Scholars LITERATURE

La Prensa Medica Argentina

Research Article

DOI: https://doi.org/10.47275/0032-745X-207
Volume 106 Issue 3

Risk Parameters of Consuming Smokeless Tobacco "Madgha": A Study in Aswan, Upper Egypt

Abdlrheem SS[1]*, Abdulkareem ES[2], El-Ebidi AM[3], Mahmoud HA[4], Abdelatif HA[5] and Ali SB[2]

[1]Department of Public Health and Community Medicine, Faculty of Medicine, Aswan University, Egypt
[2]Chest Department, Faculty of Medicine, Aswan University, Egypt
[3]Biochemistry Department, Faculty of Medicine, Aswan University, Egypt
[4]Internal Medicine Department, Faculty of Medicine, Aswan University, Egypt
[5]Clinical Pathology Department, Faculty of Medicine, Aswan University, Egypt

Abstract

Background: Smokeless tobacco (ST) use is a public practice in different places of the world. In Upper Egypt, Madgha is one of the chewable used tobacco consumed by individuals of different age groups. Being available and inexpensive has led to high consumption.

Objective: The current study aimed to examine the effect of Madgha on some hematological and biochemical parameters for Madgha users in Aswan.

Methods: We collected blood samples from 180 apparently healthy subjects, Madgha users (n=90) and their controls (n=90). Standard methods were used to examine the hematological and biochemical parameters.

Results: In a comparison of Madgha users with their controls, the results of hematological parameters showed a significant elevation in total white blood cell count, neutrophil and serum ESR, and a significant reduction in the percentage of lymphocytes and monocytes. Higher biochemical parameters like CRP, lipid contents, fasting blood glucose, and liver enzymes were observed in the blood samples of Madgha users. And a positive correlation between each of the white blood cell counts, platelet count, and CRP with the long duration of Madgha intake were reported in the study.

Conclusion: The study concluded that the consumption of Madgha might have harmed both hematological and biochemical parameters. Awareness is immensely needed to stop Madgha's usage and safeguard people's health in Aswan.

Keywords: Smokeless Tobacco; ST users; Madgha; Hematological and Biochemical parameters

Correspondence to: Shaimaa S Abdlrheem, Department of Public Health and Community Medicine, Faculty of Medicine, Aswan University, Egypt; Tel: 00201064031040; E-mail: dr_shimaasayed@yahoo.com

Citation: Abdlrheem SS, Abdulkareem ES, El-Ebidi AM, et al. (2020) Risk Parameters of Consuming Smokeless Tobacco "Madgha": A Study in Aswan, Upper Egypt. Prensa Med Argent, Volume 106:3. 207. DOI: https://doi.org/10.47275/0032-745X-207.

Received: February 11, 2020; **Accepted:** February 24, 2020; **Published:** March 02, 2020

Introduction

Over the years, the consumption of tobacco products remains an important public health issue. Nicotine is present in different tobacco forms, including smoking and smokeless tobacco (ST) [1]. Smokeless tobacco (ST) use is a public practice in different places of the world. Smokeless tobacco (ST) is used without combustion and this obliterates the hazard of direct exposure to the burned toxic compounds to the users and the individuals around them [2]. There have been significant differences in the structure and manufacturing of ST products, the two main forms of which ST comes in are snuff and chewing tobacco. Smokeless tobacco products are called Shammain Saudi Arabia, Saot in Sudan, Tombak in Yamen, and Madgha in Egypt [3].

In Upper Egypt, Madgha is one of the chewable used tobacco consumed by individuals of different age groups, formed of powdered dried tobacco leaves mixed with Atron″a stony salty material coming from Sudanese mountains″. Madghais sold in packs where each one composed of 12 pieces, each piece is 3 grams, where it is used by placing a piece between lower labile mucosa and gum for 10 min, the user spits out or swallows it [4]. Being available and inexpensive has led to high consumption. Madgha is highly prevalent among individuals with a low socioeconomic standard. They believe that the health hazards related to ST use are less than those related to smoked tobacco also they think ST has a curative effect on relieving pain and work-related stress [5].

Smokeless tobacco is easily an addictive substance as it has a high amount of nicotine as well as numerous cancer-causing substances compared to smoking tobacco [6]. Using any form of ST is an extraordinary health incident for the body organs which mainly linked with systemic illnesses depending on the way of Madgha consuming and its nature of the toxic products [2]. Earlier studies showed that ST has a durable association with a variety of oral, cardiovascular, respiratory, and renal diseases. ST seems to be influential in cellular and metabolic changes inside human bodies, particularly with long use duration [7,8]. By 2020, it is predicted that around 10 million deaths

may arise if the continuous use pattern of ST is kept on [9]. The effect of ST use on some hematologic and biochemical parameters has been discussed by the earlier studies [10-12]. Still, evidence shows that persons are not well informed about the risks of smokeless tobacco. The monitoring of these parameters for ST users is entirely required to guide them about ST health hazards. This study aims to minimize the trend of Madgha consuming in Upper Egypt.

The study aims to examine the effect of Madgha use on some hematological and biochemical parameters in Madgha users and to educate them about the health hazards of smokeless tobacco.

Methods

Design and duration

A case-control study design was conducted over two months from August to September 2017.

Study subject and sampling

The study subjects included healthy individuals aged 18-50 years old who came to Aswan university hospital as visitors to their relatives who had been admitted to inpatient departments.

The sample size was calculated using G power program version 3.1.9.2. in order to detect a significance difference in mean value of Erythrocyte Sedimentation Rate (ESR) between two independent groups under the study, and based on the following input parameters being one tailed, with the effect size of 0.49 as detected in Biswas S, et al. (2015) study [8] and with an alpha error of 0,05, power of 95%, and the allocation ratio between controls to cases was 1:1, therefore ninety subjects were included in each study group with total of 180 subjects. The required sample was collected by convenience sampling. The refusal rate was found to be 6.7%, (12 subjects refused to contribute as they did not want to go through any laboratory investigation), those subjects were not included in the study. The recruited studied persons were divided into two groups:

i) Madgha-users, people who use only ST (n=90), not any other form of tobacco, regularly >20 times per week for at least 3 consecutive years.

ii) Non-users (n=90), persons who do not use any type of tobacco. The controls were age-and sex-matched for Madgha users. People who were taking any regular medication, and those with a recent history of infection (within the last month) and people of any vascular, systemic and metabolic diseases, or immunocompromised conditions, alcoholics, and women in pregnancy or in hormonal replacement therapy were excluded from this study.

Data collection

Our data was collected through direct interviews, clinical examination and laboratory analyses. The direct interview was done to get complete demographic data, clinical history and information on Madgha consumption. After the study participants completed their data with the interviewers, clinical and anthropometric examinations were done for all subjects and blood pressure were measured twice in a sitting position, with 5 min apart.

Regarding laboratory analyses, some hematological and biochemical parameters were tested for ST-users and non-users, and then compared. To examine the studied parameters, venous blood samples (7 ml) were drawn from each subject between 7-10 a.m. under strict aseptic conditions and after 12 hours of overnight fasting. Each sample was divided into 3 parts; the first part (2 ml) was collected into tubes containing anticoagulant (K3 EDTA) used for CBC and differential count, the second part (2 ml) was collected into tubes containing (0.5 ml) 3.8% Sodium citrate anticoagulant used for ESR estimation, and the third part (3 ml) was allowed to clot in Wassermann tubes. Sera were obtained by centrifugation and divided into aliquots and used for liver enzymes, CRP, fasting blood glucose level, total lipid profile, serum creatinine, and urea estimation. Hematological parameters such as hemoglobin, red blood cells, and leukocyte total and differential count were done on (Cell Dyne 3700, Abbott diag. USA) automated blood cell counteract. ESR estimation by the Westergren method [13]. The biochemical parameters including fasting blood glucose level, total lipid profile, serum creatinine, urea, serum AST, ALT, ALP levels were measured on an automated chemistry analyzer(APX pentra 400, Horiba diag. France). CRP estimation by rapid latex agglutination kit (AVITEX- CRP) (Omega Diag. Ltd 2015).

Statistical analysis

Data were analyzed using SPSS V. 23.0 and the mean ± standard deviation (SD) were calculated for the selected hematologic and biochemical parameters. The student t-test was used to test the significance of the variance of the study parameters between Madgha users and controls. Qi square test and Pearson correlation were also used. In all cases, a P-value <0.05 was considered statistically significant.

Ethical consideration

The approval of the study was carried by the Ethical Review Committee of Aswan Faculty of Medicine before starting to work on the study. The study was in accord with the Second Declaration of Helsinki. We informed the study subjects with the details of the study procedures, and all subjects signed a written informed consent before their participation in the study. In case subjects were not able to read, an impartial witness had to be there at that time to explain accurately the content of the informed consent and sign it on the behalf of the subject in case of his\her approval.

Results

The baseline data of Madgha users and their controls are presented in table (1), there were statistically significant differences between the two groups regarding residence, education and working for cash in the last 12 months, more than half percent of Madgha consumers (55.5%) were from rural areas. Illiterate/Read and write subjects represented approximately forty percent of Madgha consumers (37.8%) and about one-third of them (33.3%) were not working for cash in the last 12 months.

In comparison to the control group, it was found that Madgha consumers experienced a significant elevation in blood pressure either systolic or diastolic (P< 0.05), while the rest of the explanatory variables in this table were not significant (P> 0.05) (Table 1).

From the data presented in table, the hematological profile of Madgha users differed from the controls group in the following: They had significantly higher total white cell count and ESR (Table 2). The results of the differential count showed that they had a significantly higher percentage of neutrophil while they had a significantly lower percentage of lymphocyte, monocyte in their blood. Moreover, the red cell count, hemoglobin level, hematocrit, PCV, MCV, MCH, MCHC, eosinophils and basophils percentages in their blood did not significantly differ from the control group.

The mean and standard deviation of the studied biochemical parameters for Madgha users and their controls are also presented in table (2). On the contrary to our controls, Madgha consumers had significantly higher levels of C reactive protein, total serum cholesterol, triglycerides, HDL, LDL, and higher fasting blood glucose levels. In addition to higher levels of serum AST and ALT. However, the other biochemical parameters as serum creatinine, serum urea, and alkaline phosphatase were not significantly different between Madgha consumers and their controls.

Nearly two-thirds of the users (64.4%) consumed Madgha for more than 6 years (Figure 1). And as shown in the figure there were 16 subjects consumed Madgha > 6 times per day (Figure 2).

Finding in the below table illustrated that there was a statistically significant positive correlation between duration of Madgha intake and each of the following: Total white cell count (P=0.001), platelet count (P= 0.008) and level of CRP in users' blood (P=0.0312). While there were no significant correlations between the duration of Madgha intake and the other assessed parameters in this table (Table 3).

Discussion

Smokeless tobacco is a deep-rooted human practice like smoking tobacco. The adverse effect of tobacco products on human systems has been well known for long-lasting years. We conducted the present study to find out whether Madgha caused unfavourable effects on selected hematological and biochemical parameters or not in a group of apparently healthy individuals.

Similar to the previous studies, the present study observed an increase in total leukocyte count among Madgha users, especially with the long use duration, such an increase might take in consideration the occurrence of tissues inflammation and damages, also the nicotine present in smokeless tobacco products speeds up the occurrence of leucocytosis [13-17]. The tobacco-specific nitrosamines present in ST (The most potent carcinogen among the known 28 carcinogens)

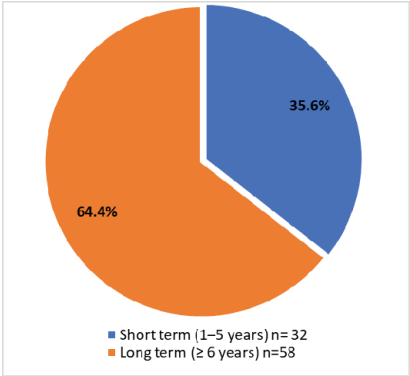

Figure 1: Madgha use duration (years).

Table 1: Baseline characteristic of the study population.

Characteristics	Madgha -users (n= 90)		Non -users (n= 90)		P value
	No.	%	No.	%	
Age in years: Mean ± SD (Range)	31.73 ± 7.44 (18 - 45)		31.47 ± 7.34 (19- 47)		0.194
Gender					
Male	60	66.7	62	68.9	0.122
Female	30	33.3	28	31.1	
Residence					
Urban	40	44.4	60	66.7	**0.011**
Rural	50	55.5	30	33.3	
Education					
Illiterate / Read and write	34	37.8	14	15.6	**0.001**
Basic	26	28.9	22	24.4	
Secondary or above	30	33.3	54	60.0	
Working for cash in the last 12 months:					
Yes	60	66.7	72	80.0	**0.041**
No	30	33.3	18	20.0	
Daily vegetable intake:					
Yes	12	13.3	18	20.0	0.094
No	78	86.7	72	80.0	
Body mass index BMI: •	27.6±2		29.7±1.9		0.071
Waist circumference (cm)••					
Male	0.89 ± 0.31		0.96 ± 0.05		0.064
Female	0.80 ± 0.12		0.82 ± 0.15		
Pulse (beats/ min)	65±23		67±24		0.521
Systolic blood pressure (mmHg): •••	132±9		121±8		**0.021**
Diastolic blood pressure (mmHg): •••	82±9		74±6		**0.011**
Madgha use duration (year):			-		-
Mean ± SD (years)	10.3±5.4				

Data presented are mean ± SD; NS: Non-Significant P < 0.05; chi square test can close; Student's t-test

• BMI was detected as body weight (kg) divided by body height (m) squared.

•• Waist circumference was measured at the midpoint between the lowest rib and the iliac crest.

••• Blood pressure was measured with a mercury Sphygmomanometer and a standard stethoscope.

Table 2: Effect of Madgha on hematological and biochemical parameters.

Parameters	Madgha -users (n= 90)	Non -users (n= 90)	P-value
Hematological parameters:			
Red cell Count ($\times 10^{12}$/L)	4.9 ± 0.3	4.5 ± 0.2	0.225 (NS)
Hemoglobin gm/dL	14.1 ± 2.0	13.1 ± 1.1	0.095 (NS)
Hematocrit (%)	44.6 ± 2.4	40.3 ± 3.0	0.054 (NS)
White cell count ($\times 10^{9}$/L)	6.3 ± 1.2	5.4 ± 0.3	**0.001**
Neutrophils (%)	68.5 ± 5.8	56.4 ± 5.3	**< 0.001**
Lymphocytes (%)	30.7 ± 5.4	38 ± 4.7	**< 0.001**
Monocytes (%)	1.8 ±1.0	2.9 ± 1.3	**< 0.001**
Eosinophils (%)	1.9 ± 1.1	1.7 ± 0.8	0.991 (NS)
Basophils (%)	0.6 + 0.6	0.6 + 1.0	0.231 (NS)
Platelet count ($\times 10^{9}$/L)	295 ± 54	279 ± 42	0.092 (NS)
ESR (mm/ hr) first hour	13.5±3.6	11.1±2.7	**0.022**
PCV (%)	40.44 ± 5.66	41.46 ± 4.88	0.124 (NS)
MCV (fl)	81.97 ± 7.30	82.63 ± 4.70	0.333 (NS)
MCH (pg)	28.31 ± 2.64	27.83 ± 4.30	0.266 (NS)
MCHC (%)	33.70 ± 0.70	33.51 ± 0.66	0.211(NS)
Biochemical parameters:			
CRP (mg/l)	2.9±0.42	0.91±0.31	**0.041**
Fasting blood glucose (mg/dl)	98±19	82±8	**0.013**
Total cholesterol (mg/dl)	200±33	179±35	**<0.001**
Triglycerides (mg/dl)	175±50	118±52	**<0.001**
HDL cholesterol (mg/dl)	38±4	45±7	**<0.001**
LDL cholesterol (mg/dl)	131±29	107±28	**<0.001**
Serum creatinine (mg/dl)	1.0 ± 0.2	0.9 ± 0.1	0.076 (NS)
Serum urea (mg/dl)	31.4 ± 6.8	28.8 ± 4.8	0.093 (NS)
AST (U/L)	21.4 ± 5.0	31.4 ± 7.1	**<0.001**
ALT (U/L)	20.8 ± 12.0	33.5 ± 10.1	**<0.001**
Alkaline phosphatase (U/L)	73.5 ± 18.6	69.7 ± 22.9	0.155 (NS)

Values represented in the table are the mean ± SD; Student's t-test; NS: Non-Significant; HDL: High-density lipoprotein. LDL: Low-density lipoprotein.

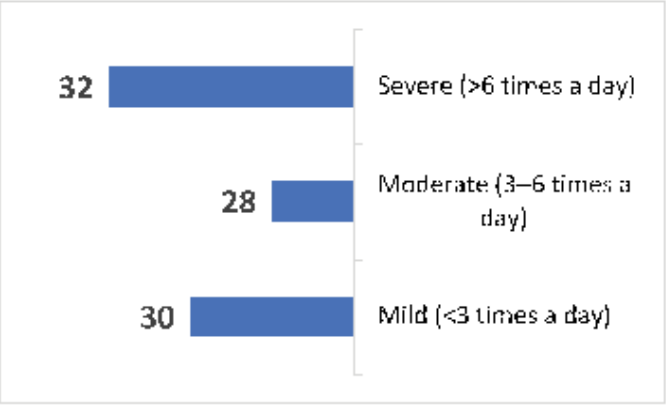

Figure 2: Daily Madgha intake among users (n=90).

altered the metabolic state gradually leading to an increase in the tissue inflammation, apoptosis, and different blood cell damage.

Like what detected in Mukherjee R, et al. (2013) study, ST users had higher levels of neutrophils and lower levels of lymphocytes and monocytes in their blood, the observed increase in neutrophil count indicated the initiation of the inflammatory reactions [15].

C-reactive protein (CRP) is one of the primary acute-phase proteins promptly elevated in response to human tissue inflammations.

Table 3: Pearson Correlation between duration of Madgha intake and some parameters.

Variable	rho	P-value
RBCs Count (10^{12}/L)	0.083	0.063 (NS)
Hemoglobin gm/dL	-0.177	0.311 (NS)
WBCs (10^{9}/L)	0.712	**0.001**
Platelet Count (10^{9}/L)	0.477	**0.008**
PCV (%)	-0.073	0.841 (NS)
MCV (fl)	-0.062	0.743 (NS)
MCH (pg)	-0.271	0.062 (NS)
MCHC (%)	-0.221	0.071 (NS)
CRP (mg/l)	0.526	**0.0312**
Fasting Blood Glucose (mg/dL)	-0.161	0.352 (NS)
Total cholesterol (mg/dl)	0.331	0.075 (NS)
Triglycerides (mg/dl)	0.531	0.055 (NS)
AST (U/L)	0.322	0.062 (NS)
ALT (U/L)	0.431	0.078 (NS)
ALP (U/L)	-0.158	0.361 (NS)
Serum Urea (mg/dl)	0.546	0.065 (NS)
Serum Creatinine (mg/dl)	0.246	0.152 (NS)

NS: Non-Significant.

A high-level of CRP refers to the occurrence of an acute infection. It is measured to monitor the disease progress [18]. Our study agrees with other studies that reported ST is accompanied by higher CRP, and other inflammatory markers [19,20].

The undesirable effects of Madgha intake on lipid profile were seen among our ST users, the total serum cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol levels were found high in the ST users group compared to the non-users group. Studies on the use of Gutka conducted among the Indian population showed a similar negative effect on serum cholesterol and fat metabolism [21]. Nicotine released from non-smoked tobacco consumption stimulates catecholamine secretion that may have raised blood cholesterol levels and increased the risk of expanding lipid-related disorders [22].

A significant increase in the mean value of fasting blood glucose levels was noted among the user participants, and this result is accepted by Jaganmohan P and Phaninanatha A (2011) study [21]. Our findings supported the fact that nicotine in tobacco may contribute in reducing insulin sensitivity in human tissue [23,24].

Smokeless tobacco products have high fatal systemic toxicity [8]. So, the prevention of ST lowers many causes of non-communicable morbidity and mortality.

Study limitations

The small sample size of the current study may have had an impact on the clarity of the results, so the results could not be generalized to the total population of the study site. No measurement of the quantity of nicotine or its metabolite was done for the users due to the unavailability of lab resources at the time of the study.

Conclusion

The consumption of Madgha might have harmed both hematological (viz. increase in white cell count, neutrophil percentages, ESR, and a decrease in the percentage of lymphocytes and monocytes) and biochemical parameters (viz. increase in CRP levels, total lipid profile, and blood glucose levels). A significant positive correlation was detected between the duration of Madgha intake and each of the following parameters: Total white cell count, platelet count, and level

of CRP. Awareness is immensely needed to stop Madgha's usage and safeguard people's health in Aswan. Our findings might help in the conduction of an awareness campaign that covers the health hazards of ST products to the users in Upper Egypt, who consume Madgha as an inexpensive alternative to tobacco smoking. Long-term follow-up studies are required with detailed measures of tobacco use to determine whether Madgha is a risk factor for most of non-communicable disorders.

References

1. Borland R, Cooper J, McNeill A, O'Connor R, Cummings KM (2011) Trends in beliefs about the harmfulness and use of stop-smoking medications and smokeless tobacco products among cigarettes smokers: Findings from the ITC four-country survey. Harm Reduct 8: 21.https://doi.org/10.1186/1477-7517-8-21
2. Jensen K, Nizamutdinov D, Guerrier M, Afroze S, Dostal D, et al. (2012) General mechanisms of nicotine-induced fibrogenesis. FASEB J 26: 4778-4487.https://doi.org/10.1096/fj.12-206458
3. Leon ME, Lugo A, Boffetta P, Gilmore A, Ross H, et al.(2016) Smokeless tobacco use in Sweden and other 17 European countries. Eur J Public Health 26: 817-821.https://doi.org/10.1093/eurpub/ckw032
4. Ali SB, Eid RM (2017) Effect of Smokeless Tobacco (Madgha) on Spirometry. Int J Adv Biomed 2: 35-37.
5. World Health Organization (2009) Global Adult Tobacco Survey (GATS) Egypt Country Report.
6. Sharma P, Murthy P, Shivhare P (2015) Nicotine quantity and packaging disclosure in smoked and smokeless tobacco products in India. Indian J Pharmacal 47: 440-443. https://dx.doi.org/10.4103/0253-7613.161273
7. Sinha DN, Palipudi KM, Gupta PC, Singhal S, Ramasundarahettige C, et al. (2014) Smokeless tobacco use: A meta-analysis of risk and attributable mortality estimates for India. Indian J Cancer 51: S73-S77.
8. Biswas S, Manna K, Das U, Khan A, Pradhan A, et al. (2015) Smokeless tobacco consumption impedes metabolic, cellular, apoptotic and systemic stress pattern: A study on Government employees in Kolkata. India Sci Rep 5:18284.https://doi.org/10.1038/srep18284
9. Hossain MS, Kypri K, Rahman B, Arslan I, Akter S, et al. (2014) Prevalence and correlates of smokeless tobacco consumption among married women in rural Bangladesh. PLoS One 9: e84470.https://doi.org/10.1371/journal.pone.0084470
10. Khan MM, Tandon SN, Khan MT, Pandey US (2008) A Comparative study of cigarette and bidi smoking on total red blood cell count, packed cell volume and hemoglobin concentration. J Biol Chem Res 25: 17-20.
11. Asif M, Karim S, Umar Z, Malik A, Ismail T, et al. (2013) Effect of cigarette smoking based on hematological parameters: comparison between male smokers and nonsmokers. Turk J Biochem 38: 75-80.https://doi.org/10.5505/tjb.2013.49369
12. Jyothirmayi B, Kaviarasi S, William E (2013) Study of glycated hemoglobin in chronic cigarette smokers. IJPCR 5: 4-6.
13. Bain B, Bates I, Laffan M, Lewis S (2016) Dacie and Lewis Practical Haematology. (12thedtn), Elsevier, United Kingdom.
14. Yasmin S, Stuti S, Rastogi N, Das J (2007) Negative impact of gutkha on certain blood parameters of Swiss mice. Bulletin PureAppl Sci 26: 75-79.
15. Mukherjee R, Chatterjee A (2013) Assessment of the effects of smoking and consuming Gutka on selected hematological and biochemical parameters: a study on healthy adult males of Hazaribag, Jharkhand. Int J Pharm Chem Biol Sci 3: 1172-1178.
16. Shukla AK, Khaitan T, Gupta P, Naik SR (2019) Smokeless tobacco and its adverse effects on hematological parameters: A cross-sectional study. Adv Prev Med.https://doi.org/10.1155/2019/3182946
17. Shenwai MR, Aundhakar NV (2012) Effect of cigarette smoking on various hematological parameters in young male smokers. Indian J Basic Appl Med Res 5: 386-392.
18. Tonstad S, Cowan JL (2009) C-reactive protein as a predictor of disease insmokers and former smokers: a review. Int J Clin Pract 63: 1634-1641.https://doi.org/10.1111/j.1742-1241.2009.02179.x
19. Ouchi N, Kihara S, Funahashi T (2003) Reciprocal association of C-reactive protein with adiponectin in the bloodstream and adipose tissue. Circulation 107: 671-674. https://doi.org/10.1161/01.CIR.0000055188.83694.B3
20. Black S, Kushner I, Samols D (2004) C-reactive protein. J Biol Chem 279: 48487-48490.https://doi.org/10.1074/jbc.r400025200
21. Jaganmohan P, Phaninanatha A (2011) Studies on changes in hematological and biochemical parameters in smokeless tobacco (Gutka) chewing auto drivers in Nellore district of Andhra Pradesh, India. J Nat Appl Sci 3: 106-107.https://doi.org/10.31018/jans.v3i1.165
22. Balhara YP (2012) Tobacco and metabolic syndrome. Indian J Endocrinol Metab 16: 81-87.https://dx.doi.org/10.4103/2230-8210.91197
23. Eliasson B, Mero N, Taskinen MR, Smith U (1997) The insulin resistance syndrome and postprandial lipid intolerance in smokers. Atherosclerosis 129: 79-88.https://doi.org/10.1016/S0021-9150(96)06028-5
24. Morgan TM, Crawford L, Stoller A, Toth D, Yeo KT, et al. (2004) Acute effects of nicotine on serum glucose insulin growth hormone and cortisol in healthy smokers. Metabolism 53: 578-582.https://doi.org/10.1016/j.metabol.2003.12.006