ABSTRACT

The study aims to describe frequency of risk factors for coronary artery disease among cardiac patients in central level hospital of Nepal. The study was descriptive cross-sectional involving 106 cardiac patients with coronary artery disease attending catheterization lab, outpatient department, coronary care unit and general cardiac ward of Manmohan Cardiothoracic Vascular and Transplant Centre (MCVTC). Data was collected by using structured questionnaire from September 2016 to October 2016. Purposive sampling technique was used to select the coronary artery disease patients. The frequency rates of nine conventional risk factors are presented as a retrospective single-center observational study. The results of the study revealed the proportion of male and female 64.2% and 35.8% respectively. Of the 106 patients the mean age of the respondents was (58.65±11.26). The most frequency of risk factors for coronary artery disease of the respondents were dyslipidemia (67.6%), smoking (53.8%), hypertension (47.2%), physically inactive (46.2%), diabetes mellitus (39.6%) and previous history of CAD (38.7%). Likewise, other less common risk factors were obesity (31.1%), alcoholic (19.8%) and family history of CAD (17.9%). This study identified coronary artery disease risk factors are highly prevalent among dyslipidemic, smokers and hypertensive patients. As management of risk factor is important aspect in the primary prevention of CAD, these patients are recommended to be trained regarding lifestyle changes. Also, prevention strategies can play an important role in reducing patient morbidity and mortality.

Contribution/ Originality: This study is one of the very few studies which have investigated cardiac patients with coronary artery disease (CAD) in central level hospital of Nepal to find out the frequency of risk factors for CAD among cardiac patients and measures the association between socio-demographic variables and risk factors for CAD.

1. BACKGROUND

Coronary artery disease (CAD) is one of the most common causes of mortality and morbidity in both developed and developing countries [1]; [2]; [3]. CAD becomes third global burdened disease ranked by WHO and leading fatal disease. As World Health Organization (WHO) [4] mentioned CVDs are the number one cause of death globally: more people die annually from CVDs than from any other cause. An estimated 17.9 million people died...
from CVDs in 2016, representing 31% of all global deaths. Of these deaths, 83% are due to heart attack and stroke. Over three quarters of CVD deaths take place in low- and middle-income countries. Out of the 17 million premature deaths (under the age of 70) due to non-communicable diseases in 2015, 82% are in low- and middle-income countries, and 37% are caused by CVDs.

The identified risk factors associated with CAD, in both developed and developing countries, are Smoking habit, alcoholism, low quality diet intakes, physical inactivity are some of the established risk factors which have 80% contribution in the development of NCDs. Developed countries showed dramatic decrease in mortality trend than developing countries. Hussain, et al. [5] mentioned CAD was responsible for each 3 out of 4 deaths in low and middle income countries; for that changing life style factors and moving towards urbanization are the major risk factors. Nevertheless, the frequency and hazards of CAD have not declined significantly especially in low and middle income countries.

According to national reports gathered by WHO's South East Asia regional office, of the total deaths in South Asia, the proportion attributable to NCDs ranged from about 7% in Nepal, in which Cardiovascular Diseases (CVDs) account for 27%. Data shows that out of the total admitted patients, 36.5% patients suffered from NCDs and out of the total (4343) NCD cases, heart diseases constituted 38%. At tertiary level, less than 10% were CAD. Frequency of CHD in eastern region was 5.7% in 2005. CAD can be prevented by addressing behavioral risk factors and early detection and management for those who are at high cardiovascular risk due to hypertension, diabetes, hyperlipidaemia or already established disease.

The burden of coronary artery disease and its risk factors are going to be national health problems even for Nepal as the number of patients with this disease is expected to increase rapidly [6]. Although CAD is an interesting area of research, in context to Nepal, studies regarding the frequency of cardiovascular risk factors are limited. So, there is a need of study on frequency of risk factors for coronary artery disease to decrease frequency of mortality and morbidity with CAD in developing country like Nepal. Therefore, this study attempts to find out the frequency of risk factors for coronary artery disease among cardiac patients. The objective of the research is therefore (i) to identify the frequency of risk factors associated with coronary artery disease and (ii) to measure the association between socio-demographic variables and risk factors of coronary artery disease.

The remaining of the paper is structured as follows. Section 2 discusses relevant literature studying the frequency and associated risk factors for Coronary Artery Disease among Cardiac Patient. Section 3 discusses the research methodology. The result and analysis discussion of the findings are discussed in section 4. Discussion is presented in section 5 and section 6 concludes the paper.

2. REVIEW OF LITERATURE

CAD, being the common causes of mortality and morbidity in both developed and developing countries, has great important to discuss further for its better solution to promote healthy lifestyle. CAD most commonly caused by various risk factors which may classified as modifiable [7]; [8]; [9]; [10] and non-modifiable [11]. Long back Black [12] has pointed out that for coronary artery disease; that cannot be changed are: age, gender and heredity; that can be changed are: high blood pressure, elevated serum cholesterol, lipoprotein, cigarette smoking, obesity, glucose intolerance, diabetes, fibrinogen, left ventricular hypertrophy, cocaine, behavioral factors (stress, type A personality); and protective factors are: HDL cholesterol, exercise, estrogen and moderate alcohol intake. It indicates multiple amendable risk factors were associated in the early onset of coronary heart disease.

Several regional studies also highlights that CAD is a leading cause of mortality and morbidity in various countries in the Americas and Europe, which are declining. Ghumman [7] observed South Asians have higher rates, higher associated mortality, and earlier onset of CAD due to genetic predisposition and lifestyle factors. Nine modifiable risk factors (smoking, DM, lipids, central obesity, hypertension, diet, physical activity, alcohol consumption, psychosocial factors) account for over 90% of CAD in all populations. South Asians have more
traditional risk factors at an earlier age, explaining premature CAD in this group. Khan, et al. [13] claimed that progressive expansion and acceptance of a western life style contributes to the rising burden of cardiovascular disease (CVD) in the developing world. The risk factors of CAD, if identified at an early stage can be extremely useful in planning primary and secondary preventive strategies. In South Asia the frequency of hypertension is 3.2 %, diabetes 2.6 %, and CAD is 3.2 % [14]. However, in urban and immigrant populations the prevalence rates are 12-20, 6-8, and 7-14 %, respectively [13].

Jiang, et al. [15] mentioned in China a total of 104393 Coronary heart Disease (CHD) deaths—55380 males (53.05%) and 49013 females (46.95%), and 67010 urban (64.19%) and 37383 rural (35.81%) residents—were recorded and validated in Tianjin's CDRS. The overall mortality from CHD stayed the same or increased over the study period. Coronary artery disease (CAD) is a leading cause of death in India, and its contribution to mortality is rising; the number of deaths due to CAD in 1985 is expected to have doubled by 2015. According to reports from the National Commission on Macroeconomics and Health, 62 million people in India will have CAD by 2015, with 23 million of these below 40 years of age [3].

In the context of Nepal, Twayana, et al. [16] observed multiple risk factors were associated in the early onset of coronary heart disease in this study population. Modification of these factors by pharmacotherapy, diet, exercise and behavioral therapy can improved the prognosis of these patients and can also lower the incidence of CHD. A recent National Non Communicable Disease (NCD) risk factors survey revealed significant levels of smoking (18.5%), alcohol consumption (17.4%), insufficient fruit and vegetable consumption (98.9%) and obesity (4%) among Nepalese [17].

Timely measuring frequency of risk factor for CAD has a significant rational as individuals affected by the disease at a particular time varies with the time span. Such measurement serves and facilitates to deal with the number of new individuals who contract a disease during a particular period of time. It then helps to reduce the mortality and morbidity associated with CAD. The frequency rate is high in CHD, In South Asia the frequency of hypertension is 3.2 %, diabetes 2.6 %, and CAD is 3.2 % [13] and In Nepal, frequency of CHD in eastern region was 5.7% in 2005 [17].

3. RESEARCH METHODOLOGY

3.1. Research Setting and Study Population

A cross sectional descriptive study design was used to identify frequency of risk factors for coronary artery disease among cardiac patients. The study was carried out in Tribhuvan University Institute of Medicine Manmohan Cardiothoracic Vascular and Transplant Center (MCVTC), Maharajgunj, Kathmandu. Selected wards of this hospital for the setting of this study were Catheterization Lab, Outpatient Department, Coronary care unit and General Cardiac ward. The total patients presented with coronary artery disease (CAD) including admitted patients, patients undergoing angiography, angioplasty and Coronary Artery Bypass Graft (CABG), and follow up cases in outpatient department included those cases who came in follow up after the intervention such as angiography, Coronary Artery Bypass Graft (CABG), angioplasty and/or regular follow up for previous CAD.

3.2. Determinants of Sample Size

The non-probability purposive sampling technique was used to determine the sample size. The patients with coronary artery disease who come to the MCVTC hospital during data collection period (i.e. 3 weeks) were taken as the sample. In this study frequency of risk factor for CAD among cardiac patient is not sure so we tale frequency of 50%. Since the N is quantified (or given) i.e. 125 CAD associated visitors for 3 weeks, the total sample size for the study is ≈ 96. This study also considered 10% of non-response error (i.e. ≈ 10). Hence, a total 106 respondents having CAD among cardiac patients were taken as a sample size for the study. However, the following exclusion conditions are applied:

- Patients with CAD who did not come for follow up.
- Patients with CAD who were lost to follow up.
- Patients with CAD who were transferred to other hospitals.
- Patients with CAD who were not willing to participate in the study.

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criteria were taken care of (i) the critically ill patients and who was in ventilator were excluded (ii) the patients who were taken for pretesting was excluded and (iii) unable or unwilling to give informed consent was excluded.

3.3. Variables of the study and Operational Definitions

The dependent variable of this study is frequency of risk factors for Coronary Artery Disease and the independent variables are age, sex, education, occupation and income of the respondents. The operational definition of the variables is:

- **Frequency:** The presence of risk factors of coronary artery disease among respondents.
- **Risk factors:** In this study the risk factors included smoking, alcohol intake, obesity, previous history of CAD, family history, sedentary lifestyle, dyslipidemia, diabetes mellitus and hypertension.
- **Cardiac Patients:** In this study the cardiac patients refers to those who come to the hospital with coronary artery disease.
- **Alcohol Intake:** In this study the respondents who consume more than 1 ounce (30ml) ethanol, 2 ounce whiskey, 10 ounce wine and 2½ ounce beer daily \[18\].
- **Smoking:** In this study smoker refers to those participants who smokes either 1 stick or more cigarettes daily. Patients will classified as non-smokers only if they had never smoked.
- **Family history of coronary artery disease:** It include the presence of coronary artery disease in three generation family members i.e. father, mother, grand-father and grand-mother.
- **Previous history of coronary artery disease:** It refers the previous attack of coronary artery disease to the respondent.
- **Sedentary lifestyle:** It refers to a type of lifestyle with lack/no or irregular physical activity. In this study it refers when respondents not engaged in either moderate intensity activities (including brisk walking) for at least 30 minutes on five or more days per week, or 20 minutes of vigorous-intensity activities on three or more days a week, or 20–30 minutes of any combination of walking, moderate-intensity or vigorous intensity activities on 5 or more days in a week \[19\].
- **Obesity:** In this study obesity refers to those who have Body Mass Index (BMI) more than 25 kg/m\(^2\) \[4\].
- **Dyslipidemia:** Dyslipidemia refers to those who have history of dyslipidemia diagnosed and/or treated by a physician or having value exceeding more than normal in one of the following condition. Total cholesterol ≥ 200 mg/dL (hypercholesterolaemia), triglycerides > 150 mg/dL, low-density lipoprotein cholesterol (LDL-C) ≥ 160 mg/dL and high-density lipoprotein cholesterol (HDL-C) ≤ 40 mg/dL (National Cholesterol Education Program \[20\].
- **Diabetes mellitus:** It refers to those patients who have a history of diabetes self-reported by patient and/or diagnosed (mention in OPD ticket or inpatient registration) by the physician.
- **Hypertension:** It refers to those patients who have a history of hypertension self-reported by patient and/or diagnosed (mention in OPD ticket or inpatient registration) by the physician.

3.4. Data Collection and Analysis

The instrument was based on the set objectives and literature review. Necessary modifications were done in the instruments after consulting with advisor and subject expert as appropriate for its validity. To maintain reliability of instrument pre-testing was performed in 10% of the total sample size i.e. 11 respondents in MCVTC. After the pretest, to check consistency of the questionnaires 1-Coefficient of Variance (CV) was applied, the result of consistency was 95.5%. Structured questionnaires were asked using face to face interview schedule which took 20-30 minutes to collect the data. Privacy of setting was maintained as the researcher was take interview in a special waiting room in OPD setting and catheterization lab setting as well as even in the bed of patients in general ward setting. The data was collected between September and October of 2016. The data obtained were analyzed on the basis of the objectives of the study using descriptive statistics which consist the parameters like mean, frequency, percentage and standard deviation. The analysis also done by using inferential statistics i.e. Chi square test to find out association between socio-demographic variables and risk factors of coronary artery disease.
3.4.1. Ethical Consideration

The study was conducted only after the approval of research committee of JF Institute of Health Sciences/LACHS. Ethical approval level was taken from Nepal Health Research Council (NHRC) and Formal written permission was taken from the concerned authority of MCVTC through written request letter from JF Institute of Health Sciences/LACHS. Self-introduction was given and explained the purpose and objectives of the study to all respondents. Verbal informed as well as written consent was taken from each of the respondents before asking questions. Confidentiality of all respondents was maintained. The content validity of the instrument was established by consulting with research advisor, subject experts and research experts, statistician, the opinion of language expert for their valuable comments and suggestion.

4. RESULT AND ANALYSIS

4.1. Socio-Demographic Information of the Respondents

This study attempts to measure age, sex, education, occupation and income as socio-economic characteristics of patients having CAD. The survey results that more than half of the respondents (52.8%) were from the age group up to 60 years with mean age 58.65 with standard deviation ±11.26. Among these respondents male were 64.2% that indicates male suffers most from CAD in terms of gender. Among 106 respondents, 66% mentioned they were literate and among literate respondents, 18.5%, 35.7% 25.8% and 20% were attended primary, secondary, higher secondary, and bachelor and above level respectively. Almost equal (28.9%) and (27.4%) respondent involved in occupation as homemaker and service respectively. Besides, respondents involved in agriculture (25.5%), business (16%) and others (2.8%) were observed as patient of CAD. Most of the respondents (47.2%) had average family income per month between USD 100 to USD 500. However, only 7.5% respondent mentioned they have sufficient income and 45.8% argued insufficient income with them.

4.2. Risk Factors for Coronary Artery Disease (CAD)

Family History of CAD: Among 106 respondents, 17.96% reported their family history of CAD. Among the respondent with family history of CAD, majority (57.9%) had mentioned family history of father having CAD and rest 42.1% argued family history of mother having CAD. Family history also supports that male patient have more risk to CAD.

Physical Activities and CAD: Among the patients having CAD, only 53.8% mentioned they were involved in physical activities, of any kind, including vigorous intensity, moderate intensity; and combination of vigorous, moderate and walking. However, 96.5% of them involved in moderate types of physical activity.

Smoking Activities and CAD: Among the respondents having CAD, only 55.8% mentioned they were current smoker. From the current smoker, only less than half (44.8%) of the respondents used less than ten stick per day and more than half (55.2%) of the respondents smoked for less than or equal to 30 years, whereas nearly half (46.4%) of the respondents had stopped smoking for more than 10 years. Likewise, the findings of the study regards to the smoking, majority of the respondents (53.8%) were smokers. Similar findings were revealed in a study conducted in Pokhara that 55.2% respondents were smokers [9].

Alcoholism Activities and CAD: Result shows that nearly half (47.61%) of the respondents were current alcoholic. Among current alcoholics, half (50%) of the respondents used more than 30 ml of ethanol (local alcohol) in one drink. Similarly, 40% respondents drink alcohol everyday and 3-5 times a week and majority (60%) of the respondents had history of alcohol intake less than 20 years. Among past alcoholic, 36.36% had already stopped alcohol intake for more than 5 years and similarly for more than 10 years. In regards to alcoholism, 19.8% were alcoholic. It is supported by the findings of the study conducted in Dharan which reported alcoholism as 22.7%

1 USD ≈ NRs. 115
In contrast with this study, a study conducted in Eastern Nepal showed that 64.9% were alcoholic [21]. According to the current study, findings regarding physical activity, one fourth of the respondents (46.2%) were physically inactive. It is supported by the findings of the study conducted in Dharan, Nepal which revealed sedentary life style among 47.1% respondents [10].

**Dyslipidemic:** The Dyslipidemic criteria indicates 2.71% respondents had high level of low density lipoprotein, 13.52% respondents had high levels of total cholesterol, 36.48% respondents had high level of triglyceride and 52.7% respondents had low level of high density lipoprotein. The findings of the study regarding dyslipidemia, 67.6% respondents had dyslipidemia which is supported by the study conducted in Iran which reported hyperlipidemia as 49.2% [22]. However, a study done in Manipal Teaching Hospital Nepal also revealed dyslipidemia among 7.6% respondents [23].

Findings regarding total cholesterol, 13.5% of respondents had more than 200 mg/dl total cholesterol. This is supported by the findings reported in a study conducted in Bharatpur, Chitwan which showed that hypercholesterolema were found in 13% respondents [16]. Similarly, a study conducted in Dharan, Nepal showed that 12.6% respondents had hypercholesterolema [10]. Regarding triglyceride, in this study 36.48% had more than 150 mg/dl triglyceride. In contrast with this study, study conducted in Bharatpur, Chitwan and Manipal Teaching Hospital, Pokhara, Nepal showed hypertriglyceridemia15% and raised triglyceride 14.7% respectively [9]; [16]. There is a contrast result with this study may be due to different setting. In the same way, findings regards to low density lipoprotein (LDL-c) 2.71% had more than 160 mg/dl low density lipoprotein (LDL-c). A study conducted in Manipal Teaching Hospital, Pokhara, Nepal showed 1.7% raised LDL [9] which supports the findings of this study. Similarly, findings of current study regarding high density lipoprotein (HDL-c), among the dislipidemic 52.7% had less than 40 mg/dl high density lipoprotein (HDL-c). Similarly a study conducted in Bharatpur, Chitwan showed that 67% were found low HDL-C [16] which supports this study.

4.3. **Association of Risk Factors with Socio-demographic Variables**

The study shows that there is significant association between the dyslipidemia and age of the respondents, at 5% significance level whereas, there was no any significant association between the age of respondents and family history, previous history, hypertension, diabetes, smoking, alcoholism, physical inactivity and obesity Table 1.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Age</th>
<th>Sex</th>
<th>Education</th>
<th>Occupation</th>
<th>Income</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family History</td>
<td>.000</td>
<td>.985</td>
<td>.138</td>
<td>.017*</td>
<td>.024*</td>
</tr>
<tr>
<td>Previous History</td>
<td>.018</td>
<td>.892</td>
<td>.262</td>
<td>.001</td>
<td>.187</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.772</td>
<td>.183</td>
<td>.663</td>
<td>.612</td>
<td>.61</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>.104</td>
<td>.747</td>
<td>.421</td>
<td>.901</td>
<td>.61</td>
</tr>
<tr>
<td>Smoking</td>
<td>.092</td>
<td>.965</td>
<td>.120</td>
<td>.003*</td>
<td>.339</td>
</tr>
<tr>
<td>Alcoholic</td>
<td>.195</td>
<td>.658</td>
<td>.194</td>
<td>.339</td>
<td>.560</td>
</tr>
<tr>
<td>Physically Active</td>
<td>.542</td>
<td>.462</td>
<td>.613</td>
<td>.485</td>
<td>.560</td>
</tr>
<tr>
<td>Obesity</td>
<td>1.006</td>
<td>.605</td>
<td>-</td>
<td>1.392</td>
<td>.499</td>
</tr>
<tr>
<td>Dyslipidemia (n=74)</td>
<td>7.00*</td>
<td>1.027</td>
<td>.311</td>
<td>1.975</td>
<td>.160</td>
</tr>
</tbody>
</table>

*Significant P-value<0.05*

In terms of sex, strongly significant association between sex of respondents and alcoholism (p-value<0.001) were observed which is tested through Fisher’s exact value. Along with alcoholism, association was found between the sex of the respondents and frequency of smoking, at 5% significance level. Frequency of family history of CAD and physical activity education of the respondents is also statistically significant at 5% significance level. There is
frequency of family history, smoking, alcoholism and hypertension and occupation of the respondents as it is statistically significant at 5% significance level. However, this study cannot measure significant association among any of the variables used in this study and income level of the respondents.

4.4. Frequency of Risk Factors for Coronary Artery Disease

The study revealed that majority (67.6%) of the respondents had dyslipidemia followed by more than half (53.8%) participants were smoker as the risk factors of coronary artery disease Table 2. Very few (17.9%) respondents had family history of CAD. Also, majority of the respondents (53.8%) were smokers. Similar findings were revealed in a study conducted in Pokhara that 55.2% respondents were smokers [9]. Further, this study found 47.2% respondents with hypertensive, which is strongly supported by findings of study which mentioned that 47.7% respondents were hypertensive [24]. Other studies done by Twayana, et al. [16] and Khan, et al. [13] also reported similar findings (52%). Regarding physical activity, one fourth of the respondents (46.2%) were physically inactive. The study conducted in Dharan, Nepal revealed sedentary life style among 47.1% respondents [10]. In terms of frequency of diabetes mellitus, 39.6% respondents were diabetic. A study conducted in Punjab supports this finding which mentioned that 39.8% were diabetic [13]. Another study done in Iran showed diabetes mellitus among 41.9% respondents [22] which also supports the findings of this study. Similarly, one third of the respondents (31.1%) were obese according to body mass index (BMI more than 25 kg/m²). It is supported by the study conducted in Bharatpur, Chitwan showed that obesity according to BMI was present among 30% respondents [16]. In regards to alcoholism, 19.8% were alcoholic. It is supported by the findings of the study conducted in Dharan which reported alcoholism as 22.7% [10]. In contrast with this study, a study conducted in Eastern Nepal showed that 64.9% were alcoholic [21]. This study found that 17.9% had positive family history of CAD. Similar finding (16%) was reported in a study done in Iraq by Mohammad, et al. [25] in Iraq. A study conducted in Kerala, South India also reported that 18% had family history of CAD [26].

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidemia (n=74)</td>
<td>50</td>
<td>67.6</td>
</tr>
<tr>
<td>Smoking</td>
<td>57</td>
<td>53.8</td>
</tr>
<tr>
<td>Hypertension</td>
<td>50</td>
<td>47.2</td>
</tr>
<tr>
<td>Physically inactive</td>
<td>49</td>
<td>46.2</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>42</td>
<td>39.6</td>
</tr>
<tr>
<td>Previous history</td>
<td>41</td>
<td>38.7</td>
</tr>
<tr>
<td>Obesity</td>
<td>33</td>
<td>31.1</td>
</tr>
<tr>
<td>Alcoholic</td>
<td>21</td>
<td>19.8</td>
</tr>
<tr>
<td>Family history</td>
<td>19</td>
<td>17.9</td>
</tr>
</tbody>
</table>

Source: Authors’ calculation from Field Data, 2017.

5. Conclusion

The present study showed that there is significant association between socioeconomic status (education and occupation) and (hypertension, smoking and low physical activity). This study also revealed the association between age and dyslipidemia of the respondents. Further, it observed that there is significant association between sex and smoking and alcoholism (p-value=0.03 and p-value=0.000 respectively. Smoking was more consistent among women than men and men had a significantly higher frequency of cigarette smoking than women. The frequency of risk factors for coronary artery disease of the respondents revealed the most prevalent coronary risk factors were dyslipidemia (67.6%), smoking (53.8%), hypertension (47.2%), physically inactive (46.2%), diabetes mellitus (39.6%) and previous history of CAD (38.7%). Likewise, other less common risk factors were obesity (31.1%), alcoholic (19.8%) and family history of CAD (17.9%). Considering the frequency of
previous history of CAD, this study reported that 38.7% respondents had previous history of coronary artery disease. As per findings, this is also concluded that various socio-economic factors i.e. age, sex, education, occupation are the contributing factors to prevalent the risk factors of CAD. Those risk factors were not diagnosed and treated before they are diagnosed to have CAD. Considering findings of study indicating high frequency of some risk factors, early screening and diagnosing of these risk factors is an important aspect in the primary prevention of CAD. The findings of the study provide a source of reference to the future researcher.

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**Competing Interests:** The authors declare that this study has no competing interests.

**Contributors:** Both authors contributed equally to the conception and design of the study.

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