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EVALUATION OF HEMATOLOGICAL, BIOCHEMICAL PARAMETERS AND CRAVING AMONG DRUG USERS

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ABSTRACT
Addiction is one of the most important issues of the 21st century that received more attention all over the world because drug addiction is associated with significant disease and death. In this study several biochemical and hematological factors were evaluated in addicted men against non-addicted volunteers as the control group. The results demonstrated the deleterious effects of opium on some liver, kidney and immune system diseases risk factors. Other finding suggests that the level of cholesterol, which is widely used in clinical practice, could be a potential marker of psychological construct related to drug-using behaviors. Thus we proposed that additional attention should be paid to dependent patients with low level of cholesterol for craving among addicted persons.

KEYWORDS: Hematological indices, biochemical parameters, craving, dependent patients.

INTRODUCTION
Addiction is non-stop issue in all over the world.[1,2] Among the illegal substances, opium has the highest consumption in Iran[2,3]; further, Iran is the first consumer of the opium in all over the world.[1] Opium poppy (Papaver somniferum) is one of the oldest cultivated plants of mankind and the commercial source for the narcotic analgesics such as morphine and codeine.[4,5] Morphine is a major alkaloid in opium poppy.[4] But more than 20 alkaloids and more than 70 ingredients are present in opium.[1,6] Addictive disorders are well known to be associated with a high level of physical and psychological disorders.[1] Opium abuse carries substantial risks of harm to health, economic and social functioning.[7-9] The drug addicts susceptible to develop killer diseases such as AIDs, cancers, cardiovascular diseases, kidney dysfunction.[10] Many studies have shown that consuming opiates have acute and chronic effects on different body systems. Some other studies also indicated that consumption of opioids may cause cofactor role in dependent people for infectious diseases.[1] Therefore, it is very important to discover the main aspect of blood toxicology, especially in drug dependent people and In this study, we tried to review the effect of addiction (heroin, opium, marijuana and synthetic drugs) on hematological and biochemical parameters of dependent people. Consequently, suitable and efficient treatments should be used in order to reduce the side effects.

MATERIAL AND METHODS
Subject group included 99 male addicted who referred to the Arad Addiction Treatment Center and control group included 99 male non addicted and healthy referred to Farabi laboratory. Several biochemical and hematological factors such as blood sugar, cholesterol, triglyceride (TG), blood urea nitrogen (BUN), creatinine (Cr), Serum glutamic oxaloacetic transaminase (SGOT or AST), serum glutamic pyruvic transaminase (SGPT or ALT), alkaline phosphatase (ALK), bilirubin direct and total, uric acid, hemoglobin (Hb), hematocrit (HCT), red blood cell (RBC) count, white blood cell (WBC) count, platelet (PLT) count and percentage of Neutrophil, Eosinophil, Basophil, Lymphocyte and Monocyte were evaluated in opium-addicted men (case) against non-addicted volunteers as the control group.

RESULT

Frequency of male addicted by age bands showed that the biggest group of them are between 20-40 years old (Fig.1). And most of them are in low degree of literacy (Fig.2). Our study also showed the age of beginning to drug abuse was under 20 years old (Fig.3). And their job or marriage were not barrier to their addiction (Fig.4, 5). This study demonstrated that background of withdrawal is not desirable and most of them had not such an experience and the others despite having withdrawal, have to experience it (F.6). In this research, it was found that abuse of natural drugs has been in the first category while synthetic drugs are in second place (F.7). Addicted person abuse the drug in different style (F.8). At the end, duration of withdrawal time showed that, this period varies from a few days to several years (F.9).

In this study, the effects of opium and heroin consumption on concentration of various biochemical parameters such as TG, Cholesterol, BUN, Cr, SGOT, SGPT, ALK, Bilirubin (D, T) and Uric acid in human's serum have been investigated. According to one way ANOVA, the concentrations of TG, Cholesterol, BUN, SGOT, ALK, Bilirubin (D) and Uric acid were significantly different in the addict groups compared to the control group (Table 1). That is, serum concentration of BUN, Bilirubin (D) and Uric acid were lower in the opium-addict group compared to the control group ($p < .05$). Addict groups showed significant decrease in serum level of cholesterol in comparison to the control group ($p < .05$). The values of parameters such as SGPT, Cr and Bilirubin (T) in the addict groups did not show significant differences with those in the control group (Table 1).

The comparison of hematological factors in dependent and control groups One-way ANOVA indicated that in addicted group, red blood cell and white blood cell count remained unchanged in comparison with that in the control group (table 2). Significant elevated Basophil and Monocyte percentage was seen but Lymphocyte was increased significantly in addict group ($p < .05$). And the PLT count actually had a significant decrease in comparison with control group ($p < .05$) (table 2).

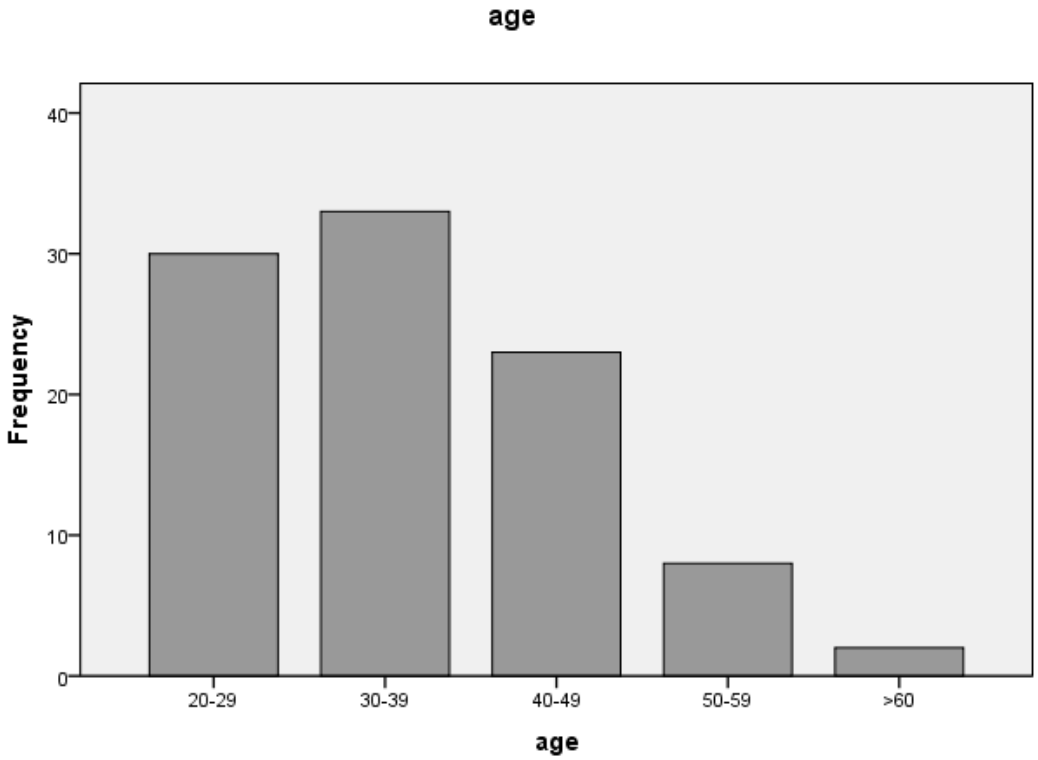

Figure 1: Frequency of male addicted by Age Bands.

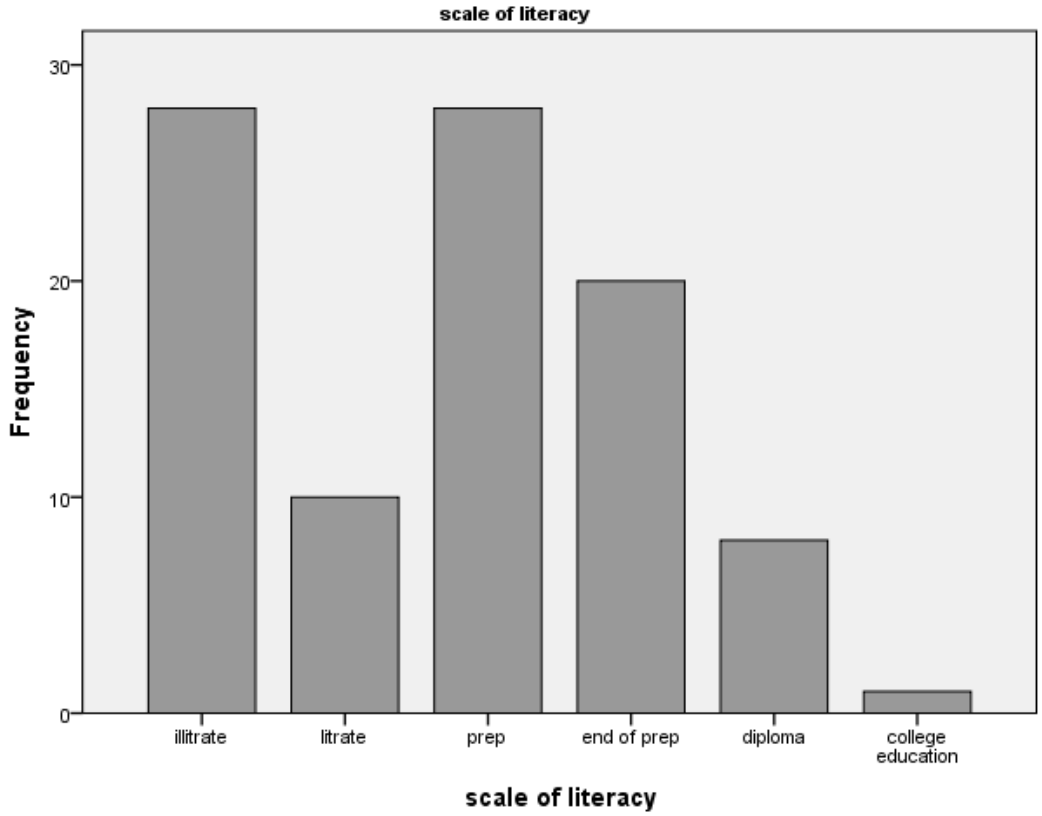

Figure 2: Frequency of male addicted in scale of literacy.

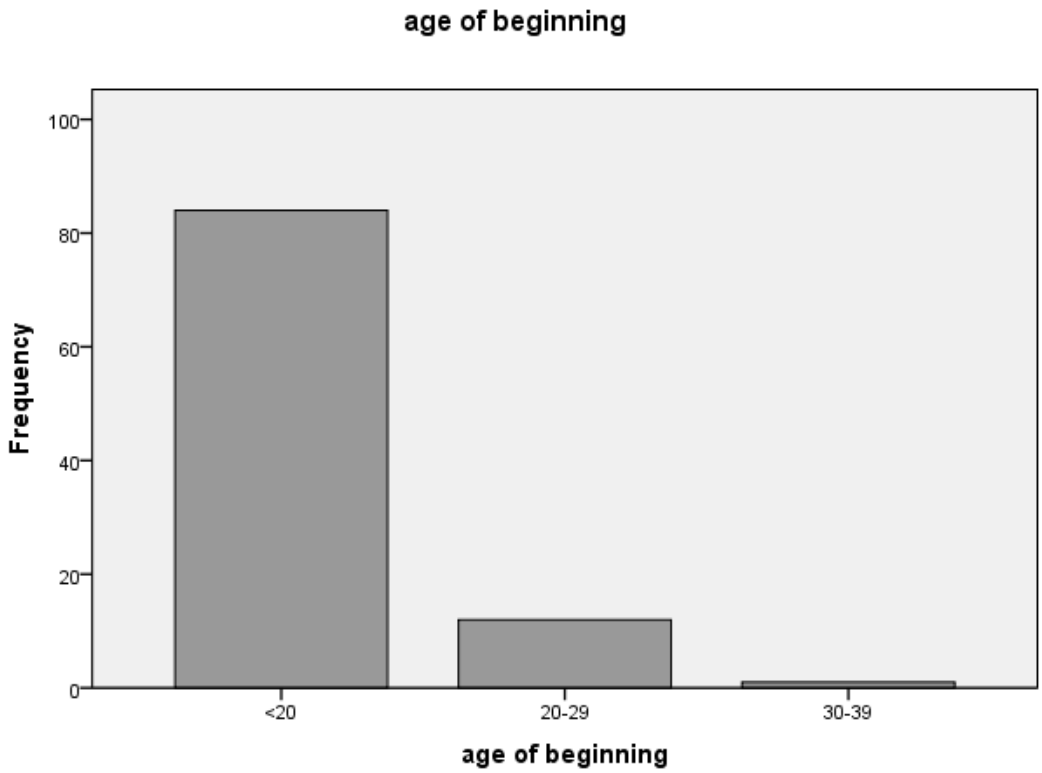

Figure 3: Frequency of male addicted by age of beginning drug abuse.

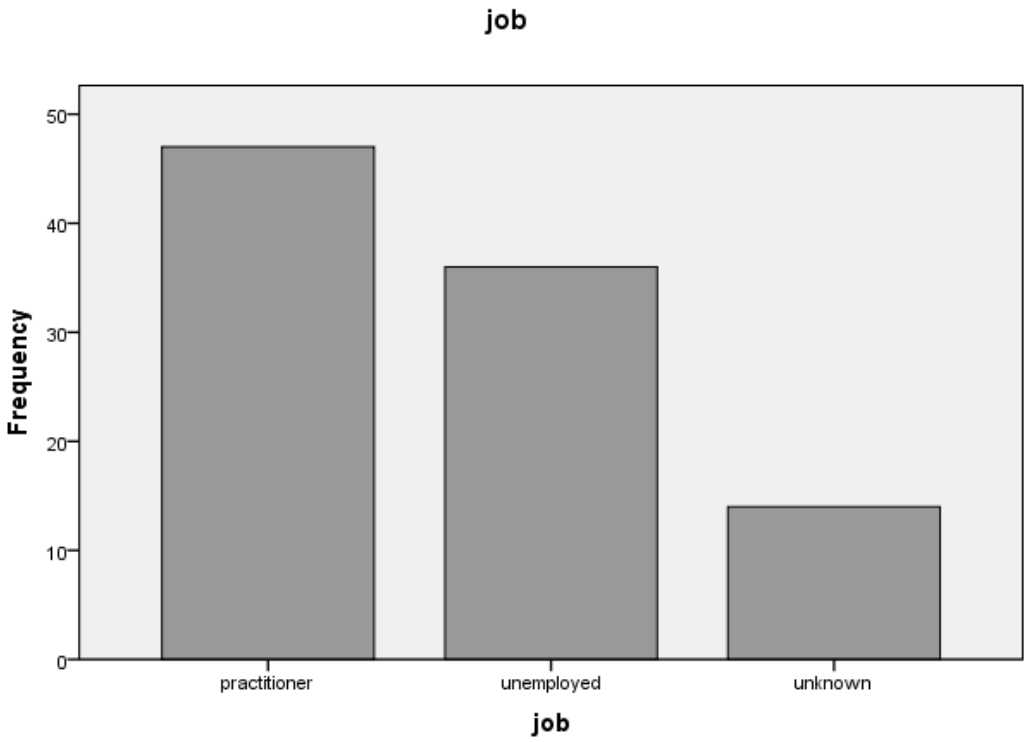

Figure 4: Frequency of male addicted in scale of their jobs.

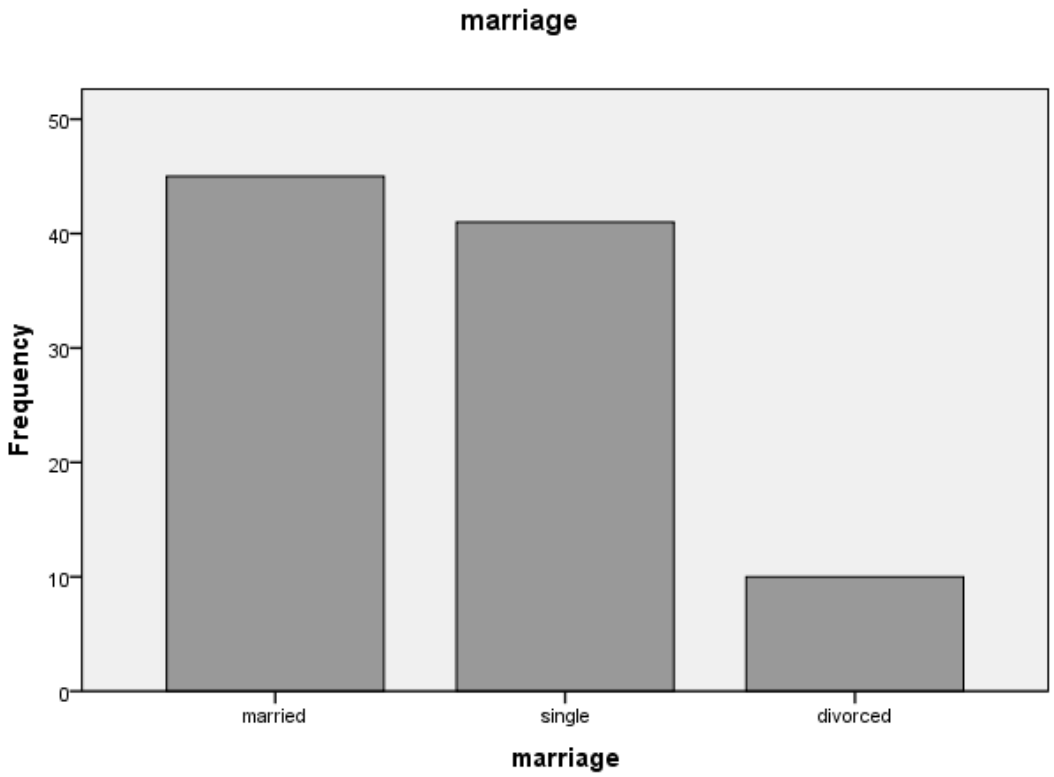

Figure 5: Frequency of male addicted in scale of marriage.

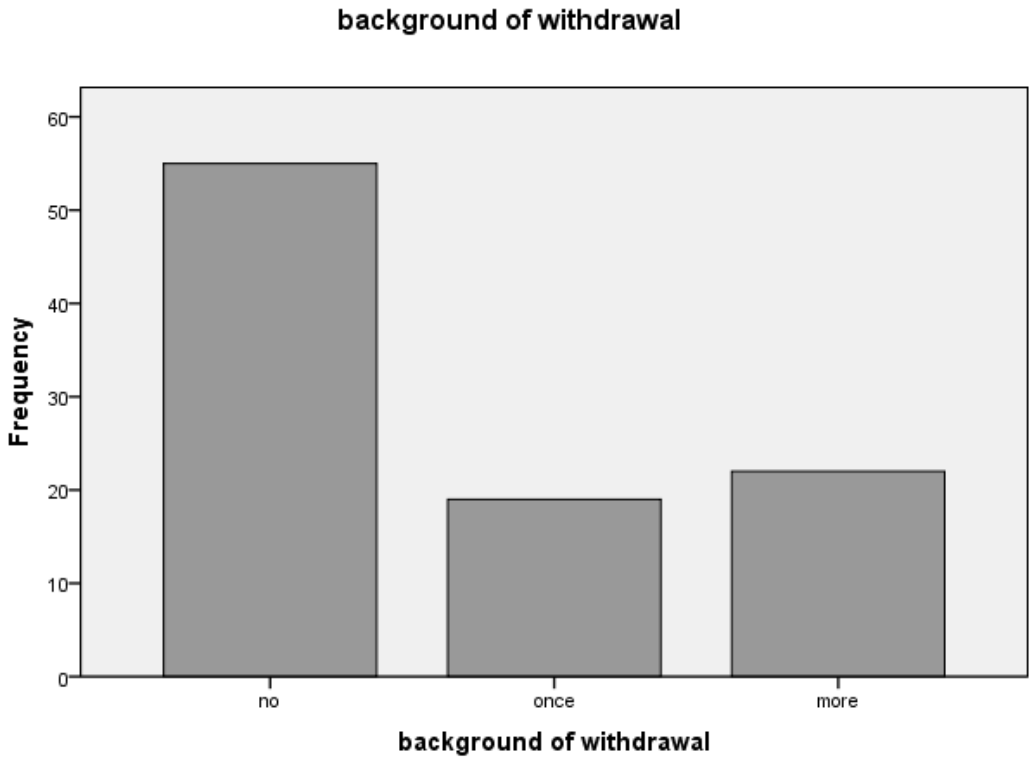

Figure 6: Frequency of male addicted by background of withdrawal.

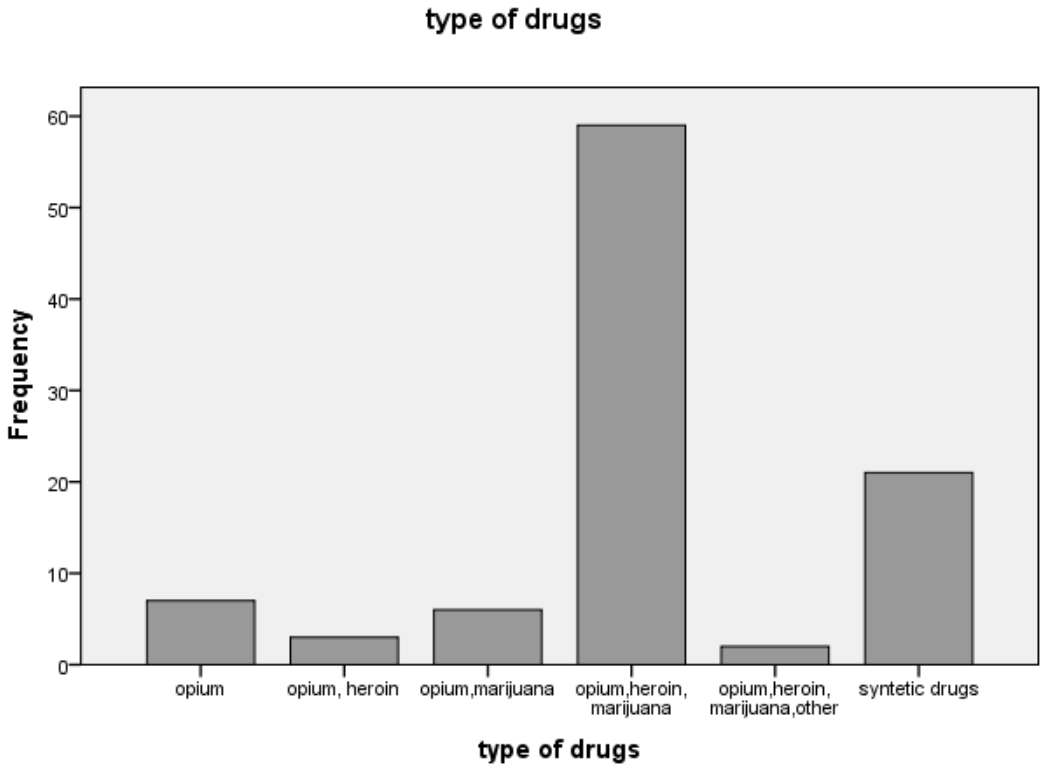

Figure 7: Frequency of male addicted by type of drugs.

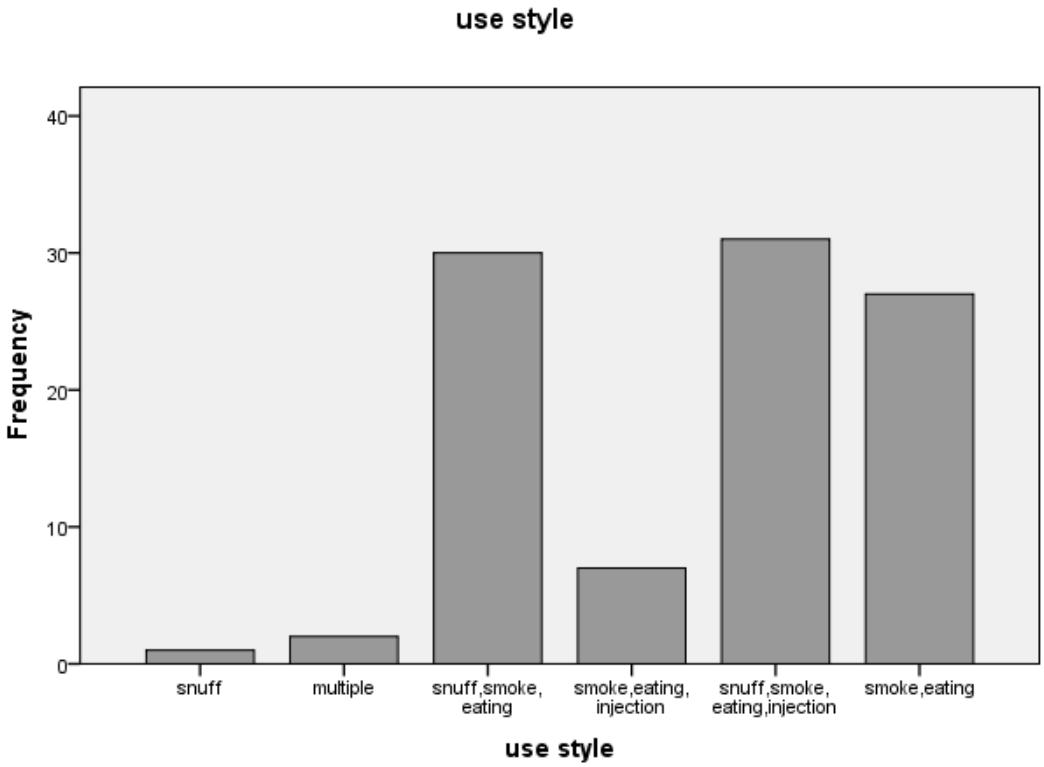

Figure 8: Frequency of male addicted by use style of drug.

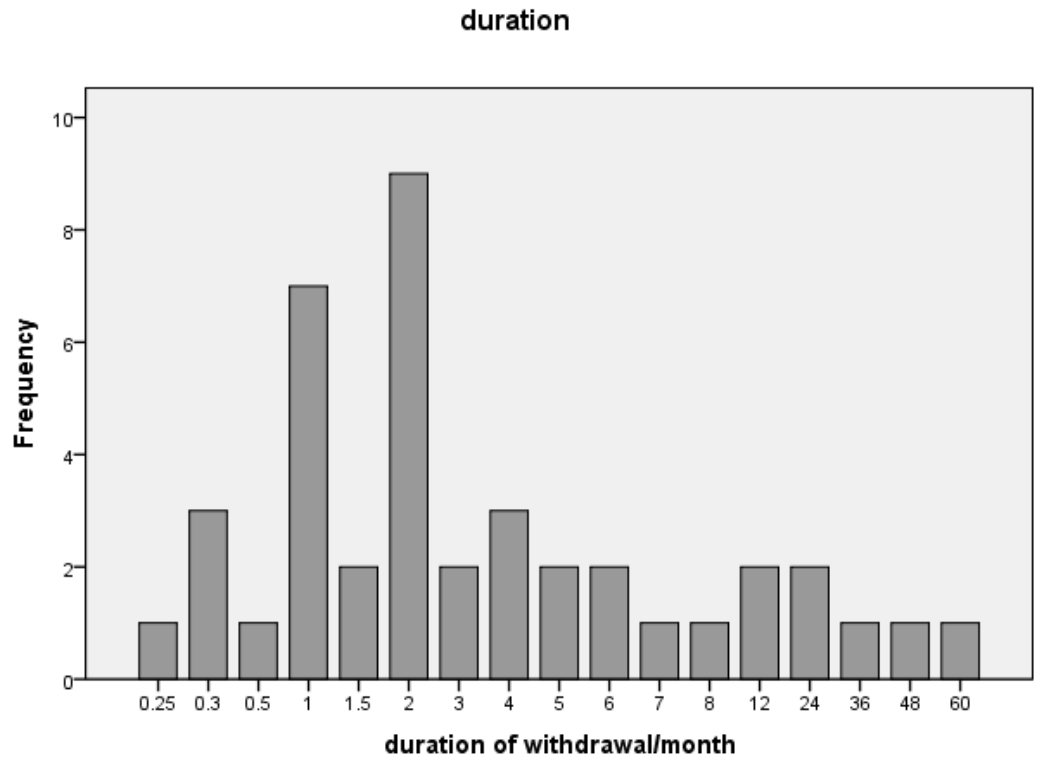

Figure 9: Frequency of male addicted by duration of withdrawal time according to month.

Table 1: Biochemical parameters in addicted and control groups.

	Addicted group	Control group	P value
TG	157.14±9.53*	97.00±3.95	<0.0001
Cholesterol	158.60±4.42*	171.91±2.32	0.006
BUN	12.04±0.29*	13.59±0.44	0.006
Cr	0.86±0.02	2.29±1.47	0.5108
SGOT	34.43±1.96*	23.81±0.85	0.0008
SGPT	23.51±1.55	22.11±0.99	0.3226
ALK	236.44±11.36*	199.14±10.78	0.0214
Bilirubin Direct	0.19±0.01*	1.26±0.77	<0.0001
Bilirubin Total	0.7±0.03	0.81±0.07	0.0664
Uric Acid	4.84±0.09*	5.28±0.16	0.023

Values are given in mean ±SEM; p values were obtained by student t test compared with control group; $p<0.05$ was considered significant.

Table 2: Hematological parameters in addicted and control groups.

	Addicted group	Control group	P value
Hemoglobin	13.92±0.15*	14.89±0.17	<0.0001
HCT	43.32±0.48	43.40±0.48	0.3743
RBC	4.72±0.06	4.81±0.063	0.0933
WBC	7636.00±320.35	7859.61±329.60	0.6085
Neutrophil	61.34±1.016	59.30±1.25	0.197
Eosinophil	0.94±0.10	1.17±0.158	0.534
Basophil	0.50±0.08*	0.0±0.0	<0.0001
Lymphocyte	30.98±1.10*	38.92±1.17	<0.0001
Monocyte	6.28±0.27*	0.59±0.092	<0.0001
PLT	209.50±12.39*	255.26±11.74	0.0004

Values are given in mean ±SEM; p values were obtained by student t test compared with control group; $p<0.05$ was considered significant.

DISCUSSION

In regard to cholesterol and TGs levels in this study, opium-dependents showed significantly lower serum cholesterol level as compared to the control group but TG was significantly higher in addicted group. In other studies, lipids levels in plasma such as cholesterol, HDL, and TG in heroin-dependents showed significant decrease.[4,11] But the other study was mentioned in diabetic opium-dependents total cholesterol decreases although non-significantly.[12] And in patients with non-malignant pain who received chronic intrathecal opioids, cholesterol, and TGs levels increased.[13] This differences might be credited to dissimilar doses used by patients and opium dependents. The variation of cholesterol and TGs is not only due to metabolic changes but also can be the concern of low levels of lipid intake in addict individuals resulting mainly from their poor nutritional status due to economic problems, unfavorable life style behavior, or loss of appetite due to the effect of opium.[5]

The metacognition about craving for drug addicts was not investigated, due to lack of access to psychiatrists, but since more than half of the subjects had not a history of drug withdrawal and the rest of the subjects had a history of one or more withdrawal, so it seems that drug craving in the group was high. Previous research[14] confirmed that an association between lipid levels and metacognition about craving may exist in abusers.[10]

Serotonin is a candidate to explain the association between cholesterol levels in serum and drug use behaviors.[14] A low level of cholesterol in plasma is associated with a decrease of tryptophan, the amino acid used to synthesize serotonin in the brain[15,16], and with membrane cholesterol that moderates serotonin transporter activity[17] So it seems that reduction of plasma cholesterol alters the metabolism of serotonin and these changes will lead to psychological problems and mood regulation.[18]

In the present study AST and alkaline phosphatase levels were higher significantly in addict group than those of control group. Similar outcomes were observed by other investigators. [14-16]

In liver, morphine is bio converted to morphine–3 glucuronide (M3G) and morphine–6 glucuronide (M6G).[19] These metabolites increase the secretion of liver enzymes. Continuous and greater dose of opium can disrupt the liver functions.[20]

Our such finding agree with the findings of the others (Balasubramaniam *et al.* (1994)) working on liver functional tests in Heroin addicts showed liver enzymes levels of addicts were significantly higher than in the control group. Liver damage due to hepatitis is also reported by Abelson (1970) when heroin is regularly taken in small doses a few times a day.[10]

Opium is considered as important cause of liver damages, and relationship between opium consumption and grade of liver damages was observed significant in hepatitis patients.[3]

In the present study, the serum creatinine levels of addicts decreased no significantly but the other study[21] mentioned that renal disease in cocaine and heroin abusers has been associated with the nephrotic syndrome, amyloidosis, acute glomerulonephritis, interstitial nephritis, and rhabdomyolysis.

In our study, Uric Acid and BUN in the serum of dependent group was lower than control group. In another study, it has been observed that consumption of morphine increases Uric Acid and creatinine levels.[22] The increased level of these end-products of nitrogen metabolism was associated with hepatotoxicity and nephrotoxicity and this is due to properties of opioids that increasing catabolism of purin nucleotides.[22,23] Interestingly, in another study, heroin withdrawal had led to the returning of Uric Acid level to the normal value.[23]

RBC count and HCT values did not report a significant change in addicted group in compare to control group($p<.05$) but there are some research that shows changes in RBC counts and HCT values in addiction group.[2]

In this study Hb was decreased without decreasing in HCT or RBC count and it might be due to Malnutrition or received low levels of folic acid. Platelets count also was decreased in addicted group in comparison with that in the control group ($p<0.05$). The others also demonstrated Hb concentration decreased in morphine dependent subject.[24] And, in a similar study, it was indicated that Hb and HCT levels decreased in heroin injection abusers.[25]

WBC count and Eosiniphil values had a non-significant decrease in dependent group, while in control group did not have any significant difference.[1] The effects of opioids could be mediated through HPA (Hypothalamus-Pituitary-Adrenal) axis and sympathetic nerves system.[26] Activity of HPA axis causes the secretion of the glucocorticoids from the adrenal cortex and activation of sympathetic nerves system increases epinephrine, norepinephrine and dopamine from the adrenal center. And studies have shown that norepinephrine and glucocorticoids both affecting WBCs so can act as suppressors of immune system.[2]

The present study showed that lymphocyte count significantly decreased in dependent group and is consistent with some previous studies.[27] While some studies were reported in heroin addicted people who had no malnutrition, increases in peripheral lymphocyte counts was seen.[28] In another study, the effect of heroin consumption was shown on reduced lymphocyte value.[29] It was demonstrated that morphine could reduce the proliferation of lymphocytes. And, these inhibitory effects gone by naloxone.[6,7] It might be due to regulate the immune system by directly via μ receptors located on the immune cells, or indirectly through activity of the μ receptors in the CNS.[30]

The monocytes increased in opium dependent people significantly in comparison to that in the control group. In previous studies, opposite results were reported; in morphine dependent group, the total neutrophil, monocyte and lymphocyte values did not change compared to the normal level of these factors.[31]

CONCLUSION

Finally, it is valuable mentioning that The alteration between the others studies and current study might be due to difference in dissimilar factors such as physiological or biochemical alterations, level of education, culture, diet, medicines, type of drug, method of Consumption, addiction period, frequency and method and duration of withdrawal.

However, the purpose of this study was to facilitate new ideas which lead to rapid, progression, development and effective treatments of diseases that associated with drugs abuse.

So, we suggest that the treatment of addicted must be according to their laboratory tests, Psychological problems and Dietary recommendations.

REFERENCES

1. Haghpanah T., Afarinesh M., Divsalar K., A review on hematological factors in opioid-dependent people (opium and heroin) after the withdrawal period. *Addiction & health*, 2010; 2(1-2): 9.
2. Hanson G. R., Analgesic, antipyretic and antiinflammatory drugs. *Remington: The Science and Practice of Pharmacy*, 1995; 2: 1196-1221.
3. Mahmoodi M., Hosseini-Zijoud S.-M., Hosseini J., Sayyadi A., Hajizadeh M., Hassanshahi G., Hashemi B., Opium withdrawal and some blood biochemical factors in addicts' individuals. *Advances in Biological Chemistry*, 2012; 2(2): 167-170.
4. Asgary S., Sarrafzadegan N., Naderi G.-A., Rozbehani R., Effect of opium addiction on new and traditional cardiovascular risk factors: do duration of addiction and route of administration matter? *Lipids in health and disease*, 2008; 7(1): 42.
5. Masoudkabir F., Sarrafzadegan N., Eisenberg M. J., ffects of opium consumption on cardiometabolic diseases. *Nature reviews Cardiology*, 2013; 10(12): 733.
6. Pawan M., Choudhary R., Mathur R., Choudhary M., Kamla M., Study on harmful effects of opium on liver and lungs in chronic opium addicts of western Rajasthan. *Journal of Bangladesh Society of Physiologist*, 2011; 6(2): 122-126.
7. Afshar A., Asadzadeh M., Kargar H., Aghdashi M. M., Mirzatolooei F., Opium and opioid abuse in

orthopedic inpatients: a cross sectional study in Urmia university of medical sciences. *Acta Medica Iranica*, 2012; 50(1): 66.
8. Divsalar K., Meymandi M. S., Afarinesh M., Zarandi M. M., Haghpanah T., Keyhanfar F., Mahmoodi M., Kruszewski S. P., Serum biochemical parameters following heroin withdrawal: an exploratory study. *The American journal on addictions*, 2014; 23(1): 48-52.
9. Asadikaram G., Sirati-Sabet M., Asiabanha M., Shahrokhi N., Jafarzadeh A., Khaksari M., Hematological changes in opium addicted diabetic rats. *International journal of high risk behaviors & addiction*, 2013; 1(4): 141.
10. Hasan M. R., Hassan P., Miah M. A. J., Evaluation of some biochemical changes in the serum of phensedyl addicts of Gaibandha District, Bangladesh. *Journal of Bio-Science*, 2014; 20: 57-65.
11. Wilczek H., Ceska R., Zlatohlávek L., Serum lipids in drug addicts. *Vnitrni lekarstvi*, 2004; 50(8): 584-586.
12. Karam G. A., Reisi M., Kaseb A. A., Khaksari M., Mohammadi A., Mahmoodi M., Effects of opium addiction on some serum factors in addicts with non-insulin-dependent diabetes mellitus. *Addiction biology*, 2004; 9(1): 53-58.
13. Abs R., Verhelst J., Maeyaert J., Van Buyten J.-P., Opsomer F., Adriaensen H., Verlooy J., Van Havenbergh T., Smet M., Van Acker K., Endocrine consequences of long-term intrathecal administration of opioids. *The Journal of Clinical Endocrinology & Metabolism*, 2000; 85(6): 2215-2222.
14. Buydens-Branchey L., Branchey M., Association between low plasma levels of cholesterol and relapse in cocaine addicts. *Psychosomatic medicine*, 2003; 65(1): 86-91.
15. Engelberg H., Low serum cholesterol and suicide. *The Lancet*, 1992; 339(8795): 727-729.
16. Steegmans P., Fekkes D., Hoes A. W., Bak A., van der Does E., Grobbee D. E., Low serum cholesterol concentration and serotonin metabolism in men. *BMJ: British Medical Journal*, 1996; 312(7025): 221.
17. Scanlon S. M., Williams D. C., Schloss P., Membrane cholesterol modulates serotonin transporter activity. *Biochemistry*, 2001; 40(35): 10507-10513.
18. Lin S.-H., Yang Y. K., Lee S.-Y., Hsieh P. C., Chen P. S., Lu R.-B., Chen K. C., Association between cholesterol plasma levels and craving among heroin users. *Journal of addiction medicine*, 2012; 6(4): 287-291.
19. Cavacuiti C. A. Principles of addiction medicine: The essentials. Lippincott Williams & Wilkins
20. Hanks G., Aherne G., Morphine metabolism: Does the renal hypothesis hold water? *The Lancet*, 1985; 325(8422): 221-222.
21. Jaffe J. A., Kimmel P. L., Chronic nephropathies of cocaine and heroin abuse: a critical review. *Clinical Journal of the American Society of Nephrology*, 2006; 1(4): 655-667.
22. Sumathi T., Devaraj S. N., Effect of Bacopa monniera on liver and kidney toxicity in chronic use of opioids. *Phytomedicine*, 2009; 16(10): 897-903.
23. Yang Y.-d., Zhang J.-z., Sun C., Yu H.-m., Li Q., Hong M., Heroin affects purine nucleotides catabolism in rats in vivo. *Life sciences*, 2006; 78(13): 1413-1418.
24. Sapira J. D., The narcotic addict as a medical patient. *The American journal of medicine*, 1968; 45(4): 555-588.
25. Pastan R. S., Silverman S. L., Goldenberg D. L., A musculoskeletal syndrome in intravenous heroin users: Association with brown heroin. *Annals of internal medicine*, 1977; 87(1): 22-29.
26. Vallejo R., de Leon-Casasola O., Benyamin R., Opioid therapy and immunosuppression: a review. *American journal of therapeutics*, 2004; 11(5): 354-365.
27. McDonough R., Madden J., Falek A., Shafer D., Pline M., Gordon D., Bokos P., Kuehnle J., Mendelson J., Alteration of T and null lymphocyte frequencies in the peripheral blood of human opiate addicts: in vivo evidence for opiate receptor sites on T lymphocytes. *The Journal of Immunology*, 1980; 125(6): 2539-2543.
28. Heathcote J., Taylor K. B., Immunity and nutrition in heroin addicts. *Drug and alcohol dependence*, 1981; 8(3): 245-255.
29. Tamba-Berehoiu R., Popa N., Popescu S., Popa C., Research regarding the toxic effects of heroin consumption on human homoleucogramma. *ROMANIAN BIOTECHNOLOGICAL LETTERS*, 12008; 3(1): 3605.
30. Sacerdote P., Opioids and the immune system. *Palliative medicine*, 2006; 20(8): 9-15.
31. Fecho K., Maslonek K. A., Dykstra L. A., Lysle D. T., Assessment of the involvement of central nervous system and peripheral opioid receptors in the immunomodulatory effects of acute morphine treatment in rats. *Journal of Pharmacology and Experimental Therapeutics*, 1996; 276(2): 626-636.