



Original article

Aspirin prescribing pattern and guidelines-adherence evaluation for primary prevention of cardiovascular diseases at a teaching hospital



Salman Almalki^{a,1}, Abdulaziz Alhossan^{b,c,*}, Bashayer Alrumayyan^b, Khansa Alanazi^b, Saja Bane Gamea^b, Marwa Alesikri^b, Ajaz Ahmad^b, Ziyad Alrabiah^b

^a College of Pharmacy, Riyadh Elm University, Riyadh, Saudi Arabia

^b Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

^c Corporate of Pharmacy Services, King Saud University Medical City, Riyadh, Saudi Arabia

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ABSTRACT

The present study investigates the aspirin prescribing pattern and guidelines-adherence evaluation for primary prevention of cardiovascular diseases at a teaching hospital. A total of 816 patients were included in the study, the patients who received aspirin aged 60–69 (29.65%), followed by patients aged 50–59 years old (29.53%) and 70–79 years old (22.91%). Demographic information shown that the majority of the patients were males (58.55%). The BMI revealed that 85.78% of patients were obese. The majority of the patients have diabetes 78.67%, hypertension 74.38%, and dyslipidemia 65.68%. The mean systolic blood pressure was 136 ± 7.4 and diastolic blood pressure was 74.9 ± 5.2 . After applying aspirin candidacy calculation, only 6% patients were highly recommended to be on aspirin, 49% patients had reasonable recommendation of aspirin, 27% patients use aspirin based on “may be considered” recommendation, and 23% patients were on aspirin with no indication or recommendation. The study highlights the importance of following the international recommendations in aspirin prescribing, and flags the inappropriate use and prescribing by our healthcare providers. The current study encourages further investigation to be carried out which should include patient and clinician education, to well understand and alleviate the inequalities in aspirin use and adherence. Further studies are also warranted to understand of the prescribing pattern and to provide solutions to avoid aspirin associated complications.

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1. Introduction

Aspirin is an antiplatelet drug which has a well-established indication in the secondary prevention of coronary and cerebrovascular diseases, however its use as a primary prevention is still controversial because the risk of bleeding (Gaziano et al., 2018). Prescribing low dose aspirin (acetylsalicylic acid) in the secondary prevention of thrombotic patients with pre-existing cardiovascular disease (patients with previous myocardial infarction or acute coronary syndromes, transient ischemic attacks, or stroke) is cur-

rently well established (Gaziano et al., 2018). However, using aspirin in the primary prevention of myocardial infarction and stroke, recommendations are different, depending upon the cases. Aspirin is not recommended in individuals who do not have cerebrovascular or cardiovascular disease, according to the ESC guidelines (Halvorsen et al., 2014; Members: et al., 2012). However, based on the ACCP guidelines, persons age 50 years or older without symptomatic CVD is candidate to take low-dose aspirin 75 to 100 mg daily (Halvorsen et al., 2014; Vandvik et al., 2012). Aspirin is one of the oldest medicine in use since the period of Hippocrates and Galen using the willow tree bark for its analgesic and anti-inflammatory effects (Ittaman et al., 2014). However, the aspirin used in current times was not introduced for public use until 1904 (Ittaman et al., 2014). Various extraction and purification methods were optimized to extract and purify the salicylic acid from bark of willow tree and to reduce the unwanted side effects (Fuster and Sweeny, 2011). Apart from its analgesic potential, aspirin was also witnessed to increase the bleeding time (Fuster and Sweeny, 2011). The increase in bleeding time exhibited the

* Corresponding author.

E-mail address: alhossan@ksu.edu.sa (A. Alhossan).

¹ Denotes equal contribution.

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utility of aspirin as anti-thrombotic agent (Patrono et al., 2017). Moreover, anti-inflammatory potential requires higher and frequent dosing (Fuster and Sweeny, 2011). Gastrointestinal bleeding is the major side effect of aspirin use is at any dose. Other common dose related side effects are renal toxicity, and hypertension (Li et al., 2020; Singh et al., 2014; Wang et al., 2020). Low dose of aspirin as an anti-thrombotic effect is being used commonly, nevertheless, the reports suggests that disagreements exists among clinical guidelines for the prescription of aspirin for primary and secondary cardiovascular disease (CVD) prevention and outlines of actual use (Naderi et al., 2012; VanWormer et al., 2012). Although evidence on the appropriate cardiovascular indications for prescribing aspirin is vague (Antithrombotic Trialists et al., 2009; Rothwell et al., 2011) further evidences has emerged in relation to aspirin's benefits and harms, clinical guidelines have varied over time in their recommendations on appropriate indications for prescribing aspirin for cardiovascular treatment and prevention (Raber et al., 2019). Till 2015, treatment guidelines have recommended aspirin be considered for primary prevention among certain higher risk groups. However, since then, guidelines have narrowed the group of patients where use is recommended, or recommended against use for primary prevention. European guidelines in 2016 on CV prevention recommend against antiplatelet agents in patients with or without CVD history (Piepoli et al., 2016). United States preventive task force (USPTF) 2016 initiates to recommend aspirin in patients aged between 50 and 59 with ten years of CVD risk of 10% or higher (Bibbins-Domingo and Force, 2016). Patients aged 60–69 years full filing the above criteria are more likely to advantage, but the prescribing decision should to be made at the individual level. These distinguish the need to balance potential benefits against known adverse effects, particularly bleeding risks (Bibbins-Domingo and Force, 2016). In order to improve quality of health in a teaching hospital, the aim of this study was to evaluate the aspirin prescribing pattern as a primary prevention against cardiovascular diseases in a teaching hospital, knowing the number of patients who take aspirin for reasonable reason, and assess the aspirin efficacy in those patients.

2. Methods

King Saud University Medical City is the largest teaching health care organization in Saudi Arabia, with 1200 beds. It provides free health services, in-patient and out-patient, the medical city has more than 40 different clinics in two different locations. All of these clinics are run by either primary care providers or specialized providers. The Medical City trains hundreds of students, residents, and fellows in different specialties annually. The Medical City's directors are eager to make the institution a pioneer in providing high-standard health services for all patients and meet the public need. Thus, our study will primarily benefit the teaching hospital. Also sample appears very homogenous (e.g. Saudi natives only), is a very important contribution to the existing literature.

2.1. Study design

A retrospective cross-sectional chart review study for all aspirin users between January–December 2018. The study was approved by the Institution Review Board (IRB) prior to data collection (IRB approval number E-19-4060; Dated July 3, 2019), King Saud University Medical City, Riyadh, Saudi Arabia. About 816 patients after applying the exclusion and inclusion criteria were enrolled for this study who were objectively diagnosed with cardiovascular and other diabetes complications. The patients were selected using systemic random sampling technique. The inclusion criteria were confirmed cases of cardiovascular and diabetes complications aged

between 40 and 90 years. Patients who take low dose of aspirin were evaluated for their use reason (either primary or secondary prevention). Patients with established cardiovascular diseases (taking aspirin as secondary prevention) were excluded. Patients taking aspirin for primary prevention were further evaluated for the validity of this indication based on AHA/Framingham/10-year CV calculated risk and whether the indication follows the local and international recommendations for aspirin use for primary prevention purposes. Data were obtained from the patients' medical records also including questions about demographic and clinical details of CVDs along with the laboratory and prescription profiles. The present was information was needed whether aspirin should be used routinely for primary prevention of CVD in patients irrespective of any other risk factors. Prescriptions were examined for other medications including any antidiabetic, statins, or antihypertensive drugs. All medications were thoroughly evaluated and the focus was on the use and daily dose of aspirin.

2.2. Data analysis

Collected data was analyzed as descriptive variables and results were reported as percentages and means using SPSS software version (SPSS Inc., Chicago, USA). Demographic, clinical characteristics, and aspirin utilization were analysed. Continuous numbers and categorical variables are presented with the number (%).

3. Results

3.1. Clinical characteristics of patients

During the study period, a total of 816 patients were enrolled in this study. The baseline characteristics of the enrolled participants are enlisted in Table 1, of which 642 patients were having diabetes. The average age was 62.5 ± 2.1 . The majority of the patients were males by 58.55% (Table 1). The BMI revealed that 85.78% of patients were obese and 14.22% normal. With respect to the clinical history, the majority of the patients have diabetes 78.67%, hypertension 74.38%, and dyslipidemia 65.68%. The mean systolic blood pressure was 136 ± 7.4 and diastolic blood pressure was 74.9 ± 5.2 . The mean systolic blood pressure was 136 ± 7.4 and diastolic blood pressure was 74.9 ± 5.2 . The participants 66.5% for those receiving aspirin as primary prevention, secondary prophylaxis were only 33.5% which shows there is abuse in prescribing aspirin for primary prophylaxis. The results of the present study evidence the knowledge gap concerning aspirin use for the primary prevention of patients with CVD. After applying aspirin candidacy calculation among participants, only 6% patients were highly recommended to be on aspirin, 49% patients had reasonable recommendation of aspirin, 27% patients use aspirin based on "may be considered" recommendation, and 23% patients were on aspirin with no indication or recommendation (Fig. 1).

4. Discussion

Despite the pervasive use of aspirin for CVD prevention, all major heart and health organizations have put guidelines regarding the use of aspirin in prevention CVD prevention including: American heart association (AHA), American stroke association (ASA), American college of chest physicians (ACCP), and European society for cardiology (ESC) (Eckel et al., 2014; Pearson et al., 2002). Aspirin is generally recommended for the primary prevention of CVD based on the risk profile (Nemerovski et al., 2012). Aspirin use for primary cardiovascular prevention has been studied for a long time with controversial recommendations (Zheng and Roddick, 2019). Most of the literature refer to the international

Table 1
Demographic data and clinical characteristics of patients. Data are in numbers (%). BMI: body mass index; CVD: cardiovascular diseases; DM: diabetic mellitus; HTN: Hypertension; DLD: dyslipidemia.

Variables	Overall (n = 816)
Gender	
Male	58.55%
Female	41.45%
Age (Years)	
≤ 40	4.41%
≥80	8.57%
40–49	4.9%
50–59	29.53%
60–69	29.65%
70–79	
BMI description	
Normal	14.22%
Obese	85.78%
CVD	
No	62.7%
Yes	37.3%
Comorbidity	
No	20.3%
Yes	79.7%
DM	
No	21.33%
Yes	78.67%
HTN	
No	34.32%
Yes	74.38%
DLD	
No	35.3%
Yes	65.68%
Blood Drugs Use	
No	94%
Yes	6%
Statin Use	
No	11.3%
Yes	88.8%

guidelines to be the most accurate and safest recommendations. The high risk of a repeat event requires secondary prevention after a severe CVD event. However initial CVD events may be fatal or

disabling, which also makes primary prevention an important consideration (Pearson et al., 2002). Patients with one or more events of CVD, such as myocardial infarction (MI) or ischemic stroke, are at extremely high risk for another case of CVD (Arboix, 2015). Although rescue procedures are aimed at stabilizing acute events, such as percutaneous coronary intervention (PCI), aspirin therapy can actually help to prevent subsequent CVD events (Patrono and Baigent, 2019).

According to the demographic finding it was found that aspirin was prescribed due to primary prevention or secondary prevention to different age groups. The percentage in age group less than 40 years old was 4.41% indicates aspirin prescribing to those with low-risk people for cardiovascular disease. The other age groups 60–69 year old that was prescribed with aspirin constitute 29.53% and those aged between 50 and 59 years old the percentage was 4.9% and the age group of 70–79 years old the percentage was 29.65%, from previous finding it was been found that people over 40 years old receiving aspirin for different reasons about 95.7% which indicates the abuse of aspirin usage. According to body mass index (BMI) it was found that 85.78% of our patient were obese, which indicates that obesity is the main risk factor for many diseases like cardiovascular disease (Akil and Ahmad, 2011). Our study revealed that almost 25% of our patients in the included sample have been using aspirin with no clear indication or risk-benefit assessment. This is a very massive percentage of patients, with high risk of complications due to aspirin use. Risk of bleeding and hospitalization may be the major concern to use this medication with no indication (García Rodríguez et al., 2016). The benefits of low-dose aspirin for the primary prevention of CVD are modest and might be offset by the risk of major bleeding has been demonstrated by meta-analysis based on individual patient data (Seidu et al., 2019). It is known that intracranial and gastro-intestinal bleeding complication are associated with the use of aspirin. The bleeding risk is high in individuals older than 70 years (De Berardis et al., 2012). The present study shows that only 35% of the patients received aspirin based on a valid recommendation. Also, the statement “can be considered” means that there is no absolute recommendation, and aspirin use should be based on

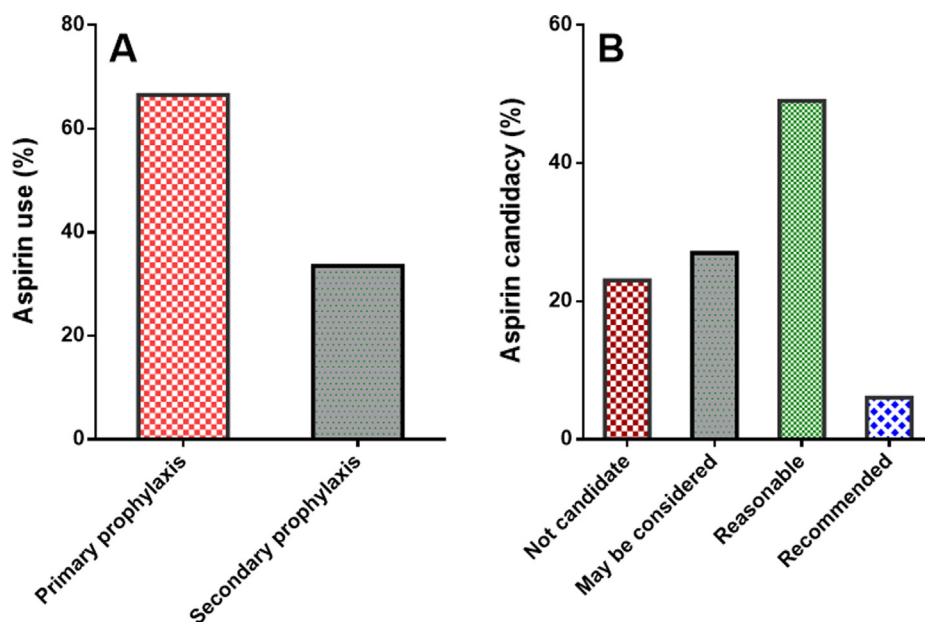


Fig. 1. Aspirin use assessment. (A) 66.5% participants for those receiving aspirin as primary prevention, Secondary prophylaxis were only 33.5%. (B) After applying aspirin candidacy (%) calculation among participants, only 6% patients were highly recommended to be on aspirin, 49% patients had reasonable recommendation of aspirin, 27% patients use aspirin based on “may be considered” recommendation, and 23% patients were on aspirin with no indication or recommendation.

patient case and further investigation should be made to make sure that the patient can tolerate the medication and no risk is associated with its use further endorses previous report on the benefits of low-dose aspirin for the primary prevention of CVD (Seidu et al., 2019). The use of aspirin in CVD prevention involves the use of aspirin in patients with diabetes (Xing and Tan, 2019). As a consequence of enhanced coronary thrombus development, increased platelet reactivity, and worsening endothelial dysfunction, individuals with diabetes have an approximately four fold increased risk of severe cardiovascular events (Patti et al., 2019). In our study it was found about 74.38% of our participant are had hypertension this give us guide that the patients need to strictly control the blood pressure, also hypertension obesity, diabetes mellitus are main risk factors for cardiovascular disease.

In primary prevention of diabetes patients, the ACCP guidelines suggest that the relative benefit of aspirin is the same in patients with and without diabetes. The American Diabetes Association, the AHA, and the ACC recommend according to cardiovascular risk as follows (Halvorsen et al., 2014; Pignone et al., 2010): 1). At low risk of cardiovascular events, aspirin should not be recommended in diabetes patients, because the potential adverse effects of bleeding are much higher than the potential benefit. 2) Aspirin may be recommended for diabetes patients at intermediate risk of cardiovascular events (patients with a 10-year risk of 5% to 10%, younger patients with at least 1 risk factor or older patients with no risk factors). 3) Aspirin use is reasonable in diabetic patients whose 10-year risk of events is >10% (men age >50 years and women age >60 years with at least 1 additional risk factor: smoking, hypertension, albuminuria, dyslipidemia, or family history of premature cardiovascular events) and who are not at increased risk of bleeding (no history of peptic ulcer disease or gastrointestinal bleeding, no concurrent use of other medications that increase risk of bleeding). The current study comprises of 78.67% of subjects having diabetes. Therefore, higher incidence of aspirin use in diabetic patients is highlighting a need for the prescribers to pay more attention in dispensing or prescribing aspirin to the diabetic patients. The use of aspirin in primary prevention patients, particularly those having diabetes, seems to be unsatisfactory as well, although this may be due to the lack of evidence. The current findings also indicate that, considering aspirin's promising cost effectiveness, statins should have been given preference as a medication for reducing CVD risk, are also in agreement with previous reports of Halvorsen et al., 2014; Pignone et al., 2010. The Journal of The American College of Cardiology recommend the use of aspirin use in the primary prevention of acute MI and other atherothrombotic cardiovascular complications, and the use of aspirin as primary prevention of CVD at a level of risk of major cardiovascular (Members: et al., 2012; Vandvik et al., 2012). Concerning about the cardiovascular events, ARRIVE Study which has investigate the use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease, patients were taking 100 mg daily and this study showed that aspirin did not lower risk of CVE, although the risk of MI was lower in patient taking aspirin but it wasn't significant (Gaziano et al., 2018). Many chronic diseases such as diabetes and hypertension are associated with increased risk of cardiovascular events. The majority of patients who are diagnosed with one of these diseases take aspirin in order to reduce the risks of cardiovascular diseases (Xing and Tan, 2019).

Previous clinical studies have consistently demonstrated that the effects of aspirin on prevention of atherosclerotic cardiovascular diseases (ASCVD) (Antithrombotic Trialists et al., 2009; Rodés-Cabau et al., 2015; Gaziano et al., 2018; Halvorsen et al., 2014). The study of Lou et al., demonstrated that aspirin may be beneficial for decreasing the incidence of CVDs in patients with dyslipidemia (Lou et al., 2016). Aspirin has now been used for the ASCVD pre-

vention owing to its compelling evidence on improving cardiovascular outcomes (Bartolucci et al., 2011). Although, aspirin also has undesirable effect on inhibiting COX and thereby reducing the platelet adhesion and activation (Lou et al., 2016). In present study most of our enrolled patients (65.68%) had clinical and laboratory proof of dyslipidemia and using statins which demonstrates the gaps in cardiovascular risk management. Consequently risk and benefits of prescribing aspirin should be monitored cautiously before applied to the patients with ASCVD risk factors such as dyslipidemia (Arnett et al., 2019). The present recommendations are also consistent with the findings of Lou and co-workers also suggests that the benefit of aspirin for dyslipidemia primary prevention capacity be possible for a definite population (Lou et al., 2016).

In a recent report from Italy indicates that only 46.3% of high-risk CVD patient used aspirin for prevention (Lugo et al., 2014), while in another study 35% of clinicians indicated that patients were using it for primary prevention (VanWormer et al., 2014). Similarly, a study revealed that a small percentage of patients were prescribed aspirin (Fiscella et al., 2015). In present study still there are high prescribing of aspirin as primary prevention of cardiovascular events, the percentage 66.5% for those receiving aspirin as primary prevention, secondary prophylaxis is only 33.5% this states there is an abuse in prescribing aspirin for primary prophylaxis. The results of the present study evidence the knowledge gap concerning aspirin use for the primary prevention of patients with CVD. Our recommendations are also in line with the results of McNeil and co-workers, reported the aspirin in reducing events in the elderly (ASPREE) trial proved that the use of aspirin is detrimental to healthy subjects causing more haemorrhagic events (McNeil et al., 2018). Conversely, this demonstrates gaps in cardiovascular risk management, and there is shortage of health care prescriber knowledge about new guidelines for prescribing aspirin as prophylaxis. Despite the large number of sample size, we recommend that other studies should be conducted to understand of this prescribing pattern and to provide solutions to avoid complications. Also, a pharmaco-economic study can show the cost of inappropriate prescribing of aspirin and helps putting a clear recommendation on its use. The available evidence of USPSTF and AHA have suggested and recommended the use of aspirin therapy in primary prevention with evidently likely to benefit from its use.

5. Conclusions

The present study highlights the importance of following the international recommendations in aspirin prescribing, and flags the inappropriate use and prescribing by our healthcare providers. The findings of this study also strengthen the evidence about aspirin use and prescription patterns for prevention in Saudi adults. A very important contribution to existing literature. Further research is needed to optimize the use of aspirin therapy in the patients likely to benefit. The current study encourages further investigation to be carried out which should include patient and clinician education, to well understand and alleviate the inequalities in aspirin use and adherence.

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7. Institutional Review Board statement

The study was approved by the Institution Review Board (IRB) prior to data collection (IRB approval number E-19-4060; Dated July 3, 2019), King Saud University Medical City, Riyadh, Saudi Arabia.

CRediT authorship contribution statement

AA (Abdulaziz Alhossan) and SA: Conceptualization, Data curation, Project administration, supervision and Resources. **AA (Abdulaziz Alhossan):** Funding acquisition. **BA:** Methodology. **K.A:** Formal analysis, investigation, Software. **S.B.G:** Methodology, Software, Validation. **MA:** Data curation, Validation, Writing-original draft. **AA (Ajaz Ahmad):** Formal analysis, Validation, Writing-original draft, review & editing. **ZA:** Methodology, Resources.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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