Original Article

Gender differences in patients presenting with premature coronary artery disease

Thamir M. Al-khlaiwi[1], Syed S. Habib[1], Hessah F. Alshammari[2], Hanan B. Albackr[3], Razan A. Alobaid[1], Lama A. Alrumaih[1], Faye W. Sendi[1], Shahad A. Almuqbil[1], Mohamed M. Khalifa[1]

[1]Department of Physiology, College of Medicine, King Saud University, Riyadh, Saudi Arabia, [2]Department of Cardiac Sciences, College of Medicine, King Saud University, Riyadh, Saudi Arabia, [3]Department of Cardiac Sciences, King Fahad Cardiac Center, College of Medicine, King Saud University Medical City, King Saud University, Riyadh, Saudi Arabia

Abstract

Objectives: To study gender differences according to severity and manifestations in patients presenting with premature coronary artery disease (PCAD). **Methods:** In this retrospective study, patients' information, including demographic data, chemical biomarkers, and coronary angiography findings, was obtained from the electronic system at King Khaled University Hospital (KKUH), Riyadh, Saudi Arabia, during the period between 2015 and 2022. Gensini and vessel scores were calculated from patients' angiographic reports. **Results:** Among males, 53.5% of the subjects had a Gensini score of > 39; only 39.5% of females had such a Gensini score ($P = 0.021$). Electrocardiography (ECG) changes revealed more frequent ST elevation in the anterior leads among females than among males. According to the vessel score, 57.4% of males and 58.2% of females had two- or three-vessel occlusions ($P = 0.150$). Approximately 8% of male patients and 3.5% of female patients had left main artery occlusion. The 45–50 years age group was associated with a higher rate of PCAD development, and this effect was more pronounced among females than among males, while in younger age groups, males were higher than females. **Conclusions:** Male patients had more severe vessel occlusion than female patients according to the Gensini score, while anterior ST elevation is more prominent in females. More than 8% of the male patients had left main artery occlusion compared to 3.5% of the female patients who had main artery occlusions.

Keywords: Coronary artery involvement, electrocardiographic changes, gender, occlusion severity, premature coronary artery disease, risk factors

Introduction

Premature coronary artery disease (PCAD) is becoming more prevalent among young adults,[1] and many of its risk factors have been studied.[1-5] However, to our knowledge, its pathogenesis has not yet been elucidated, and the wide variations in the findings of studies on its pathogenesis necessitate more focused research.[2]

As a potentially life-threatening condition and a leading cause of morbidity and mortality worldwide, PCAD is a significant public health concern; hence, broader research projects directed toward exploring multiple risk factors, elucidating its pathophysiology, implementing early preventive and therapeutic measures, and reducing morbidity and mortality outcomes are important.[3] Astonishingly, the prevalence of lack of knowledge of PCAD and its risk factors in the Kingdom of Saudi Arabia was found

Address for correspondence: Prof. Thamir Al-khlaiwi, Department of Physiology, College of Medicine, King Saud University, Riyadh, Saudi Arabia.
E-mail: talkhlaiwi@ksu.edu.sa

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to be very high in a 2023 study,[4] and healthcare providers and policymakers are responsible for taking serious action toward addressing this problem through careful planning of prophylactic and risk stratification programs for the early detection and prevention of this outcome, as well as the prevention of complications of ischemic heart disease, especially in people of younger age groups. Recently, we conducted a meta-analysis that revealed a PCAD mortality rate in Saudi Arabia of 4%, ranging from 2% to 8%, which is similar to the prevalence in older patients (2–10%).[5]

Sex disparities in PCAD prevalence and manifestations are neither properly investigated nor properly understood.[6] Generally, males are significantly more likely to experience ischemic conditions (including coronary artery disease [CAD]) than females, perhaps due to a combination of factors, including lifestyle factors, especially those related to excessive smoking or an unhealthy diet, psychological stress, and hormonal differences.[7]

Several studies have focused on the multiple risk factors involved in PCAD pathogenesis.[1-5] However, to the best of our knowledge, there is a paucity of research probing into gender variations in the Saudi Arabian population, with the goal of establishing more sex-related causative or correlative links. So, our study aim is to investigate the differences in severity and manifestations in male and female adult Saudi patients presenting with PCAD. The main goal of this project is to encourage primary care physicians to carefully examine and monitor very vulnerable group of patients, young patients, who are usually neglected and their risk factors are frequently underestimated.

Methods

This retrospective study was conducted between March 2023 and December 2023 at King Khaled University Hospital (KKUH), Riyadh, Saudi Arabia (SA). Between January 2015 and December 2022, approximately 4,000 patients presented to the KKUH emergency room with chest pain, and we found that 2000 of them experienced cardiac pain. Among these, 886 underwent coronary angiography. We studied the files of all these patients and found that 718 of them fulfilled our selection criteria. The demographic characteristics of our study population, including age, sex, body composition, and body mass index, were obtained from the records. Investigations, including electrocardiography (ECG), hemoglobin A1C (HbA1C), and lipid profile, including total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TG), were also obtained by the study investigators. Out of the 718 eligible patients, coronary angiography findings, Gensini score, and vessel scores were calculated for 283 patients for whom angiographic reports were available in the electronic system. All of these data were collected from the Electronic System for Integrated Health Information (e-SiHi) used at KKUH.

We included Saudi patients with PCAD aged 18–50 years and excluded patients with missing data, congenital heart disease, and patients older than 50 years.

Vessel and Gensini scores, widely used, were implemented to evaluate occlusion severity in coronary arteries.[8-10]

Ethical approval and guidelines for this study were granted by the Institutional Review Board, College of Medicine Research Center (CMRC), KSU, Riyadh, SA (No. E-22-6747).

Statistical analysis

We used SPSS version 25 (IBM SPSS Statistics for Macintosh), for all data analysis. Quantitative data variables are presented as mean values with standard deviations for the normally distributed data or median values with interquartile ranges for skewedly distributed data. Comparisons between quantitative variables were performed using Student's *t*-test, or Mann-Whitney *U* test for normally or skewedly distributed variables. Qualitative data variables are expressed as percentages and frequencies. To evaluate the associations between categorical variables, Pearson's Chi-square test was used. Measures of association and the 95% confidence intervals were used to present key findings, and $P < 0.05$ was considered statistically significant.

Results

Mean values of body mass index of females was significantly higher than that of males (30.9 ± 6.1 vs. 29.7 ± 7.6, $P = 0.036$); however, TG levels were higher among males (1.5 ± 1.3 vs. 1.3 ± 0.8, $P < 0.002$) where HDL levels were greater among females than among males (1.2 ± 0.3 vs. 1.0 ± 0.3, $P < 0.001$; Table 1).

A Gensini score of 39 was used as a cutoff value. In the male group, 53.5% of the subjects had a Gensini score above the cutoff value, whereas in the female group, only 39.5% had a Gensini score above this value, with the difference in the proportion of subjects with Gensini scores above the cutoff value between males and females being statistically significant, $P = 0.021$ [Figure 1].

There was no significant difference in the number of vessels involved in the PCAD between males and females ($P = 0.150$), which may represent the irrelevance of any correlation between the preinjury risk factors and the number of involved vessels represented by the vessel score. These finding points more toward microscopic functional and physiological impairment of coronary artery supply [Table 2].

Furthermore, there was no significant difference in the distribution of stenosed vessels, suggesting that the greater severity in males is related to microscopic pathophysiological events and the degree of premorbid atherosclerosis and stenosis rather than macroscopic vascular occlusion [Tables 3]. Also, there were no statistically significant sex differences in the specific vessel distribution of PCAD. However, the left main artery was more involved in males than in females.

The 45–50 years age group was associated with a higher rate of PCAD development, and this effect was more pronounced

among females than among males, while in younger age groups, males were higher than females [Figure 2].

Figure 3 shows that ECG results were normal in approximately 23% of the patients (22.6% of the male subjects and 23.6% of the female subjects). Moreover, anterior ST elevation was significantly greater among females than among males (16.9% in males and 36.4% in females). In contrast, inferior-lead ST elevation was more common among males than among females (8.5% vs. 0.3%, $P < 0.001$). Other ECG findings (nonspecific ST segment or T wave changes) did not differ significantly between males and females.

Discussion

The study revealed that male patients had more severe occlusion than female patients according to the Gensini score. Our results regarding the Gensini score are consistent with those of Avci *et al.*[11] and Yang *et al.*,[12] who also reported higher Gensini scores in male patients with CAD than in female ones in the Chinese population, possibly reducing the impact of ethnicity. Nonetheless, our results contrast with those of He *et al.*,[13] who reported higher Gensini scores in females. This difference in findings probably exists because the study by He *et al.*[13] was limited to patients with CVD with concomitant DM.

We found that the 45–50 years age group was associated with a higher rate of PCAD development, and this effect was more

Table 1: Basic characteristics of male and female groups

Parameter	Male (*n*=540)	Female (*n*=178)	*P*
Age (years)	43.0±6.0	46.2±4.9	0.000*
BMI (kg/m²)	29.7±7.6	30.9±6.1	0.036*
HbA1c %	7.5±3.0	7.4±2.3	0.753
TC (mmol/L)	4.5±1.4	4.6±1.0	0.500
HDL (mmol/L)	1.0±0.3	1.2±0.3	0.000*
LDL (mmol/L)	2.7±1.3	2.7±0.9	0.729
TG (mmol/L)	1.5±1.3	1.3±0.8	0.002*

The data are presented as the means and standard deviations. *t tests are used to assess significance. BMI=Body mass index, HbA1c=Glycated hemoglobin, TC=Total cholesterol, HDL=High-density lipoprotein, LDL=Low-density lipoprotein, TG=Triglyceride

Table 2: Number of coronary arteries involved in relation to gender

Degree of vessel score	Male	Female	*P*
0	4 (2.0%)	0 (0.0%)	0.150
1	80 (40.6%)	36 (41.9%)	
2	53 (26.9%)	30 (34.9%)	
3	60 (30.5%)	20 (23.3%)	

The data are presented as frequencies and percentages. Significance was assessed by Pearson's Chi-square test. 0=no occlusion, 1=one main vessel occlusion, 2=two main vessel occlusions, 3=three main vessel occlusions

Table 3: Comparison of sex and specified vessel types

Stenosed vessel	Male	Female	*P*
Left anterior descending (LAD)	164 (83.2%)	76 (88.4%)	0.178
First diagonal artery	37 (18.9%)	11 (12.8%)	0.139
Second diagonal artery	14 (7.1%)	9 (10.5%)	0.234
Left main artery (LM)	16 (8.1%)	3 (3.5%)	0.117
Right coronary artery (RCA)	116 (58.9%)	45 (52.3%)	0.243
Posterior descending artery (PDA)	14 (7.1%)	7 (8.1%)	0.466
Left circumflex artery (LCx)	78 (39.9%)	33 (38.4%)	0.477
Obtuse	40 (20.3%)	17 (19.8%)	0.528
Posterolateral	6 (3.0%)	4 (4.7%)	0.359
Apical	5 (2.5%)	2 (2.3%)	0.639

The data are presented as frequencies and percentages. Significance was evaluated by the Pearson Chi-square test

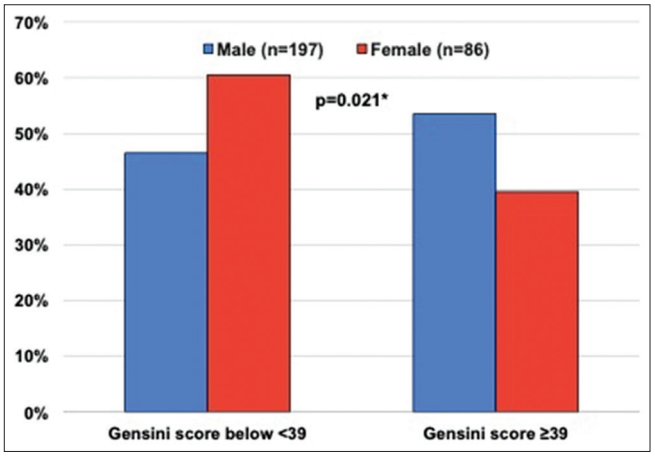

Figure 1: Comparison of Gensini scores between male and female patients who presented with PCAD

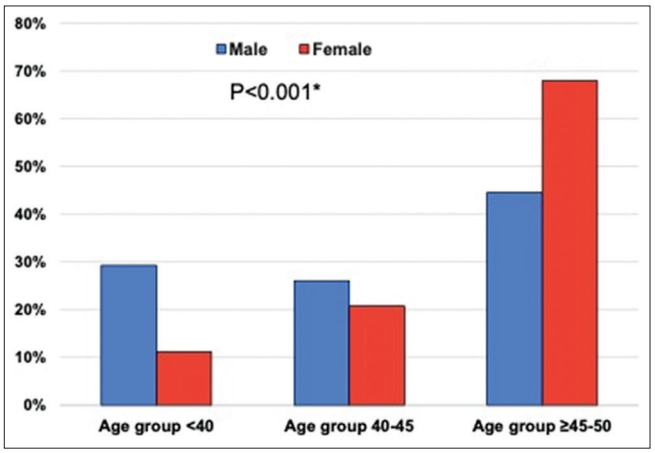

Figure 2: Comparison of the age groups of male and female patients who presented with PCAD

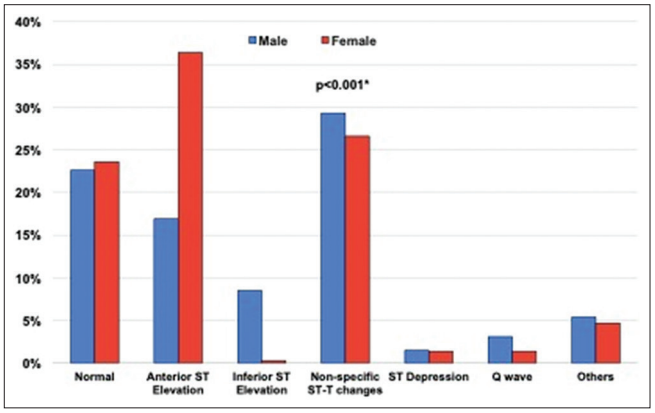

Figure 3: ECG pattern distribution among the study population (%)

pronounced among females than among males while in younger age groups males were higher than females. Aging is well-known as a risk factor for normal-onset CAD. However, its relation to PCAD pathogenesis still requires further confirmation. Our findings may be explained by the fact that females are naturally protected against the development of ischemic cardiac conditions because they have hormones (especially estrogen and progesterone) protecting them from coronary atherosclerosis during the childbearing period. In addition, the PCAD risk is significantly increased in the presence of hypertension, hyperlipidemia, or a family history of at least one of the established risk factors for CAD development.[14-18]

ECG, one of the primary diagnostic modalities for acute coronary syndrome (ACS), serves as not only a diagnostic method but also an essential tool for follow-up, risk detection and stratification, and the determination of therapeutic steps and subsequent work-up plans.[19] Recent guidelines use ECG criteria to differentiate ACS into two main categories—ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (non-STEMI).[20] This differentiation plays a crucial role in emergency settings. Thus, ECG is often the first and most readily available tool for confirming the diagnosis and guiding treatment decisions with potentially life-saving consequences.[21] The hallmark of STEMI is the persistent elevation of the ST segment in at least two contiguous leads. This finding indicates a transmural infarction caused by the complete blockage of one coronary artery and ongoing cell death in the underlying heart muscle. Early reperfusion therapy is essential for preventing further necrosis and preserving cardiac function.[22] Non-STEMI indicates subendocardial infarction (hence not full-thickness necrosis). ECG findings, which are variable, include ST-segment elevation or depression, T-wave inversion, or flattening. The ECG may even be normal in some cases.[23] The exact determination of the importance, diagnostic and prognostic value, and risk stratification significance of ECG findings in PCAD needs to be researched further.

Our finding regarding the ECG may partly explain the controversial fact that mortality rates are higher among females than among males.[23,24] This finding is consistent with the results of previous studies showing that female subjects presenting with PCAD have a smaller vascular diameter than male subjects do.[23]

Because females exhibit certain cardioprotective factors, such as regular menstruation, high estrogen levels, and a prepubertal delay in atherogenesis, the fact that their mortality rates related to ACS are higher than those of males remains controversial. This paradox has ignited intense scientific scrutiny, hypothesizing a complex interplay of hormonal fluctuations, vessel-related factors, or other unknown factors, highlighting the need for more extensive studies.[24]

Unraveling this complex interplay of biological factors is crucial for developing tailored preventive and therapeutic strategies for women. By navigating deeper into the subtle differences in sex-specific causes, pathophysiological mechanisms, and sex disparities in ACS or PCAD, we can unlock the potential for more effective sex-specific therapeutic approaches. However, in this study, we may have identified a more favorable prognostic marker for patients with PCAD, as mortality rates from STEMI are significantly lower in the younger population than in the older population.[25]

Understanding the sex-specific risk factor distribution and the role of each specific factor in the pathophysiological progression of the disease is crucial to developing specific management strategies and targeted interventions, including primary and secondary preventive measures, together with proper public awareness and robust health education efforts and campaigns, which may address the lack of knowledge that contributes to poorer outcomes, both in terms of morbidity and mortality, in patients with PCAD.[26,27] It is well known that some risk factors such as diabetes can increase the inflammatory biomarkers in the blood and hence accelerate the inflammation process that might affect cardiovascular system.[28] On the other hand, preventive measures that reduce the calcification process and consequently reduce the development of CADs events should be taken into considerations from primary physicians in order to protect very young individuals from deleterious complications.[29]

Conclusions

Male patients have more severe occlusions than female patients according to the Gensini score. More than 57% of male patients and more than 58% of female patients have two- or three-vessel occlusions according to the vessel score. Since these patients are young, the severity of occlusion is alarming and astonishing. More than 8% of the male patients had left main artery occlusion, and 3.5% of the female patients had main artery occlusions. Anterior ST elevation is more apparent in females than in males. The 45–50 years age group was associated with a higher rate of PCAD development, and this effect was more pronounced among females than among males, while in younger age groups, males were higher than females.

Limitations

The sample size was relatively small, and there was missing data due to the retrospective study design. In view of these limitations, larger-scale multicenter studies involving direct patient interviews, recruitment, and prospective follow-up are needed to determine the exact role of each risk factor in sex-specific PCAD development and study the evolution and outcome of CADs and their complications.

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Author contributions

TA: designed and supervised the study. TA and SSH analysed and organized the data. HAA: interpreted ECG findings.

HEA, RA, LA, FS, and SA: collected the data. TA and MK wrote the manuscript. All authors read and approved the final manuscript.

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Conflicts of interest

There are no conflicts of interest.

References

1. Smith CL, Seigerman M, Adusumalli S, Giri J, Fiorilli PN, Kolansky DM, *et al.* Evolution and outcomes of premature coronary artery disease. Curr Cardiol Rep 2021;23:36.
2. Al-Murayeh MA, Al-Masswary AA, Dardir MD, Moselhy MS, Youssef AA. Clinical presentation and short-term outcome of acute coronary syndrome in native young Saudi population. J Saudi Heart Assoc 2012;24:169-75.
3. Khoja A, Andraweera PH, Lassi ZS, Zheng M, Pathirana MM, Ali A, *et al.* Risk factors for premature coronary artery disease (PCAD) in adults: A systematic review protocol. F1000Research 2021;10:1228.
4. Al-Khlaiwi T, Alshammari H, Habib SS, Alobaid R, Alrumaih L, Almojel A, *et al.* High prevalence of lack of knowledge and unhealthy lifestyle practices regarding premature coronary artery disease and its risk factors among the Saudi population. BMC Public Health 2023;23:908.
5. Al-Khlaiwi T, Habib SS, Bayoumy N, Al-Khliwi H, Meo SA. Identifying risk factors and mortality rate of premature coronary artery disease in young Saudi population. Sci Rep 2024;14:12727.
6. Zwischenberger BA, Jawitz OK, Lawton JS. Coronary surgery in women: How can we improve outcomes. JTCVS Tech 2021;10:122-8.
7. Zeitouni M, Clare RM, Chiswell K, Abdulrahim J, Shah N, Pagidipati NP, *et al.* Risk factor burden and long-term prognosis of patients with premature coronary artery disease. J Am Heart Assoc 2020;9:e017712.
8. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, *et al.* Heart disease and stroke statistics—2013 update: A report from the american heart association. Circulation 2013;127:e6-245.
9. Neeland IJ, Patel RS, Eshtehardi P, Dhawan S, McDaniel MC, Rab ST, *et al.* Coronary angiographic scoring systems: An evaluation of their equivalence and validity. Am Heart J 2012;164:547-552.e1.
10. Wang KY, Zheng YY, Wu TT, Ma YT, Xie X. Predictive value of gensini score in the long-term outcomes of patients with coronary artery disease who underwent PCI. Front Cardiovasc Med 2022;8:778615.
11. Avci A, Fidan S, Tabakçı MM, Toprak C, Alizade E, Acar E, *et al.* Association between the gensini score and carotid artery stenosis. Korean Circ J 2016;46:639-45.
12. Yang B, Ma K, Xiang R, Yang G, Luo Y, Wu F, *et al.* Uric acid and evaluate the coronary vascular stenosis gensini score correlation research and in gender differences. BMC Cardiovasc Disord 2023;23:546.
13. He LY, Zhao JF, Han JL, Shen SS, Chen XJ. Correlation between serum free fatty acids levels and Gensini score in elderly patients with coronary heart disease. J Geriatr Cardiol 2014;11:57-62.
14. Yetkin E, Topal E, Erguzel N, Senen K, Heper G, Waltenberger J. Diabetes mellitus and female gender are the strongest predictors of poor collateral vessel development in patients with severe coronary artery stenosis. Angiogenesis 2015;18:201-7.
15. Al-Shahrani MS, Katbi FA, Al-Sharydah AM, AlShahrani SD, Alghamdi TM, Al-Sharidah MA. Differences in clinical nature and outcome among young patients suffering from an acute coronary syndrome. J Blood Med 2021;12:1011-7.
16. Abazid RM, Kattea MO, Sayed S, Saqqah H, Qintar M, Smettei OA. Visceral adipose tissue influences on coronary artery calcification at young and middle-age groups using computed tomography angiography. Avicenna J Med 2015;5:83-8.
17. Al-Saif SM, AlHabib KF, Ullah A, Hersi A, AlFaleh H, Alnemer K, *et al.* Age and its relationship to acute coronary syndromes in the Saudi Project for Assessment of Coronary Events (SPACE) registry: The SPACE age study. J Saudi Heart Assoc 2012;24:9-16.
18. Al-Khlaiwi T, Habib SS, Alshammari H, Albackr H, Alobaid R, Alrumaih L, *et al.* Severity and risk factors associated with premature coronary artery disease in patients under the age of 50 in Saudi population: A retrospective study. J Clin Med 2025;14:1618.
19. Al-Khadra AH. Clinical profile of young patients with acute myocardial infarction in Saudi Arabia. Int J Cardiol 2003;91:9-13.
20. Rosiek A, Leksowski K. The risk factors and prevention of cardiovascular disease: The importance of electrocardiogram in the diagnosis and treatment of acute coronary syndrome. Ther Clin Risk Manag 2016;12:1223-9.
21. Bhatt DL, Lopes RD, Harrington RA. Diagnosis and treatment of acute coronary syndromes: A review. JAMA 2022;327:662-75.
22. Baloglu UB, Talo M, Yildirim O, San Tan R, Acharya UR. Classification of myocardial infarction with multi-lead ECG signals and deep CNN. Pattern Recognition Letters 2019;122:23-30.
23. Kingma JG. Myocardial infarction: An overview of STEMI and NSTEMI physiopathology and treatment. World J Cardiovasc Dis 2018;8:498-517.
24. Habib SS, Al-Khlaiwi T, Alhowikan A, Al Aseri Z, Habib SM, Al-Khliwi H, *et al.* Gender differences in plasma levels of cardiovascular risk markers and severity indices in Saudi patients with angiographic evidence of coronary artery disease. Khyber Med Univ J 2023;15:71.
25. Lawton JS. Sex and gender differences in coronary artery disease. Semin Thorac Cardiovasc Surg 2011;23:126-30.
26. Sakr H, Azazy AS, Hillani A, Ebada M, Alharbi A, Alshalash S, *et al.* Clinical profiles and outcomes of acute ST-segment elevation myocardial infarction in young adults in a tertiary care center in Saudi Arabia. Saudi Med J 2021;42:1201-8.
27. Habib SS, Al-Khlaiwi T, Almushawah A, Alsomali A, Habib SA. Homocysteine as a predictor and prognostic marker of atherosclerotic cardiovascular disease: A systematic review and meta-analysis. Eur Rev Med Pharmacol Sci 2023;27:8598-608.

28. Habib SS, Al-Khlaiwi T, Al-Khliwi H, Habib SM, Habib SA, Habib SH, *et al*. Adiponectin and TNFα in relation to glucometabolic control in patients with type 2 diabetes mellitus. J Family Med Prim Care 2024;13:2741-5.
29. Al-Khlaiwi T, Alsaleh A, Alghamdi F, Abukhalaf F, Alghannam M, Alzaid S, *et al*. Correlations between coronary artery calcium scores and Vitamin A, the triglyceride/high-density lipoprotein ratio, and glycated hemoglobin in at-risk individuals in Saudi Arabia: A comprehensive cross-sectional study. J Clin Med 2025;14:3645.