Association of Opium Addiction with Coronary Artery Ectasia and Coronary Artery Disease

Naemeh Bahrami¹, Gholamreza Asadikaram², Mohammad Masoumi¹

Abstract

Background: 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 (CVDs) have also been documented previously. This project was designed to assess the relationship between opium and CAE and coronary artery disease (CAD).

Methods: This cross-sectional study was performed on 46 patients with CAE, 30 patients with CAD, and 42 cases without CAE and CAD (controls). Demographic data and information regarding opium consuming and also smoking were collected using a standard checklist. Serum levels of homocysteine, creatinine (Cr), urea, fasting blood glucose (FBG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), and cholesterol were determined.

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

Conclusion: The results of study showed that opium addiction was associated with increased risk of CAE and CAD, independent of homocysteine serum levels.

Keywords: Coronary artery disease; Opium; Homocysteine

Citation: Bahrami N, Asadikaram G, Masoumi M. Association of Opium Addiction with Coronary Artery Ectasia and Coronary Artery Disease. Addict Health 2021; 13(2): 77-84.

Received: 03.12.2020

Accepted: 07.02.2021

1- Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
2- Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran

Correspondence to: Mohammad Masoumi; Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran; Email: masoomidr@yahoo.com
Opium Addiction and Coronary Artery Ectasia

Bahrami et al.

Introduction

Cardiovascular diseases (CVDs) are the main causes of the morbidity and mortality among Iranian population and also developed and developing countries. The diseases are associated with several complications, including coronary artery ectasia (CAE), which play key roles in the induction of the cardiovascular-related morbidities and mortalities. It has been demonstrated that several genetic and environmental factors play significant roles in the induction of CVDs, including CAE and coronary artery disease (CAD). CAE, as a rare CVD-related complication, occurs in only 0.3%-4.9% of the patients. The complication is characterized by the non-local coronary artery enlargement to 1.5 times or more, when compared to its normal diameter. It is plausible in 0.22%-1.40% of angiographies and most of them are induced due to the atherosclerosis; however, some of them have the congenital or percutaneous coronary intervention (PCI) sources. It has been hypothesized that CAE may increase the risk of acute myocardial infarction (MI). However, some of the patients with CAD suffer from CAE, implying that different mechanisms are 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. It has been reported that opium is an inducer of inflammation and its significant association with CVDs has been documented by several investigators. The roles played by opium in the pathogenesis of CAE are yet to be defined. Due to the relation between opium and CVDs and their related complications, it has been hypothesized that opium may alter the risk of CAE. Therefore, this project was designed to investigate the prevalence of opium consumption in patients with CAD and CAE and possible association 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 CVDs, and it also can be considered as a risk factor for induction of the diseases. Nevertheless, its roles in the pathogenesis of CAE are yet to be clarified completely. Thus, another aim of this project was to explore the association between homocysteine serum levels and CAE/CAD among an Iranian population from Kerman Province, Iran.

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 Department of Cardiovascular Diseases, Shafa Hospital, Kerman. CAE was defined as dilatation of an arterial segment to a diameter at least 1.5 times that of the adjacent normal coronary artery.

CAD was defined as more than 50% diameter stenosis of one or more major coronary artery. Patients without CAE and any coronary artery stenosis were determined as control group (normal coronary artery).

Opium consumption was diagnosed due to the patients’ self-declaration. In addition to the variables, sex, age, smoking, and history of CVDs were collected using a standard checklist. Body mass index (BMI) was calculated as weight (kg) divided by height in meters squared (m²). All the patients who were under angiography and had CAE and CAD were entered to the study except the patients that suffered from other CVDs, heart failure (HF) with a left ventricular ejection fraction (LVEF) < 40%, atrial fibrillation (AF), 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 participants’ characteristics, including demographic information, screening records, drug use, and clinical features/manifestations were recorded using a checklist.

Angiography: An expert Doctor of Medicine (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.

**Biochemical measurements:** High-performance liquid chromatography (HPLC) technique (KNAUER, Germany), coupled with fluorescence detector, was 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 (CV), respectively.

Low-density lipoprotein (LDL), high-density lipoprotein (HDL), fasting blood glucose (FBG), urea, creatinine (Cr), triglyceride (TG), and cholesterol were measured for the participants. To evaluate serum levels of these factors, 5 ml blood samples were collected in the tubes without anticoagulant agents and sera were separated and kept in -20 ºC. Serum levels of FBG, urea, Cr, TG, LDL, and HDL were evaluated using commercial kits (Man Company, Tehran, Iran) according to the manufacturer instructions.

The SPSS software (version 20, IBM Corporation, Armonk, NY, USA) was used to analyse the raw data. Accordingly, for the normal distribution of the data, the groups were compared regarding the variables using the parametric tests. One-way analysis of variance (ANOVA) was used to analyse the differences between the groups regarding age, BMI, ejection fraction (EF), and serum levels of FBG, urea, Cr, TG, cholesterol, LDL, and HDL. To analyse the differences between the groups regarding gender and status of smoking and opium consuming, chi-square test was used.

### Results

Data analysis demonstrated that although the groups were not different regarding smoking (P = 0.132), the opium consumers were significantly higher in the patients with CAE and CAD 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. 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). Table 1 illustrates the raw data regarding the variables.

The statistical analysis revealed that the patients were different regarding opium consumption significantly. Table 2 shows the data regarding EF, FBG, TG, cholesterol, LDL, HDL, urea, Cr, and homocysteine between three 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), cholesterol (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). EF (P < 0.001) was significantly decreased in the CAD in comparison to both CAE and control groups.

| Variables | Groups | Value | P   |
|-----------|--------|-------|-----|
| Age (year) | Control | 55.97 ± 1.74 | 0.448 |
|           | CAE    | 55.00 ± 1.41 |
|           | CAD    | 51.21 ± 1.57 |
| BMI (kg/m²) | Control | 25.33 ± 0.89 | 0.113 |
|           | CAE    | 26.60 ± 0.38 |
|           | CAD    | 24.61 ± 0.62 |
| Sex (%)   | Control | Male 50.0 | 0.219 |
|           | CAE    | Male 54.3 |
|           | CAD    | Male 70.0 |
| Opium (%) | Control | Yes 26.2 | 0.001 |
|           | CAE    | Yes 60.9 |
|           | CAD    | Yes 66.7 |
| Smoking (%) | Control | Yes 11.9 | 0.132 |
|            | CAE    | Yes 26.1 |
|            | CAD    | Yes 13.4 |

*P < 0.001 versus control group
SE: Standard error; BMI: Body mass index; CAE: Coronary artery ectasia; CAD: Coronary artery disease

The statistical analysis revealed that the patients were different regarding EF, TG, cholesterol, HDL, and LDL serum levels significantly. Table 3 shows the data regarding EF, FBG, TG, cholesterol, LDL, HDL, urea, Cr, BMI, and homocysteine between the smokers vs. non-smokers and opium consumers vs. non-consumers in participants. Statistical analysis revealed that smoking was associated with decreased EF and opium consumption was associated with decreased serum levels of HDL in the patients (Table 3). In addition, smoking and opium were associated with increased serum levels of Cr (Table 3).

The statistical analysis revealed that smoking and opium were associated with changes in EF, HDL, and Cr serum levels.
Table 2. Comparison of ejection fraction (EF), fasting blood glucose (FBG), triglyceride (TG), cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), urea, creatinine (Cr), body mass index (BMI), and homocysteine between control, coronary artery ectasia (CAE), and coronary artery disease (CAD) groups

| Group     | EF      | FBG    | TG      | Cholesterol | LDL     | HDL     | Urea | Cr   | Homocysteine |
|-----------|---------|--------|---------|-------------|---------|---------|------|------|--------------|
| Control   | 55.97 ± 0.43 | 104.78 ± 3.66 | 168.92 ± 12.57 | 167.82 ± 5.23 | 92.30 ± 4.40 | 43.16 ± 1.78 | 30.26 ± 1.68 | 0.96 ± 0.03 | 9.67 ± 0.74 |
| CAE       | 55.04 ± 0.55 | 106.27 ± 3.82 | 214.88 ± 10.92 | 199.02 ± 7.89 | 130.67 ± 6.98 | 38.11 ± 1.09 | 33.04 ± 1.61 | 1.01 ± 0.02 | 9.38 ± 0.91 |
| CAD       | 51.21 ± 1.20 | 97.75 ± 4.10 | 144.86 ± 13.03 | 165.33 ± 5.45 | 96.08 ± 3.33 | 39.33 ± 1.01 | 33.29 ± 1.74 | 1.06 ± 0.03 | 9.12 ± 0.57 |

P < 0.05 versus non-smokers, opium consumers, and non-consumers, *P < 0.05 versus control group. †P < 0.001 versus control and coronary artery ectasia (CAE) groups.
CAE: Coronary artery ectasia; CAD: Coronary artery disease; EF: Ejection fraction; FBG: Fasting blood glucose; TG: Triglyceride; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; Cr: Creatinine
Data are presented mean ± standard deviation (SD)

Table 3. Comparison of ejection fraction (EF), fasting blood glucose (FBG), urea, creatinine (Cr), triglyceride (TG), cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), body mass index (BMI), and homocysteine between the smokers vs. non-smokers and opium consumers vs. non-consumers in participants

| Smoking | EF      | FBG    | TG      | Cholesterol | LDL     | HDL     | Urea | Cr   | Homocysteine |
|---------|---------|--------|---------|-------------|---------|---------|------|------|--------------|
| Yes     | 46.22 ± 2.33 | 91.30 ± 4.44 | 153.00 ± 15.53 | 157.33 ± 11.93 | 81.81 ± 4.16 | 45.11 ± 11.31 | 22.30 ± 11.50 | 1.11 ± 0.06 | 25.53 ± 1.53 |
| No      | 53.13 ± 1.33 | 101.21 ± 3.53 | 146.31 ± 19.30 | 158.12 ± 9.69 | 85.67 ± 3.55 | 25.65 ± 13.82 | 0.81 ± 0.03 | 24.55 ± 1.63 |

P < 0.05 versus non-smokers, opium consumers, and non-consumers, *P < 0.05 versus opium non-consumers. †P < 0.05 versus non-smokers and opium non-consumers.
EF: Ejection fraction; TG: Triglyceride; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; Cr: Creatinine; FBG: Fasting blood glucose; BMI: Body mass index
Data are presented mean ± standard deviation (SD)
Discussion
The results demonstrated that the prevalence of opium addiction was significantly higher in CAE and CAD groups compared to control group (Table 1). Due to the results, it appears that opium addiction increases the risk of CAE and CAD. As mentioned previously, opium is a risk factor for deterioration of CVDs. Additionally, the roles played by opium in the cardiovascular-related complications, such as atherosclerosis and coronary microvascular dysfunction (CMD), have also been documented previously. Our results also showed that there was an association between opium consumption and 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 was a risk factor for CVDs. The results of the current study demonstrated that homocysteine levels were not changed between cases and controls. Smoking and opium consumption also did not have significant effects on the serum levels of homocysteine. Thus, it may be concluded that opium can probably induce CAE or CAD in homocysteine independent pathways and it may alter other risk factors for the diseases. For example, it has been reported that opium can lead to CAD via up-regulation of plasminogen activator inhibitor (PAI). In parallel with our results, Azdaki et al. revealed that opium had no effects on the homocysteine serum levels. Although there are some investigations showing increased plasma/serum levels of homocysteine in the opium-addicted patients, their participants did not suffer from CVDs. Therefore, it may be hypothesized that probably opium increases the risks of CAE and CAD incidence, but it did not induce the disorders via up-regulation of homocysteine.

The results showed that the smoking was associated with decrease in EF compared to non-smokers, opium consumers, and non-consumers. Besides, opium consumption was associated with decrease in HDL serum levels when compared to non-addicted patients.

Conclusion
Due to the results, it may be concluded that there is an association between opium consumption and smoking with the risk of CVDs (including CAD and CAE), independent of homocysteine and kidney diseases incidence.

Conflict of Interests
The Authors have no conflict of interest.

Acknowledgements
This project was funded by Kerman University of Medical Sciences with grant number of IR.KMU.AH.REC.1397.031.

Authors’ Contribution
Data curation, data analysis, funding, investigation, methodology, software, supervision, writing-original draft, review and editing: NB; conceptualization, data curation, funding, investigation, methodology, project administration, resources, writing-review and editing: GA; conceptualization, data curation, funding acquisition, investigation, methodology, project administration, supervision, resources, writing–reviewing and editing: MM.

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; 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; 50(3): 201-8.

3. Devabhaktuni S, Mercedes A, Diep J, Alhsan 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 renelase activity in hypertension but not coronary artery diseases: The role of gene polymorphism. J Cell Biochem 2019; 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; 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; 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; 37(12): 2350-5.

8. Antonopoulos AS, Siasos G, Okonomou 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; 215: 138-9.

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

10. Dahhan A. Coronary artery ectasia in atherosclerotic coronary artery disease, inflammatory disorders, and sicle cell disease. Cardiovasc Ther 2015; 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; 1(3): 182-6.

12. Momeni-Moghadam MA, Asadikaram G, Nematollahi MH, Esmaeili Tarzi M, Faramarz-Gaznagh S, Mohammadpour-Gharehbagh A, et al. Effects of cigarette smoke and opium on the expression of CD9, CD36, and CD68 at mRNA and protein levels in human macrophage cell line THP-1. Iran J Allergy Asthma Immunol 2020; 19(1): 45-55.

13. Nakhaee S, Amirabadizadeh A, Qorbani M, Lamarine RJ, Mehrpour O. Opium use and cardiovascular diseases: A systematic review and meta-analysis. Crit Rev Toxicol 2020; 50(3): 201-12.

14. Ghazavi A, Mosayebi G, Solhi H, Rafiei M, Moazzeni SM. Serum markers of inflammation and oxidative stress in chronic opium (Taryak) smokers. Immunol Lett 2013; 153(1-2): 22-6.

15. Asgry S, Sarrafa-zadegan N, Naderi GA, Rozbehani R. Effect of opium addiction on new and traditional cardiovascular risk factors: Do duration of addiction and route of administration matter? Lipids Health Dis 2008; 7: 42.

16. Ebdalí RT, Tabaei SS, Tabaei S. Cardiovascular complications and related risk factors underlying opium consumption. J Cell Physiol 2019; 234(6): 8487-95.

17. Ganguly P, Alam SF. Role of homocysteine in the development of cardiovascular disease. Nutr J 2015; 14: 6.

18. 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. J Nat Sc Biol Med 2019; 10(1): 72-6.

19. 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; 9(1): FC01-FC04.

20. 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; 219: 301-7.

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

22. 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.

23. 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; 6(3-4): 119-26.

24. Azdaki N, Zardast M, Anani-Sarab G, Abdorrazaghnaejad 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; 9(1): 17-23.

25. Masoomi M, Azdaki N, Shahouzehi B. Elevated plasma homocysteine concentration in opium-addicted individuals. Addict Health 2015; 7(3-4): 149-56.
26. 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; 10(3): 198-204.

27. Regalado M, Yang S, Wesson DE. Cigarette smoking is associated with augmented progression of renal insufficiency in severe essential hypertension. Am J Kidney Dis 2000; 35(4): 687-94.

28. Bleyer AJ, Shemanski LR, Burke GL, Hansen KJ, Appel RG. Tobacco, hypertension, and vascular disease: Risk factors for renal functional decline in an older population. Kidney Int 2000; 57(5): 2072-9.

29. Sumathi T, Niranjali DS. Effect of Bacopa monniera on liver and kidney toxicity in chronic use of opioids. Phytomedicine 2009; 16(10): 897-903.

30. Orth SR. Smoking and the kidney. J Am Soc Nephrol 2002; 13(6): 1663-72.
بررسی ارتباط مصرف تریاک با اکتاسی عروق کرونر و بیماری عروق کرونر
نیایه بهرامی، غلامرضا اسدی کرم، محمد معصومی

چکیده
مقدمه: اکتاسی عروق کرونر (CAE) با Coronary artery ectasia (CAE) با Coronary artery disease (CAD) مرتبط می‌باشد. نقص هموضیعی در ابداع بیماری‌های قلبی- عروقی بیشتر ناگهانی است. نیاز می‌باشد به مانور بررسی ارتباط بین مصرف تریاک، اکتاسی عروق کرونر و بیماری عروق کرونر (CAE) با Coronary artery disease (CAD) تحقیقاتی باعث شده است.

روش‌ها: این مطالعه مقطعی بر روی 46 بیمار مبتلا به CAD، 200 بیمار مبتلا به CAD و 42 بیمار بدون CAD و CAE انجام شد. یافته‌های دموگرافیک و اطلاعات مرتبط با مصرف تریاک و سیگار برابر بر اساس جمع‌آوری گردید. سطح سرمی هموضیعی، کریتینین (LDL) Low density lipoprotein، FBG و ناشتا اوره، سطح خون ناشتا Cr با و سطح HDL High density lipoprotein، Triglyceride و کلسترول محاسبه شد.

یافته‌ها: مصرف کندگان تریاک به صورت قابل توجه بیشتر بود که بیشتر CAD و CAE را در افراد طبیعی افزایش می‌بیند. بیماران 41 مبتلا به CAD، سطح سرمی Cr و 41 مبتلا به CAE کاهش یافته بودند. سطح سرمی هموضیعی و تفاوت قابل توجه بین هر دو گروه نداشت.

نتیجه‌گیری: مصرف تریاک بدون ارتباط با سطح سرمی هموضیعی، با افزایش خطر CAD و CAE و افزایش خطر و قلبی کلیدی: بیماری عروق کرونر؛ تریاک؛ هموضیعی

واژگان کلیدی: بیماری عروق کرونر؛ تریاک؛ هموضیعی

ارجاع: بهرامی نیایه، غلامرضا اسدی کرم، محمد معصومی. بررسی ارتباط مصرف تریاک با اکتاسی عروق کرونر و بیماری عروق کرونر. مجله اعتیاد و سلامت. 1400، 13 (2): 9-17.

تأخیر پذیرش: 1399/11/19

رنگ زاویه: 1399/9/13

Email: masoomidr@yahoo.com

http://ahj.kmu.ac.ir, 04 April