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LOW DOSE ASPIRIN USE FOR PRIMARY CARDIOVASCULAR PREVENTION AMONG LEBANESE POPULATION

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LOW DOSE ASPIRIN USE FOR PRIMARY CARDIOVASCULAR PREVENTION AMONG LEBANESE POPULATION

Abstract

In spite of the controversies regarding low-dose aspirin safety and efficacy, aspirin is widely used by individuals for the primary prevention of myocardial infarction and ischemic stroke. This study assesses the appropriateness of low dose aspirin use in a sample of Lebanese population. A cross-sectional study was conducted using a community-based questionnaire to assess each patient's risk factors for Myocardial Infarction and ischemic stroke and possible contraindications for aspirin use. WHO risk score was used to calculate the cardiovascular risk of patients and determine the appropriateness of aspirin use for the primary prevention of cardiovascular diseases accordingly. Data were analyzed using Statistical Package for the Social Science (SPSS®) version 20. Chi-square test was used to compare between nominal data. P-value was considered significant at values less or equal to 0.05. Results showed that 34% of 505 patients were on aspirin therapy for primary prevention of cardiovascular disease. Eighty-two percent of the sample had low cardiovascular disease risk, while only 4% had very high risk and were eligible for aspirin use for primary prevention according to the WHO guideline. Of the total sample 30.5% were over-utilizing aspirin and 3% only were using it appropriately. Moreover, all self and pharmacists' prescriptions as well as 88% of the physician's prescriptions were inappropriate. As a conclusion, aspirin is being over-utilized by the Lebanese population for primary prevention of Myocardial Infarction and ischemic stroke. Physicians and pharmacists should collaborate in order to insure proper prescription of aspirin.

Keywords

Aspirin, Primary Prevention, Myocardial Infarction, Stroke

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ABSTRACT: *In spite of the controversies regarding low-dose aspirin safety and efficacy, aspirin is widely used by individuals for the primary prevention of myocardial infarction and ischemic stroke. This study assess the appropriateness of low dose aspirin use in a sample of Lebanese population. A cross sectional study was conducted using a community based questionnaire to assess each patient's risk factors for Myocardial Infarction and ischemic stroke and possible contraindications for aspirin use. WHO risk score was used to calculate the cardiovascular risk of patients and determine the appropriateness of aspirin use for the primary prevention of cardiovascular diseases accordingly. Data were analyzed using Statistical Package for the Social Science (SPSS®) version 20. Chi-square test was used to compare between nominal data. P-value was considered significant at values less or equal to 0.05. Results showed that 34% of 505 patients were on aspirin therapy for primary prevention of cardiovascular disease. Eighty two percent of the sample had low cardiovascular disease risk, while only 4% had very high risk and were eligible for aspirin use for primary prevention according to the WHO guideline. Of the total sample 30.5% were over utilizing aspirin and 3% only were using it appropriately. Moreover, all self and pharmacists' prescriptions as well as 88% of the physician's prescriptions were inappropriate. As a conclusion, aspirin is being over-utilized by the Lebanese population for primary prevention of Myocardial Infarction and ischemic stroke. Physicians and pharmacists should collaborate in order to insure proper prescription of aspirin.*

KEYWORDS: *Aspirin, Primary Prevention, Myocardial Infarction, Stroke*

1. INTRODUCTION

According to the world health organization (WHO), cardiovascular disease (CVD) is the leading cause of death worldwide, representing 31% of all global deaths in 2016 (WHO, 2017). Similarly, in Lebanon, CVD accounted for 47% of deaths due to non-communicable diseases, making it the number one cause of death between the ages of 30- 70 years (WHO, 2015).

Most of the CVD risk factors are controllable, treatable or modifiable such as hypertension (HTN), diabetes mellitus (DM), dyslipidemia (DL), sedentary lifestyle, smoking, and obesity. Nevertheless, age, gender, and genetic factors are non-modifiable CVD risk factors. Accordingly, treating and controlling risk factors are the major CVD preventive measures to be taken and recommended by health care providers. In addition, a low dose of aspirin has been advocated. In fact, aspirin has been proven to produce a statistically significant reduction in cardiovascular events as secondary prevention out-weighting its drawback, the major bleeding. However, aspirin use as primary prevention of CVD is less clear (WHO, 2012; Maas, 2010).

Some of the guidelines support the use of aspirin in primary prevention of CVD. The WHO 2007 guidelines for the prevention of cardiovascular diseases, for example, recommend the use of aspirin for people who have a 10-year risk of cardiovascular events of 30% and more (WHO, 2007). Similarly, the American College of Chest Physicians (ACCP) 2012 (Vandvik, 2012) recommends the use of a low dose of aspirin 75 – 100 mg for those ages 50 years and older without symptomatic CVD. In 2016, the U.S. Preventive Services Task Force (USPSTF) recommend the use of aspirin for patients with a 10-year risk of cardiovascular disease of 10% and more and aged between 50 and 69 years, if its benefit outweighs the risks (Domingo, 2016). On the other hand, the FDA mentioned that evidence doesn't support the general use of aspirin for primary prevention of heart attack or stroke due to the increased risk of bleeding in the gastrointestinal tract and brain. The FDA reaffirmed the use of aspirin only in secondary prevention (FDA, 2015). The European Society of Cardiology (ESC), NICE guidelines 2015 for the management of type 2 diabetes in adults and The American Heart Association / American Stroke Association (AHA/ASA) guidelines for the primary prevention of stroke state that the usefulness of aspirin in low

– risk diabetic patients is still unclear (Halvorsen, 2014; NICE, 2015; Meschia, 2014). Newer studies and guidelines are showing that prescribers should be more prudent while prescribing aspirin for the primary prevention of CVD. The American Diabetes Association (ADA) 2019 guidelines included data from the ASPREE, ASCEND and ARRIVE trials and stated that aspirin can be considered in patients with high 10-years risk of CVD after discussing the possible risks (ADA, 2019). Furthermore, a systematic review and meta-analysis from 13 trials published in JAMA journal showed that the role of aspirin in primary prevention is still controversial since it lowers the risk of CVD but increases the risk of bleeding (Gaziano, 2019). In fact, according to Baigent et.al., it is essential to estimate the patient's baseline risk to have CVD and to balance this risk against the side effects of aspirin therapy before initiating aspirin for primary prevention (Baigent, 2009). In Lebanon, according to Drouby et al, in a sample of 315 patients, 49% were on aspirin for primary prevention of CVD (Drouby, 2015). Accordingly and since the appropriateness of aspirin use was not studied, the aim of the current study was to assess the compatibility of aspirin use with the WHO guideline (WHO, 2007).

2. METHOD

A cross sectional descriptive study was conducted by completing anonymous data collection forms. Patients aged 45 to 79 years old were included in the survey while pregnant women, patients with chronic kidney disease or connective tissue diseases, cancer patients and patients with a history of myocardial infarction or ischemic stroke were excluded. The questionnaire was administered by interview to volunteer patients visiting different community pharmacies in Beirut, Tripoli, saida, and Bekaa areas, during may till September 2015. No compensation was given to them.

The questionnaire was developed in English then translated to Arabic, the native language. It included demographic information such as age, gender and body weight, the risk factors of CVD, aspirin use and indication as well as its contraindications if present. World Health Organization/ International Society of Hypertension (WHO/ISH) CVD risk score was calculated, using WHO risk score charts, for each patient to categorize them as candidate or not for aspirin use (WHO, 2007). The questionnaire was tested for content validity by 2 experts and further adjustments were done after pilot testing with 20 patients. The sample size was calculated using the online sample size calculator assuming that the Lebanese population is around 5,851,000. A total of 385 patients and above would provide a representative sample with 5% margin error and 95% confidence level.

The Results were analyzed using Statistical Package for the Social Science (SPSS®) version 20. Categorical data were expressed as percentage while continuous data as mean \pm standard deviation (SD). Chi-Square was used when appropriate to compare between groups. Difference was considered significant at P-value less or equal to 0.05.

3. RESULTS

A total of 505 participants answered the survey with a mean age of 58.37 ± 8.41 years old. They were gathered from Beirut (46.3%), South (14.9%), North (14.7%), and Bekaa valley (24.2%). Two hundred forty two participants 242 (47.9%) were females and 263 (52.1%) were males. Fifty eight percent were overweight or obese and 58% followed a sedentary lifestyle. Forty two point eight percent were smoker and 40.6% had a family history of CVD. Hypertension, diabetes, and dyslipidemia accounted for 43.6%, 25.2% and 35.5%, respectively (Table 1).

Table 1: Studied sample characteristics

Characteristics	Frequency (%) or mean \pm SD
Regional distribution	
Beirut	234 (46.3%)
South	75 (14.9%)
North	74 (14.7%)
Bekaa Valley	122 (24.2%)
Age	58.37 \pm 8.41
Gender	
Female	242(47.9%)
Male	263 (52.1%)
Obesity	
Normal weight	212 (42%)
Overweight/Obese	293 (58%)
Smoking status	
Non-smoker	289 (57.2%)
Smoker	216 (42.8%)
Sedentary lifestyle	
Yes	216 (42.8%)

No	289 (57.2%)
Family History of CVD	
Yes	205 (40.6%)
No	300 (59.4%)
Comorbidities*	
Diabetes	127 (25.2%)
Dyslipidemia	179 (35.5%)
Hypertension	220 (43.6%)

*Patients may had more than one comorbidity

According to the WHO calculator, 81.6% of the total sample had low CVD risk, 12.9% had moderate CVD risk, 1.6% had high CVD risk and 4% had very high CVD risk (Fig. 1).

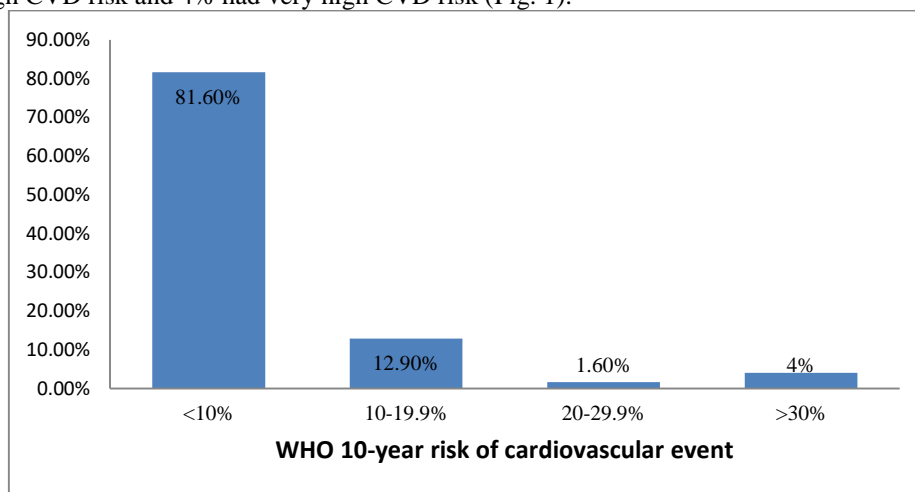


Fig. 1 Percentage of cardiovascular risk according to WHO

Thirty three percent of the sample was on aspirin therapy for the primary prevention of myocardial infarction and ischemic stroke (Fig. 2). Aspirin was prescribed in 79% of the cases by physicians, recommended in 3% by the pharmacists and self-used by 18%. The self-users of aspirin had the common perspective that any patient above 50 years of age should be on aspirin regardless of his or her comorbidities.

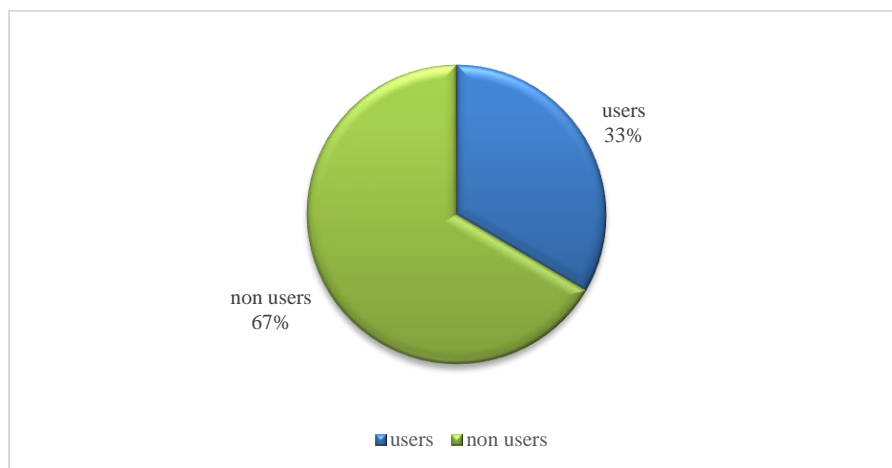


Fig. 2 Aspirin use among the participants

The pattern of aspirin use significantly increases by the presence of serious risk factors and comorbidities such as DM, HTN, age and smoking. Results showed that the use of aspirin was 2.42 times higher in diabetic participants than non-diabetic (CI=1.60-3.65; p <0.001), 2.10 times more in participants with SBP of 140-159 mmHg than those with SBP of 120 – 139 mmHg (CI=1.13-3.89; p <0.05), 2.7 times more in participants aged 70 to 80 years old than patients aged 40 to 49 years (CI=1.28-5.75; p <0.05) (Table 2).

Table 2: Pattern of aspirin use according to the risk factors of cardiovascular disorders

Risk Factors		Not on Aspirin count (%)	Using aspirin count (%)	OR	CI	P value
DM	Non-Diabetic	271 (80.65)	107 (63.31)	2.42	1.60-3.65	<0.001
	Diabetic	65 (19.34)	62 (36.68)			
SBP range	120-139	305 (90.77)	139 (82.24)	2.10	1.13-3.89	0.02
	140-159	23 (6.84)	22 (13.01)			
	160-180	8 (2.38)	8 (4.73)			
Age Range	40-49	59 (15.55)	17 (10.05)	1.46	0.79-2.71	0.23
	50-59	145 (43.15)	61 (36.09)			
	60-69	100 (29.76)	66 (39.05)			
	70-80	32 (9.52)	25 (14.79)			
Smoking	Non-smoker	179 (53.27)	97 (57.39)	0.81	0.56-1.17	0.27
	Smoker	136 (46.72)	72 (42.60)			

X² test was performed

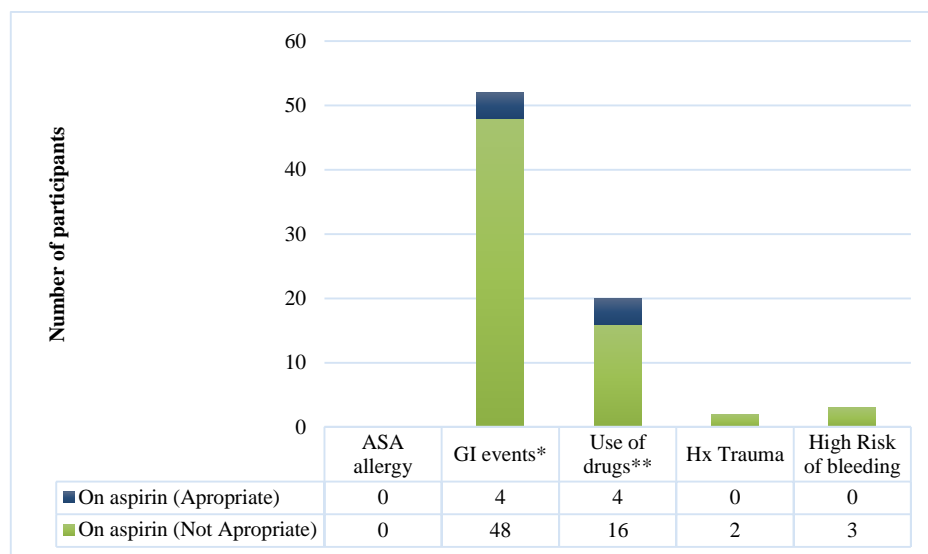
Regarding the pattern of aspirin use versus the population's CVD risk, a higher percentage of the participants used aspirin in higher CVD risk categories than those with low CVD risk: 7.39 times (CI=2.6-20.6; p<0.001) more participants with very high CVD risk, and 2.24 times (CI=1.36-3.89; p<0.001) more participants with moderate CVD risk used aspirin than those with low CVD risk (Table 3).

Table 3: Pattern of aspirin use according to patients' collective CVD risk

CVD risk	Total Frequency	Not on aspirin # (%)	Using aspirin # (%)	OR	CI	P value
Low (<10%)	412	293 (71.11%)	119 (28.88%)	2.24	1.32-3.82	<0.001
Moderate (10-20%)	65	34 (52.30%)	31 (47.69%)			
High (20-30%)	8	4 (50.0%)	4 (50.0%)	2.46	0.61-10.01	0.19
Very High (>30%)	20	5 (25.0%)	15 (75%)	7.39	2.63-20.78	<0.001

X² test was performed

Fifty-two participants were using aspirin even-though they had GI events. Only 4 of them had very high CVD risk, justifying the use of aspirin. Results also showed that 20 participants are using other drugs such as antiplatelet, anticoagulants, other non-steroidal anti-inflammatory drugs or steroids, with aspirin concomitantly. Only 4 of them had very high CVD risk, thus justifying the reason for aspirin use. Two participants using aspirin had history of trauma and 3 had high risk of bleeding, with a low to moderate CVD risk, making them non-appropriate users of aspirin (Fig. 3).



*Gastrointestinal events: history of, or active ulcer

**Antiplatelet, anticoagulants, NSAIDs, steroids

Fig. 3 Appropriate use of aspirin in patients with contraindications

The WHO guideline recommends the use of aspirin for primary prevention only in patients with very high CVD risk. Results showed that 154 participants out of 485 non-candidate participants were on aspirin therapy and 5 participants out of 20 candidate participants were not on aspirin therapy thus accounting to a total of 31.5% inappropriate use of aspirin. These findings are suggestive of wrong practice concerning aspirin prescribing and counseling, where participants are being either over-prescribed aspirin (30.5%) or under-prescribed aspirin (1%) due to lack of patient risk assessment and risk to benefit risk calculation (Fig. 4).

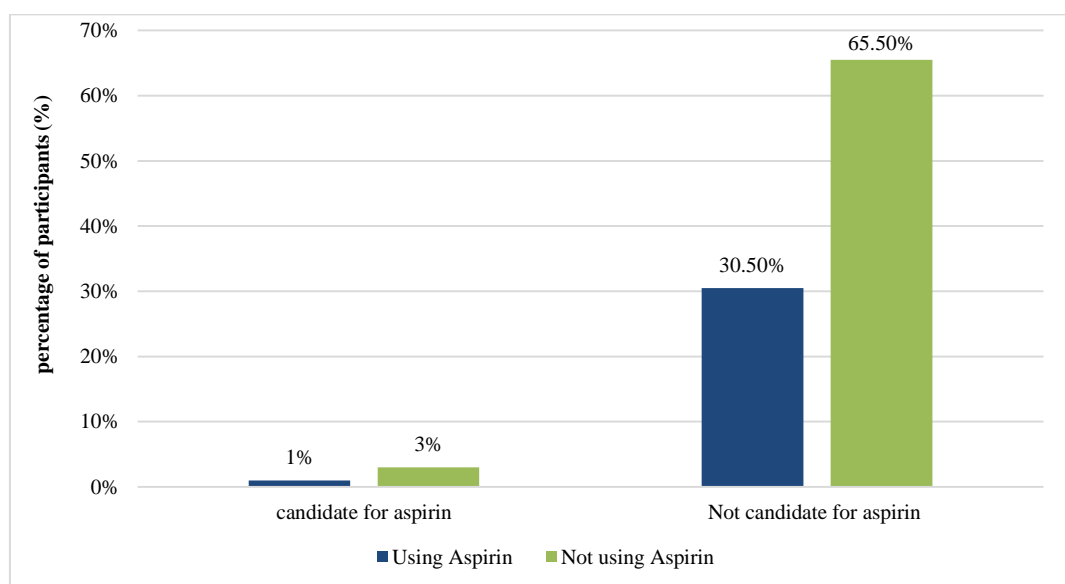


Fig. 4 Appropriateness of aspirin use in the sample studied

All self-used aspirin and those recommended by pharmacists as well as 88% of the physicians' prescriptions were inappropriate (Fig. 5).

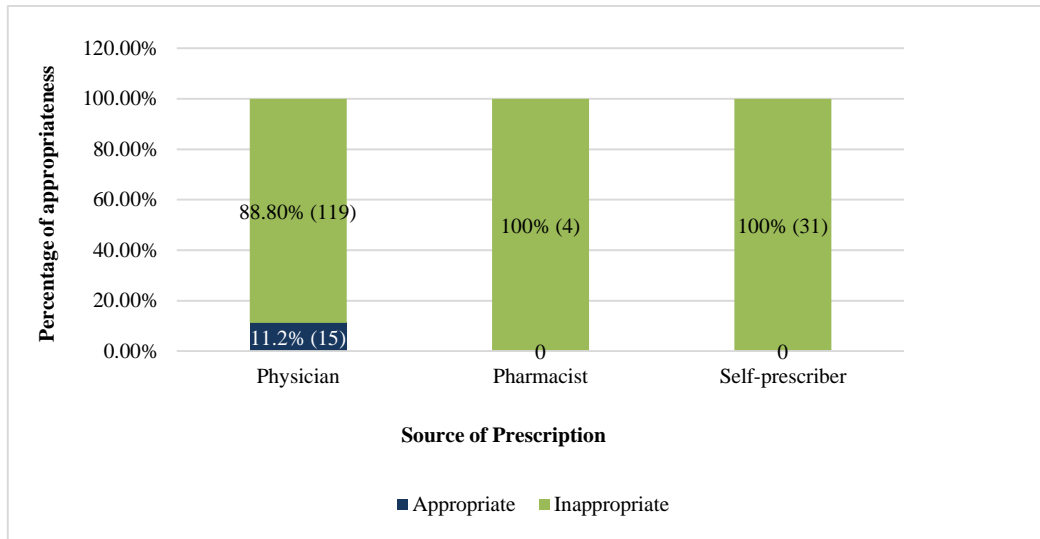


Fig. 5 Appropriateness of prescription of aspirin

4. DISCUSSION

Atherosclerosis begins early in life and continues through adulthood putting humans at middle age and elderly at high risk for CVD. Its rate of development is not only related to age but also to cardiovascular risk factors such as smoking, unhealthy diet or sedentary lifestyle resulting in obesity, hypertension, dyslipidemia and diabetes (WHO, 2017). According to the WHO risk score charts, the 10-year risk of cardiovascular event is determined by taking into consideration the age, gender, smoking status, presence of diabetes, cholesterol and systolic blood pressure levels (WHO, 2017). Accordingly, 12.9% of the studied sample had a moderate CVD risk and 5.6% had a high or very high risk, while 81.6% had low CVD risk. Nevertheless, 33 %of the studied sample were using aspirin.

Knowing that diabetes and hypertension are major risk factors for CVD (Petrie, 2018), participants with diabetes or elevated blood pressure used more aspirin than non-diabetic or normotensive ones, respectively. Moreover, AHA 2014 guideline for the prevention of stroke considers older age as a risk factor for CVD due to heart physiologic changes (Meschia, 2014). As a consequence, in the studied sample, old participants used more aspirin than younger ones. Smoking status, on the other hand, did not affect the use of aspirin although it was proven that it increase the risk of stroke by 2to 4 times (Benjamin, 2019). The sum of all risk factors, in the studied sample, revealed that only 4% of the participants were candidate for aspirin use taking into consideration that the WHO advocates the use of aspirin in only very high CVD risk group (WHO, 2017). As a matter of fact, 30.5% of the studied sample were misusing aspirin. This finding is consistent with a cross-sectional study done in the United States of America which showed that aspirin is over utilized (Wormer, 2014).

Moreover, 48 participants on aspirin had GI ulcers and 16 participants used concomitantly other antiplatelet, anticoagulants, non-steroidal anti-inflammatory drugs or steroids with no justified reason of its use. In fact, based on the ACC/AHA 2019 recommendations, aspirin should be avoided in persons with a history of GI bleeding, peptic ulcer disease, and concurrent use of NSAIDs, steroids, and anticoagulants (Arnett, 2019).

The inappropriate aspirin use was not only owed to self-prescription but also to physician over-prescription and pharmacist improper counseling. This implicate that physicians should calculate, as recommended by the new guideline for primary prevention of aspirin (Arnett, 2019), patient's risk for CVD and evaluate the benefit/risk of aspirin use since newer recommendations state that aspirin should not be used in the routine primary prevention of CVD due to lack of benefit. Pharmacists also has an important role by counseling patients to visit their physicians instead of self-medicating themselves as well by screening for drug-drug interactions and contraindications.

5. CONCLUSIONS

The use of aspirin for primary prevention of CVD is inappropriate in 31.5% of the population where only 4% of the population should be on aspirin according to the WHO recommendations. This inappropriateness is accounted for the wrong interpretation of the healthcare providers for the risks of CVD, along with the lack of patient awareness regarding the aspirin side effects. As a consequence, patients' risks of CVD as well as the benefit/risk of aspirin use should be determined before prescribing aspirin.

6. CONFLICT OF INTEREST

The authors declare that they have no conflict of interest. The study was self-funded.

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