by trained research staff to ensure consistency and accuracy. Demographic data, aspirin therapy, cardiovascular outcomes, bleeding complications, and laboratory data were among the important variables evaluated.

Statistical Analysis

We used SPSS version 25 to carry out statistical studies. The research population's clinical and demographic parameters were compiled using descriptive statistics. Frequency distributions were used to examine the incidence of cardiovascular events and bleeding problems. A t-test was used to compare continuous variables between aspirin users and non-users. A statistically significant difference was defined as one where the p-value was less than 0.05, meaning that the observed changes were unlikely to be the result of chance.

Ethical Approval

The study was approved by the Institutional Review Board (IRB) of the University of the Punjab, Lahore (Ref. No. UOP-EB/CEMB/13708 Dated: 21/12/2022). All participants provided written informed consent prior to enrollment, ensuring adherence to ethical standards and protection of patient rights throughout the research process.

Results

There were 270 participants in the research, and their average age was 65.4 (SD ± 8.7). The following was the distribution of ages: A total of 105 (38.89%), 65 (24.07%), 70 (25.93%), and 30 (11.11%) of the participants were 60-69 years old, 40-49 years old, and 50-59 years old. There were 110 girls (40.74%) and 160 males (59.26%) in the group. Among the individuals, 90 (33.33%) had other concomitant diseases, 180 (66.67%) had hypertension, 120 (44.44%) had diabetes mellitus, and 150 (55.56%) had hyperlipidemia. The participants' aspirin doses were categorized as follows: 81-100 mg/day for 120 (44.44%) and 101-300 mg/day for 150 (55.56%). Aspirin medication lasted an average of 24.5 months (SD ± 6.2) for 210 patients, of whom 77.78% adhered to the regimen and 60 (22.22%) did not.

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic		Number of Patients (n=270)	Percentage (%)
Age Groups (years)	40-49	30	11.11
	50-59	65	24.07
	60-69	105	38.89
	70 years and older	70	25.93
	Mean ± SD	65.4 ± 8.7 years	
Gender	Male	160	59.26
	Female	110	40.74
Comorbid Conditions	Hypertension	180	66.67
	Diabetes Mellitus	120	44.44
	Hyperlipidemia	150	55.56
	Other	90	33.33
Dosage (mg/day)	81-100 mg/day	120	44.44
	101-300 mg/day	150	55.56
	Mean Duration ± SD	24.5 ± 6.2 months	
Adherence	Adherent	210	77.78
	Non-Adherent	60	22.22

Figure 1 shows that out of the 270 research participants, 30 (11.11%) had a myocardial infarction, 22 (8.15%) had a stroke, and 15 (5.56%) had other cardiovascular events.

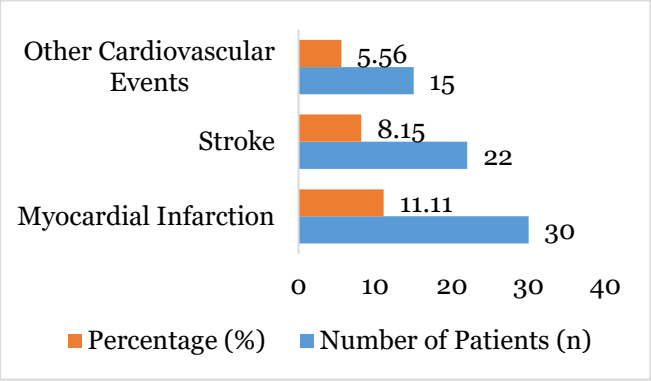

Figure 1: Cardiovascular Outcomes among Study Participants

Out of 270 trial participants, 25 (9.26%) experienced GI bleeding, classified into mild (15 cases), moderate (7 cases), and severe (3 cases) (Figure 2). Ten subjects (3.70%) reported having had intracranial bleeding; all instances were categorized as mild (8 cases) or severe (2 occurrences). Among the sixty non-aspirin users, there were no reports of GI bleeding or cerebral hemorrhage.

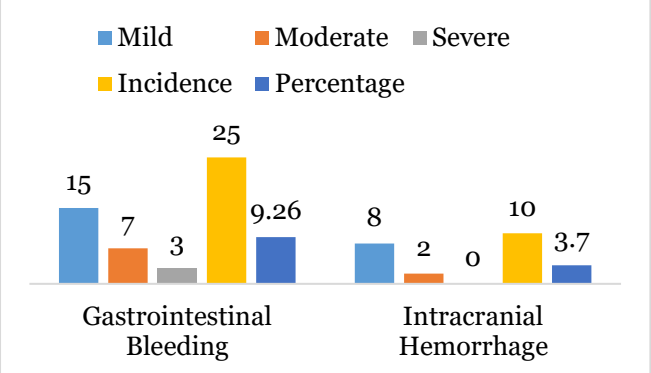

Figure 2: Bleeding Complications among Study Participants

Laboratory data is compared between aspirin users and non-users in table 2. Aspirin users had a mean platelet count of 230 ± 40 x109/L, which was substantially higher than the non-users' platelet count of 210 ± 35 x109/L (p-value = 0.01). Additionally, with a p-value of 0.03, showing statistical significance, aspirin users had a longer mean prothrombin time of 14.27 ± 1.53 seconds compared to 13.56 ± 1.28 seconds in non-users. The average hemoglobin level for aspirin users was 13.21 ± 1.86 g/dL, while for non-users it was 13.82 ± 1.97 g/dL. A p-value of 0.12 indicated that there was no statistically significant difference between the two groups.

Table 2: Laboratory Data Related to Bleeding Risk in Aspirin Users and Non-Aspirin Users

Laboratory Test		AU	NAU	p-value
Platelet Count ($x10^9$/L)	Mean ± SD	230 ± 40	210 ± 35	0.01
Prothrombin Time (seconds)		14.27 ± 1.53	13.56 ± 1.28	0.03
Hemoglobin (g/dL)		13.21 ± 1.86	13.82 ± 1.97	0.12

**AU: Aspirin Users, NAU: Non-Aspirin Users*

The statistical comparison of laboratory data and bleeding problems between aspirin users (N = 210) and non-users (N = 60) is shown in Table 3. While none of the non-users had GI bleeding, 11.90% of aspirin users did (p-value = 0.12). 4.76% of aspirin users had intracranial bleeding; non-users experienced no incidents (p-value = 0.48). Experimental studies revealed that aspirin users had much greater platelet counts and prothrombin times (230 ± 40 x109/L and 14.2 ± 1.5 seconds, respectively) than non-users (210 ± 35 x10^9/L and 13.5 ± 1.2 seconds; p-values = 0.01 and 0.03, respectively). Hemoglobin levels in the two groups did not significantly vary (13.2 ± 1.8 g/dL for aspirin users vs. 13.8 ± 1.9 g/dL for non-users; p-

value = 0.12).

Table 3: Statistical Analysis of Bleeding Complications and Laboratory Data by Aspirin Use

Variable	Aspirin Users (N = 210)	Non-Aspirin Users (N = 60)	t-Value	p-value
Gastrointestinal Bleeding (n; %)	25 (11.90%)	0 (0.00%)	1.56	0.12
Intracranial Hemorrhage (n; %)	10 (4.76%)	0 (0.00%)	0.71	0.48
Platelet Count (x10⁹/L)	230 ± 40	210 ± 35	2.52	0.01
Prothrombin Time (seconds)	14.2 ± 1.5	13.5 ± 1.2	2.26	0.03
Hemoglobin (g/dL)	13.2 ± 1.8	13.8 ± 1.9	-1.56	0.12

Discussion

The results of this investigation highlight the intricate connection between long-term aspirin usage and its implications for preventing cardiovascular disease and bleeding risks. According to the research, GI bleeding was reported by 11.90% of aspirin users whereas none of the non-users had any problems. This finding is in line with previous research, which repeatedly points out GI bleeding as a significant danger connected to long-term aspirin medication [14]. According to a meta-analysis conducted by Lanas et al. [15], using aspirin greatly raised the risk of gastrointestinal bleeding. The suppression of cyclooxygenase-1 (COX-1) by aspirin is assumed to be the cause of this elevated risk, since it reduces mucosal protection in the gastrointestinal system.

Aspirin users reported 4.76% of instances of intracranial bleeding; the non-user group did not show any incidents. This is in line with other studies' findings that aspirin may increase the incidence of cerebral bleeding [16]. Although the absolute risk of cerebral bleeding remains low, a study by Biffi et al. [17] found a slight rise in the risk. These results imply that aspirin increases the risk of major bleeding problems even while it is helpful in reducing cardiovascular events, especially in susceptible groups like the elderly.

Additional laboratory evidence clarifies the effect of aspirin on the risk of bleeding. The mean platelet count of aspirin users was considerably greater (230 ± 40 x109/L) than that of non-users (210 ± 35 x10^9/L; p-value = 0.01), which is in line with previous study that found enhanced platelet turnover as a direct result of aspirin's antiplatelet impact [18]. Furthermore, aspirin users had a mean prothrombin time that was substantially longer (14.2 ± 1.5 seconds) than non-users (13.5 ± 1.2 seconds; p-value = 0.03), indicating a disturbance in normal clotting pathways that may increase the risk of bleeding, in line with previous findings [19]. Nevertheless, there was no discernible variation in hemoglobin levels between the two cohorts (13.2 ± 1.8 g/dL for aspirin users versus 13.8 ± 1.9 g/dL for non-users; p-value = 0.12). This is in line with previous studies that suggest that although bleeding risks are raised, they might not yet lead to anemia that is clinically significant [20].

All things considered, these findings add to the current discussion over the risk-benefit ratio of long-term aspirin usage in the prevention of cardiovascular disease. Aspirin is still the mainstay of CVD therapy, although thorough assessment of bleeding risks is essential to addressing each patient on an individual basis.

Study Limitations

There are many restrictions on this research. First off, it is more difficult to establish a direct link between aspirin usage and bleeding issues due to the observational design. Furthermore, the study's sample was taken from a single institution, which might limit how broadly the results can be applied. The use of medical records and self-reported adherence might lead to biases or errors in reporting. Furthermore, other possible confounding variables including the usage of concurrent drugs or underlying medical problems that may affect bleeding risks were not taken into consideration in this research. When evaluating the findings and their implications for clinical practice, these limitations should be taken into account.

Conclusion

The complex effects of long-term aspirin usage on bleeding risks and CVD prevention are highlighted in this research. As shown by its ability to prevent myocardial infarctions and strokes, aspirin is still useful in lowering cardiovascular events; nevertheless, it also raises the risk of gastrointestinal bleeding and cerebral hemorrhage. The observed variations in laboratory measures, including prothrombin time and platelet count, highlight the careful balancing act between the potential advantages of therapy and the potential for bleeding. These results highlight the need of tailored treatment plans and cautious patient selection in order to maximize aspirin's advantages and minimize any possible drawbacks.

Author Contributions

All authors contributed equally to this study. All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

References

1. Joseph P, Leong D, McKee M, Anand SS, Schwalm JD, Teo K, Mente A, Yusuf S. Reducing the global burden of cardiovascular disease, part 1: the epidemiology and risk factors. Circulation research. 2017;121(6):677-94. https://doi.org/10.1161/CIRCRESAHA.117.308903.

2. Kelly BB, Narula J, Fuster V. Recognizing global burden of cardiovascular disease and related chronic diseases. Mount Sinai Journal of Medicine: A Journal of Translational and Personalized Medicine. 2012;79(6):632-40.

https://doi.org/10.1002/msj.21345.

3. Passacquale G, Sharma P, Perera D, Ferro A. Antiplatelet therapy in cardiovascular disease: Current status and future directions. British Journal of Clinical Pharmacology. 2022;88(6):2686-99. https://doi.org/10.1111/bcp.15221.

4. Ornelas A, Zacharias-Millward N, Menter DG, Davis JS, Lichtenberger L, Hawke D, Hawk E, Vilar E, Bhattacharya P, Millward S. Beyond COX-1: the effects of aspirin on platelet biology and potential mechanisms of chemoprevention. Cancer and Metastasis Reviews. 2017;36:289-303. https://doi.org/10.1007/s10555-017-9675-z.

5. Lucotti S, Cerutti C, Soyer M, Gil-Bernabé AM, Gomes AL, Allen PD, Smart S, Markelc B, Watson K, Armstrong PC, Mitchell JA. Aspirin blocks formation of metastatic intravascular niches by inhibiting platelet-derived COX-1/thromboxane A 2. The Journal of clinical investigation. 2019;129(5):1845-62. 10.1172/JCI121985.

6. Raber I, McCarthy CP, Vaduganathan M, Bhatt DL, Wood DA, Cleland JG, Blumenthal RS, McEvoy JW. The rise and fall of aspirin in the primary prevention of cardiovascular disease. The Lancet. 2019;393(10186):2155-67. https://doi.org/10.1016/S0140-6736(19)30541-0.

7. Walker J, Cattaneo M, Badimon L, Agnelli G, Chan AT, Lanas A, Rocca B, Rothwell P, Patrignani P, Langley R, Vilahur G. Highlights from the 2019 International Aspirin Foundation Scientific Conference, Rome, 2019: benefits and risks of antithrombotic therapy for cardiovascular disease prevention. ecancermedicalscience. 2020;14. doi: 10.3332/ecancer.2020.998.

8. Dai Y, Ge J. Clinical use of aspirin in treatment and prevention of cardiovascular disease. Thrombosis. 2012;2012(1):245037. https://doi.org/10.1155/2012/245037.

9. Zheng SL, Roddick AJ. Association of aspirin use for primary prevention with cardiovascular events and bleeding events: a systematic review and meta-analysis. Jama. 2019;321(3):277-87. doi:10.1001/jama.2018.20578.

10. García Rodríguez LA, Martín-Pérez M, Hennekens CH, Rothwell PM, Lanas A. Bleeding risk with long-term low-dose aspirin: a systematic review of observational studies. PLoS one. 2016;11(8):e0160046. https://doi.org/10.1371/journal.pone.0160046

11. Whitlock EP, Burda BU, Williams SB, Guirguis-Blake JM, Evans CV. Bleeding risks with aspirin use for primary prevention in adults: a systematic review for the US Preventive Services Task Force. Annals of internal medicine. 2016;164(12):826-35. https://www.acpjournals.org/doi/full/10.7326/M15-2112?download=true&journalCode=aim.

12. Li L, Geraghty OC, Mehta Z, Rothwell PM. Age-specific risks, severity, time course, and outcome of bleeding on long-term antiplatelet treatment after vascular events: a population-based cohort study. The Lancet. 2017;390(10093):490-9. https://doi.org/10.1016/S0140-6736(17)30770-5.

13. Wu IC, Hsieh HM, Yu FJ, Wu MC, Wu TS, Wu MT. A long-term risk-benefit analysis of low-dose aspirin in primary prevention. European journal of clinical investigation. 2016;46(2):130-40. https://doi.org/10.1111/eci.12575.

14. Iwamoto J, Saito Y, Honda A, Matsuzaki Y. Clinical features of gastroduodenal injury associated with long-term low-dose aspirin therapy. World journal of gastroenterology: WJG. 2013;19(11):1673. doi: 10.3748/wjg.v19.i11.1673.

15. Lanas A, Wu P, Medin J, Mills EJ. Low doses of acetylsalicylic acid increase risk of gastrointestinal bleeding in a meta-analysis. Clinical Gastroenterology and Hepatology. 2011;9(9):762-8. https://doi.org/10.1016/j.cgh.2011.05.020.

16. Huang WY, Saver JL, Wu YL, Lin CJ, Lee M, Ovbiagele B. Frequency of intracranial hemorrhage with low-dose aspirin in individuals without symptomatic cardiovascular disease: a systematic review and meta-analysis. JAMA neurology. 2019;76(8):906-14. doi:10.1001/jamaneurol.2019.1120.

17. Biffi A, Halpin A, Towfighi A, Gilson A, Busl K, Rost N, Smith EE, Greenberg MS, Rosand J, Viswanathan A. Aspirin and recurrent intracerebral hemorrhage in cerebral amyloid angiopathy. Neurology. 2010;75(8):693-8. https://doi.org/10.1212/WNL.0b013e3181eee40f.

18. Di Minno G. Aspirin resistance and platelet turnover: a 25-year old issue. Nutrition, Metabolism and Cardiovascular Diseases. 2011;21(8):542-5. https://doi.org/10.1016/j.numecd.2011.04.002.

19. Gulpinar K, Ozdemir S, Ozis E, Sahli Z, Demirtas S, Korkmaz A. A preliminary study: aspirin discontinuation before elective operations; when is the optimal timing?. Journal of the Korean Surgical Society. 2013;85(4):185-90. https://doi.org/10.4174/jkss.2013.85.4.185.

20. Gaskell H, Derry S, Moore RA. Is there an association between low dose aspirin and anemia (without overt bleeding)?: narrative review. BMC geriatrics. 2010;10:1-7. https://doi.org/10.1186/1471-2318-10-71.