Opium is an important risk factor for coronary artery ectasia; a cross-sectional study

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Research article

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Abstract

Introduction Coronary artery ectasia (CAE) is a rare cardiovascular disorder with unknown mechanisms and related risk factors. The roles played by homocysteine in induction of cardiovascular diseases have also been documented previously. This project was designed to explore the roles played by opium in the pathogenesis of CAE disorder and the roles of the plausible risk factors on the homocysteine and other biochemical factors.

Material and methods This cross-sectional study was performed on the 46 patients with CAE, 30 patients with coronary artery disease (CAD) and 42 cases without CAE and CAD (controls). Demographic data and information regarding opium consuming and also smoking were collected using standard check list. Serum levels of homocysteine, creatinin (Cr), urea, fasting blood glucose (FBG), low density lipoprotein (LDL), high density lipoprotein (HDL), triglyceride (TG) and cholesterol (Chol) were determined.

Results Statistical analysis revealed that opium consumers were significantly higher in CAD and CAE patients when compared to healthy controls. Opium increased serum levels of Cr in the normal controls, and decreased HDL in the CAD patients. Homocysteine serum levels were not altered among the groups.

Discussion Due to the results it appears that opium may be considered as a risk factor for either CAE or CAD independent of homocysteine and also may be the risk factor for kidney diseases in the normal population.

Background

Cardiovascular diseases are the main causes of the morbidity and mortality among Iranian population and also developed and developing countries [1, 2]. The diseases are associated with several complications, including coronary artery ectasia, which play key roles in the induction of the cardiovascular-related morbidities and mortalities [3]. It has been demonstrated that several genetic and environmental factors play significant roles in the induction of cardiovascular diseases, including coronary artery ectasia (CAE) and coronary artery disease (CAD) [4-6]. CAE, as a rare cardiovascular disease-related complication occurs in only 0.3-4.9% of the patients [7]. The complication is characterized by the non-local coronary artery enlargement to 1.5 times, or more, when compared to its normal diameter [8]. It is plausible in 0.22-1.4 percents of angiographies and most of them are induced due to the atherosclerosis, however some of them have the congenital or percutaneous coronary intervention sources [8]. It has been hypothesized that CAE may increase the risk of acute myocardial infarction [7]. However, some of the CAD patients suffer from CAE [9], demonstrated different mechanisms involved in the induction of CAE.

Although the main causes of CAE are yet to be clarified, it has been proposed that inflammation and its related environmental inducers can stimulate the disease ranges [10]. It has been reported that opium is an inducer of inflammation and its significant association with cardiovascular diseases have been documented by several investigators [11]. The roles played by opium in the pathogenesis of CAE are yet to be defined. Due to the relation between opium and cardiovascular diseases and their related complications [12], it has been hypothesized that opium may alter the risk of CAE. Therefore, this project
was designed to investigate the correlation between opium consumption and the risk of CAD and CAE in the patients who were under angiography.

Additionally, it has also been documented that serum levels of homocysteine are elevated among the patients who are suffering from cardiovascular diseases and it also can be considered as a risk factor for induction of the diseases [13]. Nevertheless, its roles in the pathogenesis of CAE are yet to be clarified completely. So, another aim of this project was to explore the relationship between homocysteine serum levels and CAE/CAD among an Iranian population from Kerman province.

**Methods**

**Subjects**

In this cross-sectional study, 46 patients with CAE, 30 patients with CAD and 42 cases without CAE and CAD (controls) were evaluated regarding opium consumption and also serum levels of homocysteine. The participants were selected from the patients under angiography who referred to the Cardiovascular Diseases Department, Shafa hospital, Kerman, Iran. CAE was defined as dilatation of an arterial segment to a diameter at least 1.5 times that of the adjacent normal coronary artery [14]. Opium consumption was diagnosed due to the patients self-declaration and clinical presentation, based on the DSM-1V criteria [15], by an expert specialist in internal medicine. In addition to the variables, sex, age, low density lipoprotein (LDL), high density lipoprotein (HDL), fasting blood glucose (FBG), urea, creatinin (Cr), triglyceride (TG), cholestrol (Chol), body mass index (BMI), smoking and history of cardiovascular diseases were also calculated for the participants. To evaluate serum levels of homocysteine, FBG, TG, Chol, LDL and HDL, 5 mL blood samples were collected in the tubes without anti-coagulant agents and serum were separated and kept in the -20ºC. All the patients who were under angiography and had CAE and CAD were entered to the study except the patients that suffered from other cardiovascular diseases, heart failure with a left ventricular ejection fraction (LVEF) <40%, atrial fibrillation, a history of any revascularization, autoimmune diseases, cancer, splenectomy, active infectious diseases, alcohol drinking, drug administration, allergy, hypersensitivity disorders and other systematic disorders. All the participants filled out the consent form and the Ethical Committee of Kerman University of Medical Sciences approved the protocol study (Code: IR.KMU.AH.REC.1397.031). The study participant’s characteristics, including demographic information, screening records, drug use, and clinical features/manifestations were recorded using a checklist.

**Angiography**

An expert MD cardiologist performed the angiography based on the comparison of the damaged to normal vessels. The selective coronary angiography was carried out after local anesthesia using 6 French sheath and judkins catheters (left and right catheters). So, the contrast media (Visipaque) was injected into the right and left coronary arteries directly, in multiple projections.

**Homocysteine, FBG, urea, Cr, TG, LDL and HDL measurement**
High-performance Liquid Chromatography (HPLC) technique (KNAUER, Germany), which was coupled with fluorescence detector, were used to evaluate homocysteine serum levels. It was validated over a linearity range of 1–100 μmol/L with 4% and 6% intra-assay and inter-assay coefficient of variation, respectively.

Serum levels of FBG, urea, Cr, TG, LDL and HDL were evaluated using commercial kits (Man-company, Tehran, Iran) according to the manufacture instructions.

Statistical analysis

The SPSS software, version 20, were used to analyse the raw data. Accordingly, the normal distribution of the data, the groups were compared regarding the variables using the parametric tests. Accordingly, One way ANOVA were used to analyse the differences between the groups regarding age, BMI, ejection fraction, and serum levels of FBG, urea, Cr, TG, Chol, LDL and HDL. To analyse the differences between the groups regarding gender and statuses of smoking and opium consuming, Chi-square test were used. The differences of variables in the male versus (vs) the female, smokers vs non-smokers and opium consumers vs non-consumers were calculated using student t test.

Results

Data analysis demonstrated that, although the groups were not different regarding smoking (p = 0.132), the opium consumer were significantly higher in the CAE and CAD patients in comparison to the controls (p = 0.001). Table 1 shows the frequency of the cigarette and opium consumers in the case and control groups.

The results showed that the serum levels of FBG (p = 0.308), urea (p = 0.430), Cr (p = 0.178), and homocysteine (p = 0.881) were not different between the groups, while serum levels of TG (p < 0.001), Chol (p < 0.001), and LDL (p < 0.001) were significantly increased in the CAE when compared to both CAD and control groups. HDL serum levels were significantly decreased in the CAD and CAE groups when compared to the controls (p = 0.024). Additionally, the One Way ANOVA test revealed that the groups were similar regarding age (p = 0.448), sex (p = 0.219) and BMI (p = 0.113). Ejection fraction (p < 0.001) were significantly decreased in the CAD in comparison to both CAE and control groups. Table 1 illustrates the raw data regarding the variables.

Table 2 shows the data regarding ejection fraction, FBG, TG, Chol, LDL, HDL, urea, Cr, BMI and homocysteine between the male vs female, smokers vs non-smokers and opium consumers vs non-consumers in the control group. Statistical analysis revealed that FBG as significantly higher in the female when compared to male normal participants (p = 0.004). Although smoking has no effects on the variables in the normal participants, opium increased serum levels of Cr significantly (p = 0.004).

Comparison of the variable in the CAE showed that TG (p = 0.012) and Cr (p = 0.026) were significantly increased in the smoker when compared to the non-smoker CAE patients. Cr serum levels also were
significantly higher in the male than female CAE patients \((p = 0.008)\). Table 3 shows the details of the analysis.

Analysis of CAD group demonstrated that HDL was higher \((p = 0.024)\) and Cr was lower \((p = 0.013)\) in the CAD female patients when compared to the male patients. Smoking significantly decreased EF \((p = 0.046)\) and was associated with decreased serum levels of urea \((p < 0.001)\), while opium decreased serum levels of HDL in the CAD patients (Table 4).

**Discussion**

The results demonstrated that the prevalence of opium addiction was significantly associated with CAE and CAD (Table 1). Due to the results it appears that opium addiction increases the risk of CAE and CAD disease. As mentioned previously, opium is a risk factor for deterioration of cardiovascular diseases [12]. Additionally, the roles played by opium in the cardiovascular-related complications, such as atherosclerosis and coronary microvascular dysfunction has also been documented previously [16]. Our results also confirmed the pathologic roles of opium in the human to increase the risk of either CAE or CAD. The main mechanisms used by opium to increase the risk of the disease are yet to be clarified. Meanwhile, previous investigations revealed that homocysteine is a risk factor for cardiovascular diseases [17, 18]. The results of the current study demonstrated that homocysteine levels were not changed between cases and controls. Smoking and opium consumption also had not significant effects on the serum levels of homocysteine. Thus, it may be concluded that opium induces CAE in homocysteine independent pathways and it may alter other risk factors for the disease. For example, it has been reported that opium can lead to CAE via up-regulation of plasminogen activator inhibitor [19]. In parallel with our results, Azdaki and colleagues revealed that opium had no effects on the homocysteine serum levels [20]. Although there are some investigations showed increased plasma/serum levels of homocysteine in the opium addicted patients, their participants were not suffered from cardiovascular diseases [21, 22]. Therefore, it may be hypothesized that although opium increases the risks of CAE and CAD incidences, it did not induce the disorders via up-regulation of homocysteine.

The results were confirmed by the fact that HDL serum levels were decreased in the opium addicted patients when compared to non-addicted patients in the CAD patients. So, it may be hypothesized that opium increases the risk of CAD indirectly via down-regulation of HDL related molecules, which needs to be explored by further investigations. Opium also may be considered as a risk factor for other disorders including kidney disease, as the results demonstrated that opium consumers had higher levels of Cr than non-opium consumers in normal controls. Nevertheless, it appears that smoking has the same side effects in the CAE patients because it increased serum levels of Cr in the patients. Additionally, smoking significantly decreased ejection fraction in the CAD patients.

Collectively, it appears that opium and smoking are two important risk factors for deterioration of CAE and CAD independent of homocysteine.
Additionally, it appears that gender may be considered as risk factor for kidney diseases in both CAE and CAD patients. Accordingly, the results demonstrated that male CAD and CAE patients had higher levels of Cr. However, based on the fact that the female participants in the CAD group are significantly higher than male, but not in CAE group, it appears that the roles played by gender on the Cr serum levels in the CAD patients need to be explored by same sample size of the male and female. Nevertheless, the pattern of the male and female were similar in the CAE group and increased serum levels of Cr may be associated with male gender.

Conclusions

Finally, due to the results it may be concluded that opium significantly increases the risk of cardiovascular diseases including CAD and CAE independent of homocysteine.

Declarations

Competing Interest

The authors declare no Competing Interest

Acknowledgements

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References

[1] Sepehri ZS, Masoomi M, Ruzbehi F, Kiani Z, Nasiri AA, Kohan F, et al. Comparison of serum levels of IL-6, IL-8, TGF-beta and TNF-alpha in coronary artery diseases, stable angina and participants with normal coronary artery. Cell Mol Biol (Noisy-le-grand) 2018 Apr 30;64(5):1-6.

[2] Kwasny C, Manuwald U, Kugler J, Rothe U. Systematic Review of the Epidemiology and Natural History of the Metabolic Vascular Syndrome and its Coincidence with Type 2 Diabetes Mellitus and Cardiovascular Diseases in Different European Countries. Horm Metab Res 2018 Mar;50(3):201-8.

[3] Devabhaktuni S, Mercedes A, Diep J, Ahsan C. Coronary Artery Ectasia-A Review of Current Literature. Curr Cardiol Rev 2016;12(4):318-23.

[4] Akbari H, Asadikaram G, Vakili S, Masoumi M. Atorvastatin and losartan may upregulate renalase activity in hypertension but not coronary artery diseases: The role of gene polymorphism. J Cell Biochem 2019 Jun;120(6):9159-71.

[5] Asadikaram G, Ram M, Izadi A, Sheikh Fathollahi M, Nematollahi MH, Najafipour H, et al. The study of the serum level of IL-4, TGF-beta, IFN-gamma, and IL-6 in overweight patients with and without diabetes mellitus and hypertension. J Cell Biochem 2019 Mar;120(3):4147-57.
[6] Qin Y, Tang C, Ma C, Yan G. Risk factors for coronary artery ectasia and the relationship between hyperlipidemia and coronary artery ectasia. Coron Artery Dis 2019 May;30(3):211-5.

[7] Doi T, Kataoka Y, Noguchi T, Shibata T, Nakashima T, Kawakami S, et al. Coronary Artery Ectasia Predicts Future Cardiac Events in Patients With Acute Myocardial Infarction. Arterioscler Thromb Vasc Biol 2017 Dec;37(12):2350-5.

[8] Antonopoulos AS, Siasos G, Oikonomou E, Mourouzis K, Mavroudeas SE, Papageorgiou N, et al. Characterization of vascular phenotype in patients with coronary artery ectasia: The role of endothelial dysfunction. Int J Cardiol 2016 Jul 15;215:138-9.

[9] Ovali C, Morrad B. Associations between coronary artery disease, aneurysm and ectasia. Kardiochir Torakochirurgia Pol 2017 Sep;14(3):158-63.

[10] Dahhan A. Coronary artery ectasia in atherosclerotic coronary artery disease, inflammatory disorders, and sickle cell disease. Cardiovasc Ther 2015 Apr;33(2):79-88.

[11] Masoomi M, Ramezani MA, Karimzadeh H. The relationship of opium addiction with coronary artery disease. Int J Prev Med 2010 Summer;1(3):182-6.

[12] Ebdali RT, Tabaee SS, Tabaei S. Cardiovascular complications and related risk factors underlying opium consumption. J Cell Physiol 2019 Jun;234(6):8487-95.

[13] Ganguly P, Alam SF. Role of homocysteine in the development of cardiovascular disease. Nutr J 2015 Jan 10;14:6.

[14] Ahmed R, Khandelwal G, Bansal A, Jain A, Khandelwal K, Singla R. Prevalence and clinical profile of angiographic coronary artery ectasia among North Indian population. Journal of Natural Science, Biology and Medicine 2019;10(1):72.

[15] Hussain SS, Farhat S, Rather YH, Abbas Z. Comparative trial to study the effectiveness of clonidine hydrochloride and buprenorphine-naloxone in opioid withdrawal - a hospital based study. J Clin Diagn Res 2015 Jan;9(1):FC01-4.

[16] Esmaeili Nadimi A, Pour Amiri F, Sheikh Fathollahi M, Hassanshahi G, Ahmadi Z, Sayadi AR. Opium addiction as an independent risk factor for coronary microvascular dysfunction: A case-control study of 250 consecutive patients with slow-flow angina. Int J Cardiol 2016 Sep 15;219:301-7.

[17] Naruszewicz M. [Homocysteine as a residual risk factor in cardiovascular diseases]. Kardiol Pol 2010 Mar;68(3):283-4.

[18] Ebesunun MO, Obajobi EO. Elevated plasma homocysteine in type 2 diabetes mellitus: a risk factor for cardiovascular diseases. Pan Afr Med J 2012;12:48.
[19] Forood A, Malekpour-Afshar R, Mahdavi A. Serum level of plasminogen activator inhibitor type-1 in addicted patients with coronary artery disease. Addict Health 2014 Summer-Autumn;6(3-4):119-26.

[20] Azdaki N, Zardast M, Anani-Sarab G, Abdorrazaghnajad H, Ghasemian MR, Saburi A. Comparison between Homocysteine, Fibrinogen, PT, PTT, INR and CRP in Male Smokers with/without Addiction to Opium. Addict Health 2017 Jan;9(1):17-23.

[21] Masoomi M, Azdaki N, Shahouzehi B. Elevated Plasma Homocysteine Concentration in Opium-Addicted Individuals. Addict Health 2015 Summer-Autumn;7(3-4):149-56.

[22] Gholamhossenian A, Shahouzehi B, Shokoohi M, Najafipour H. B12 and Folate Concentrations in Opium Addicts Compared to Healthy Subjects: A Case Control Study from Kerman Coronary Artery Disease Risk Study. Addict Health 2018 Jul;10(3):198-204.

Tables

Table 1. Demographic data, ejection fraction and serum levels of FBG, TG, Chol, LDL, HDL, urea, Cr and Homocysteine in the patients with coronary artery ectasia (CAE), coronary artery disease (CAD) and the patients without CAE and CAE (control).
| Variables       | Groups | Mean ± SE        | P value |
|----------------|--------|-----------------|---------|
| Age            | Control | 55.97 ± 1.74    | 0.448   |
|                | CAE    | 55.00 ± 1.41    |         |
|                | CAD    | 51.21 ± 1.57    |         |
| Ejection fraction | Control | 55.97 ± 0.43    | <0.001* |
|                | CAE    | 55.04 ± 0.55    |         |
|                | CAD    | 51.21 ± 1.20    |         |
| FBG            | Control | 104.78 ± 3.66   | 0.308   |
|                | CAE    | 106.27 ± 3.82   |         |
|                | CAD    | 97.75 ± 4.10    |         |
| TG             | Control | 168.92 ± 12.57  | <0.001* |
|                | CAE    | 214.88 ± 10.92  |         |
|                | CAD    | 144.86 ± 13.03  |         |
| LDL            | Control | 92.30 ± 4.40    | <0.001* |
|                | CAE    | 130.67 ± 6.98   |         |
|                | CAD    | 96.08 ± 4.33    |         |
| HDL            | Control | 43.16 ± 1.78    | 0.024*  |
|                | CAE    | 38.11 ± 1.09    |         |
|                | CAD    | 39.33 ± 1.01    |         |
| Chol           | Control | 167.82 ± 5.23   | <0.001* |
|                | CAE    | 199.02 ± 7.89   |         |
|                | CAD    | 165.33 ± 5.45   |         |
| Urea           | Control | 30.26 ± 1.68    | 0.430   |
|                | CAE    | 33.04 ± 1.61    |         |
|                | CAD    | 33.29 ± 1.74    |         |
| Cr             | Control | 0.96 ± 0.03     | 0.178   |
|                | CAE    | 1.01 ± 0.02     |         |
|                | CAD    | 1.06 ± 0.03     |         |
| BMI            | Control | 25.33 ± 0.89    | 0.113   |
|                | CAE    | 26.60 ± 0.38    |         |
|                | CAD    | 24.61 ± 0.62    |         |
| Homocysteine   | Control | 9.67 ± 0.74     | 0.881   |
|                | CAE    | 9.38 ± 0.91     |         |
|                | CAD    | 9.12 ± 0.57     |         |
| Sex            | Control | Male 21          | 0.219   |
|                |        | Female 21        |         |
|                | CAE    | Male 25          |         |
|                |        | Female 21        |         |
|                | CAD    | Male 21          |         |
|                |        | Female 9         |         |
| Opium          | Control | Yes 11           | 0.001*  |
|                |        | No 31            |         |
|                | CAE    | Yes 28           |         |
|                |        | No 18            |         |
|                | CAD    | Yes 20           |         |
|                |        | No 10            |         |
| Smoking        | Control | Yes 5            | 0.132   |
|                |        | No 37            |         |
*The statistical analysis revealed that the patients were different regarding ejection fraction, TG, Chol, HDL and LDL serum levels and opium consumption significantly.

Table 2 Comparison of ejection fraction (EF), FBG, TG, Chol, LDL, HDL, Urea, Cr, BMI and homocysteine (Hom) between the male vs female, smokers vs non-smokers and opium consumers vs non-consumers in the control group.

|        | EF      | FBG     | TG      | Chol    | LDL     | HDL     | Urea    | Cr      | BMI     | Hom     |
|--------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Male   | 56.19±  | 94.38±  | 160.66± | 168.42± | 94.57±  | 43.09±  | 29.18±  | 1.04±   | 24.33±  | 9.32±   |
| ± 0.58 | ± 2.22± | ± 14.54±| ± 8.53± | ± 7.58± | ± 3.00± | ± 2.37± | ± 0.06± | ± 1.44± | ± 0.81± |         |
| Female | 55.75±  | 115.70± | 177.19± | 167.20± | 90.04±  | 43.23±  | 31.06±  | 0.92±   | 26.28±  | 11.45±  |
| ± 0.65 | ± 6.33± | ± 20.72±| ± 6.14± | ± 4.62± | ± 2.00± | ± 2.38± | ± 0.03± | ± 1.07± | ± 1.73± |         |
| Male   | 0.619   | 0.004*  | 0.908   | 0.969   | 0.613   | 0.590   | 0.102   | 0.283   | 0.293   |         |
| Female | 56.00±  | 90.20±  | 143±    | 167.40± | 37.80±  | 86.80±  | 25.50±  | 1.20±   | 23.70±  | 9.33±   |
| ± 1.87 | ± 3.54± | ± 15.33±| ± 7.99± | ± 4.66± | ± 3.13± | ± 9.50± | ± 0.16± | ± 1.19± | ± 1.93± |         |
| Male   | 55.97±  | 106.80± | 172.37± | 167.88± | 432.89± | 93.05±  | 30.66±  | 0.95±   | 25.56±  | 9.79±   |
| ± 0.43 | ± 4.03± | ± 14.07±| ± 5.88± | ± 1.91± | ± 4.97± | ± 1.70± | ± 0.03± | ± 1.00± | ± 0.81± |         |
| Female | 0.984   | 0.504   | 0.462   | 0.976   | 0.651   | 0.274   | 0.424   | 0.066   | 0.817   | 0.504   |
| Male   | 55.90±  | 98.18±  | 147.54± | 161.54± | 88.45±  | 43.76±  | 31.33±  | 1.15±   | 23.66±  | 9.95±   |
| ± 0.90 | ± 5.65± | ± 11.69±| ± 6.93± | ± 4.90± | ± 3.63± | ± 2.04± | ± 3.96± | ± 0.08± | ± 1.09± | ± 1.27± |
| Female | 56.00±  | 107.20± | 176.51± | 170.13± | 93.67±  | 456120± | 29.95±  | 0.91±   | 25.94±  | 9.44±   |
| ± 0.50 | ± 4.52± | ± 16.40±| ± 6.69± | ± 5.72± | ± 2.21± | ± 1.88± | ± 0.03± | ± 1.14± | ± 0.88± |         |
| Male   | 0.928   | 0.281   | 0.317   | 0.474   | 0.607   | 0.064   | 0.736   | 0.004*  | 0.264   | 0.741   |
| Female |        |         |         |         |         |         |         |         |         |         |

Data analysis using student t test revealed that FBG serum levels were higher in the female in comparison to male normal participants. Smoking has no effects on the variables and opium increased Cr serum levels in the participants.

Table 3. Comparison of ejection fraction, FBG, Urea, Cr, TG, CHol, LDL, HDL, BMI and homocysteine between the male vs female, smoker vs non-smoker and opium consumers vs non-consumers in the CAE group.
|       | EF    | FBG   | TG    | Chol  | LDL   | HDL   | Urea  | Cr    | BMI   | Hom   |
|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| male  | 54.58 | 112.08| 230.80| 191.63| 136.16| 38.20 | 33.23 | 1.07  | 26.84 | 7.92  |
|       | ± 5.98| ±     | ±     | ±     | ±     | ±     | ±     | ±     | ±     | ±     |
| female| 55.47 | 99.30 | 150.00| 204.64| 123.80| 38.00 | 32.85 | 0.94  | 26.33 | 11.06 |
|       | ± 4.03| ±     | ± 9.72| ± 7.74| ±     | ±     | ±     | ±     | ±     | ±     |
| male  | 0.68  | 12.91 | 19.12 | 11.82 | 10.96 | 1.73  | 2.94  | 0.03  | 0.44  | 0.82  |
| female| 0.425 | 0.097 | 0.104 | 0.400 | 0.385 | 0.929 | 0.908 | 0.008*| 0.522 | 0.085 |

Table 4. Comparison of ejection fraction, FBG, Urea, Cr, TG, Chol, LDL, HDL, BMI and homocysteine between the male vs female, smoker vs non-smoker and opium consumers vs non-consumers in the CAD group.

*Data analysis using student t test revealed that Cr serum levels were significantly higher in the male and smoker when compared to the female and non-smoker CAE patients, respectively. Smoking also was associated with increased serum levels of TG in the participants.*
|     | EF    | FBG   | TG     | Chol   | LDL   | HDL   | Urea  | Cr    | BMI   | Hom   |
|-----|-------|-------|--------|--------|-------|-------|-------|-------|-------|-------|
| e   | 51.26 | 97.15 | 153.66 | 170.28 | 100.41| 37.85 | 33.11 | 1.12  | 24.73 | 8.84  |
|     | ± 1.40 | ± 5.79 | ± 17.75| ± 7.28 | ± 5.81| ± 1.02| ± 2.26| ± 0.04| ± 0.63| ± 0.70|
| ile | 51.11 | 99.11 | 124.33 | 153.77 | 85.95 | 42.77 | 33.66 | 0.92  | 24.33 | 9.77  |
|     | ± 2.46 | ± 3.59 | ± 11.77| ± 5.09 | ± 3.37| ± 2.05| ± 2.78| ± 0.06| ± 1.52| ± 0.98|
| ue  | 0.956 | 0.830 | 0.311  | 0.169  | 0.128 | 0.024*| 0.884 | 0.013*| 0.771 | 0.467 |
| Yes | 45.12 | 92.00 | 137.25 | 166.75 | 101.55| 35.50 | 25.00 | 1.11  | 22.80 | 7.73  |
|     | ± 3.53 | ± 14.02| ± 27.31| ± 15.28| ± 9.68| ± 2.95| ± 1.00| ± 0.11| ± 0.70| ± 0.52|
| No  | 52.15 | 98.68 | 146.03 | 165.11 | 95.23 | 39.92 | 34.33 | 1.05  | 24.89 | 9.33  |
|     | ± 1.20 | ± 4.31 | ± 14.60| ± 5.95 | ± 4.81| ± 1.05| ± 1.85| ± 0.04| ± 0.69| ± 0.64|
| ue  | 0.046*| 0.584 | 0.823  | 0.921  | 0.629 | 0.141 | <0.001*| 0.663 | 0.259 | 0.073 |
| Yes | 51.30 | 100.57| 153.80 | 168.15 | 101.00| 37.75 | 32.22 | 1.02  | 24.42 | 9.29  |
|     | ± 1.38 | ± 6.03 | ± 18.79| ± 7.66 | ± 6.07| ± 1.09| ± 1.85| ± 0.3  | ± 0.67| ± 0.74|
| No  | 51.05 | 92.40 | 127.00 | 159.70 | 86.24 | 42.50 | 35.44 | 1.12  | 25.00 | 8.78  |
|     | ± 2.43 | ± 3.01 | ± 9.82 | ± 5.85 | ± 3.05| ± 1.78| ± 3.76| ± 0.07| ± 1.33| ± 0.90|
| ue  | 0.924 | 0.353 | 0.341  | 0.475  | 0.109 | 0.025*| 0.394 | 0.215 | 0.671 | 0.683 |

*Data analysis using student t test revealed that HDL and Cr serum levels were higher and lower, respectively, in the CAD female patients in comparison to CAD male patients. Smoking led to decreased serum levels of both FBG and urea. Opium decreased serum levels of HDL in the CAD patients.