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# A COMPARATIVE STUDY OF LIPID PROFILE, ATHEROGENIC INDEX OF PLASMA (AIP) AND LIPID ACCUMULATION PRODUCT (LAP) IN DIABETIC NON-SMOKERS AND SMOKERS IN JEDDAH, SAUDI ARABIA

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**ABSTRACT**
Cigarette smoking is a well-known risk factor in many diseases, including various kinds of cancer and cardiovascular disease (CVD).Various studies have also reported the unfavorable effects of smoking for diabetes mellitus (DM). Smoking increases the risk of developing diabetes, alters the lipid profile and aggravates the micro- and macro-vascular complications of DM. Atherogenic index of plasma (AIP) is found to be useful marker in patients with diabetes as it increases the risk of cardiovascular disease. Lipid accumulation product (LAP) is a novel biomarker of central lipid accumulation related to risk of diabetes and CVD. The present study aimed to compare the fasting serum glucose (FSG), glycated hemoglobin (HbA1c), lipid profile, AIP and LAP in diabetic non-smokers and diabetic smokers. Mean FSG and HbA1c levels were significantly higher in diabetic patient who are smokers compared to diabetic patients who are non-smokers. Our study showed the higher incidence of poor glycemic control as reflected by HbA1c ≥ 7% among diabetics with smoking in comparison with those non-smokers diabetics. There was significant increase in total cholesterol (TC) ($p<0.01$), triglycerides (TG) ($p<0.01$), AIP ($p<0.001$) and LAP ($p<0.001$) and significant decrease in HDL ($p<0.05$) in diabetic smokers as compared to diabetic non-smokers. Smokers had a wider waist circumference and a proatherogenic lipid profile. Pearson's correlation study revealed a significant positive correlation between FSG and AIP ($r = 0.29$, $p<0.01$) and LAP ($r =0.40$, $p<0.001$). In addition, we found significant positive correlations between AIP and LAP with HbA1c ($r=0.34$, $p =0.004$ and $r=0.57$, $p<0.001$, respectively). It is concluded that both AIP and LAP could be used as simple parameters to early assessment of risk for development of atherosclerosis in diabetic smokers.

**KEYWORDS:** Smoking, diabetes mellitus, dyslipidemia, AIP, LAP, cardiovascular disease.

## INTRODUCTION

Smoking is one of the most potent and prevalent addictive habits, influencing behavior of human beings. Smoking is now increasing rapidly through the developing world and is one of the biggest threats to current and future world health. Smoking, a global escalating public health problem, is estimated to kill 6 million people, causes hundreds of billions of dollars of economic damage worldwide each year[1]. It is reported that a smoker's life expectancy is, on average, 13 years shorter than a nonsmoker's life expectancy [2]. Cigarette smoking is now acknowledged to be one of the leading causes of preventable morbidity and mortality and is one of the largest single preventable causes of ill health particularly associated with/ of coronary artery diseases. It is also found that smokers are at risk of coronary heart disease and stroke at a rate of about 2-3 times higher than non-smokers[3,4]. Cigarette smoking is a well-known risk factor in many diseases, including various kinds of cancer and cardiovascular disease[5,6]. Several studies have also reported the unfavorable effects of smoking for diabetes. Smoking increases the risk of developing diabetes, and aggravates the micro- and macro-vascular complications of diabetes mellitus. Smoking is associated with insulin resistance, inflammation and dyslipidemia. Although smoking is known to decrease body weight, it is associated with central obesity[7,8]. Smoking also increases inflammation and oxidative stress [9], to directly damage β cell function[10] and to impair endothelial function[11]. Smoking is a major risk factor for atherosclerosis and coronary artery disease. Smoking is also recognized as a major risk factor for the development of ischaemic heart disease may lead to alter the normal plasma lipoprotein pattern. Incidence of developing CHD is directly related to the number of cigarette smoked [12].Sudden death is 2-4 times more often in heavy smokers than nonsmokers[13].

The prevalence of smoking in Saudi Arabia ranges from 2.4-52.3%. Among university students, the prevalence of smoking ranges from 2.4-37%, and among adults from 11.6-52.3%. In elderly people, the prevalence of smoking is 25%. The number of Saudi smokers is expected to rise from the current 5 million to 10 million by 2020, according to the Saudi Diabetes and Endocrine Association in the Eastern province. It is reported very recently that the number of men and women who smoke in the Kingdom is more than 9 million, mainly between the ages of 17 and 40 [14-16]. Obesity is fast turning out to be a major cause of concern for the Kingdom with seven out of 10 Saudis suffering from obesity, and 37 percent of Saudi women facing problems related to overweight[17]. Overweight and obesity affect more than 75% of the total population in Saudi Arabia. Almost all age groups are affected in general and adults particularly[18]. With the obesity epidemic on the rise, research on obesity has intensified. Obesity is an important risk factor for cardiovascular and other diseases and the high prevalence

of obesity is an increasing worldwide problem; in particular, the rapid increase in abdominal obesity might lead to a rise of obesity-associated morbidity and mortality [19,20]. Commonly, obesity is defined as an increased BMI >30. For long period BMI was considered to be an indicator of metabolic syndrome and cardiovascular risk. With the introduction of newer index like 'Lipid Accumulation Product' (LAP) and BMI's failure to differentiate adipose mass from muscle mass – the credibility of BMI has been questioned [21]. Central obesity is the most prevalent manifestation of metabolic syndrome. Obesity is measured mainly with BMI but it does not measure central adiposity whereas indices such as waist circumference (WC) are known to be better index for central adiposity or visceral adiposity [22,23]. According to various studies researchers has explored another index known as LAP which is based on a combination of WC and fasting triglyceride.

LAP is known to be a good marker of lipid accumulation in ectopic sites like the liver, skeletal system and in the beta cells of pancreas. Ectopic lipid accumulation eventually leads to insulin resistance and hence LAP can be a better marker to diagnose metabolic syndrome and associated morbidities like type 2 DM in obese subjects [24,25]. The LAP has been shown to be a better discriminator for diabetes than BMI[24,26] and to be associated with risk of cardiovascular disease[26.27]. LAP combines WC and TG levels, reflecting both the anatomic and physiological changes associated with lipid over accumulation. LAP was closely associated with CVD, diabetes and metabolic syndrome and outperformed BMI for identifying these diseases[28-30]. LAP is based on a combination of two measurements – one is WC, a measure of truncal fat that includes the visceral (intra-abdominal) depot and the other is the fasting concentration of triglycerides (TG) which measures circulating fat. LAP for men is calculated using the formula [24,25,29,30]:

LAP = [waist circumference (cm)- 65] x [triglycerides concentration (mmol/l)]

It has been demonstrated that the atherogenic index of plasma (AIP), a new indicator of atherogenity, significantly increases with atherogenic risk[31]. Dobiasova and Frohlic[32,33] defined the atherogenic index as the logarithm of the ratio of plasma triglyceride to HDL-c levels. The association of TGs and HDL-c in this simple ratio theoretically reflects the balance between risk and protective lipoprotein forces, and both TGs and HDL-c are widely measured and available. It is suggested that AIP values of <0.1 are related to low cardiovascular risk, between 0.1 and 0.24 are related to moderate cardiovascular risk, and >0.24 are related to high cardiovascular risk[34-36]. Different investigators concluded that AIP has a better prediction of coronary artery disease than individual lipids, and / or TC/HDL-c, LDL-c/HDL-c ratios. AIP which can easily be calculated from standard lipid profile can act as an adjunct that significantly adds predictive value for cardiovascular events beyond that of the individual lipid parameters [35-37]. According to some authors, calculating AIP can be more reliable in predicting the risk for development of atherosclerosis in diabetes mellitus patients. This parameter is easy to calculate every time a lipid profile is asked for, so that the cardiovascular risk of the patient can be assessed [32,34,35,36,37].

The present study was conducted (1) to determine and compare the levels of fasting serum glucose (FSG), glycated hemoglobin (HbA1c), fasting lipid profile, AIP and LAP in diabetic smokers and diabetic non-smokers and (2) to correlate the AIP and LAP with FSG and HbA1c.

## MATERIALS & METHODS

The present study was carried out on total 85 male type 2 diabetes mellitus (T2 DM) patients and they were grouped into, group I consisting of 40 patients who are non-smokers and group II consists of 45 patients who are cigarette smokers. Study subjects were recruited from volunteers attending King Abdulaziz University health clinic, Jeddah (Saudi Arabia) with average history of diabetes mellitus from last 5-6 years. The subjects who have smoked more than 20 cigarettes per day for at least 5 yrs or more were included in the study. Patients with history of alcoholism or drug use were excluded from the study. Informed consent was sought and obtained from individuals before enrollment into the study. The study protocol was approved by institutional ethical committee. After taking a brief medical history, a detailed physical examination was conducted for all participants by a physician and the data was recorded in a predesigned questionnaire. The height and weight were measured according to standard protocols. The body mass index (BMI) was calculated as weight in kilograms divided by height in squared meters. Waist circumference (WC) was obtained with a plastic, flexible, inelastic measuring tape in the middle point between the lower costal rib and the iliac crest in a perpendicular plane, with patient standing in both feet, approximately 20 cm apart, and with both arms hanging freely.

Venous blood samples were collected from group I and group II patients after at least 10 hours fasting into centrifuge tubes. Serum was separated by centrifugation at 3000 rpm for 15 minutes. The sera were analyzed for glycated hemoglobin (HbA1c), fasting serum glucose (FSG), total cholesterol (TC), triglycerides (TG), and high density lipoprotein cholesterol (HDL-c) using an auto analyzer (Roche Modular P-800, Germany). Serum low density lipoprotein cholesterol (LDL-c) was calculated by Friedewald's formula shown below [38,39]:

LDL-c = TC – [(HDL-c) + (TG/5)]

AIP was calculated using formula [34,35,38,39],

AIP = log (TG / HDL-c)

LAP for men was calculated using the formula [24,25,29,30]:

LAP = [waist circumference (cm) - 65] x [triglycerides concentration (mmol/l)]

The results were reported as mean ± SD. The statistical analysis was done by SPSS version 17.0 software. The results were evaluated using the independent sample't' test and the Pearson's correlation coefficient test. The results were considered significant when $p < 0.05$.

## RESULTS

The study sample consisted of 85 males. We divided our study group into 40 non-smokers (group I) and 45 smokers

(group II). The mean age of non-smokers (57.87± 6.28 years) and smokers (58.42 ±7.13 years) did not significantly differ between groups. Both groups did not differ in body mass index (BMI), but smokers had a wider waist circumference, showing higher amount of visceral fat smokers. The smokers had a proatherogenic lipid profile (higher TC, TG, AIP, LAP and lower HDL-c). Data are presented in Table 1.

**TABLE 1:** Comparison of lipid profile, AIP and LAP between diabetic smokers and non-smokers

| Parameters | Diabetic non-smokers (Gr. I) (n = 40) | Diabetic smokers (Gr. II) (n = 45) | p-value |
|---|---|---|---|
| Age (y) | 57.87 ± 6.28 | 58.42 ± 7.13 | |
| BMI (kg/m$^2$) | 29.51 ± 1.86 | 30.29 ± 2.05 | |
| Waist circumference (cm) | 95.42 ± 7.61 | 98.85 ± 8.35 | < 0.05 |
| Duration of diabetes (y) | 5.12 ± 3.26 | 5.38 ± 4.05 | |
| Fasting Serum Glucose (mg/dl) | 180.36 ± 60.71 | 196.53 ± 69.22 | < 0.05 |
| HbA1c ( % ) | 8.85 ± 1.92 | 9.77 ± 2.39 | < 0.01 |
| Total cholesterol ( mg/dl ) | 202.63 ± 44.31 | 242.47 ± 54.50 | < 0.01 |
| Triglycerides ( mg/dl ) | 164.02 ± 21.82 | 191.61 ± 21.83 | < 0.01 |
| HDL-c ( mg/dl ) | 44.57 ± 8.34 | 39.89 ± 6.27 | < 0.05 |
| LDL-c ( mg/dl ) | 121.43 ± 20.05 | 134.24 ± 21.12 | |
| Atherogenic index of plasma (AIP) | 0.51 ± 0.063 | 0.68 ± 0.058 | < 0.001 |
| Lipid accumulation product (LAP) (cm.mmol/l) | 52.92 ± 8.76 | 72.36 ± 10.31 | <0.001 |

**TABLE 2 :** Pearson correlation coefficient (r) for AIP and LAP with FSG and HbA1c in diabetic smokers

| Parameters | HbA1c | FSG |
|---|---|---|
| AIP | r = 0.34 , p < 0.004 | r = 0.29, p < 0.01 |
| LAP | r = 0.57, p < 0.001 | r = 0.40, p < 0.001 |

As depicted in the Table 1, there was significant increase in WC, FSG, HbA1c, TC, TG, AIP and LAP and significant decrease in HDL-c in group II (smokers) patients compared to group I (non-smokers) patients. The mean ± SD of AIP were 0.68 ±0.058 and 0.51 ±0.063 in diabetic smokers and non-smokers respectively. According to the category that mentioned before, both smokers and non-smokers groups of the participants were in increased risk of CVD. The risk of CVD for smokers group is higher than for non-smokers group.

The mean ± SD of LAP were 72.36±10.31 and 52.92 ±8.76 in diabetic smokers and non-smokers respectively. The mean LAP of smoker patients is significantly higher than that of non-smoker patients. Thus the risk of CVD for smoker patients is higher than that of non-smoker patients.

Table 2 shows the strengths and directions of association between AIP and LAP with FSG and HbA1c in diabetic smoker patients. The results revealed a mild, positive and significant correlation between FSG (r = 0.40), HbA1c (r = 0.57) and LAP. A weak, positive and statistically significant correlation was obtained between FSG (r = 0.29), HbA1c (r= 0.34) and AIP.

## DISCUSSION

Smoking has been shown to be a significant risk factor for all-cause mortality, and for mortality due to CVD and coronary heart disease (CHD) in diabetics. Cigarette smoking is associated with higher serum levels of cholesterol and lower plasma concentrations of HDL-c; also smokers have higher plasma triglyceride concentrations than nonsmokers and smoking impairs lipoprotein metabolism, and reduces the distensibility of blood vessel walls [40]. In our study, we have found a significant increase in TC, TG, LDL-c, FSG and HbA1c and a significant decrease in HDL-c in diabetic smokers compared to diabetic non-smokers (Table 1). It was also found that smokers had a higher percentage of uncontrolled HbA1c (HbA1c ≥ 7%) than that of the non-smokers. This was in accordance with the studies of different authors [29,41,42,43] in which it was found that the patients with type 2 diabetes who were smokers had a level of HbA1c higher than non-smokers. Several studies have demonstrated that the smokers were more likely to have uncontrolled diabetes more than the non-smokers [41,44,45]. The results of our study also revealed that smokers had a pro-atherogenic lipid profile (higher TC, TG, AIP and lower HDL-c). Previous studies showed that cigarette smoking was associated with a more atherogenic lipid profile [46,47]. The study of Gepner et al.[47] revealed that smoking cessation improved HDL-c, total HDL, and large HDL particle concentrations, despite weight gain, especially in women. Increases in HDL may mediate part of the reduced cardiovascular disease risk observed after smoking cessation. In population-based studies, a 1-mg/dl increase in HDL-c has been associated with a 2% to 3% decrease in CVD events and the results of a large, prospective study revealed smoking abstinence could reduce CVD events by 4% to 6% over a decade [47]. The clinicians may be encouraged by this important finding to emphasize abstinence even in light smokers. A number of experimental and clinical studies suggest that smoking decreases insulin sensitivity, and consequently results in the disorders of glucose and lipid metabolism such as hyperglycemia and dyslipidemia including low HDL-c and postprandial lipid intolerance. Particular in diabetic patients, it is clear that cigarette smoking worsens the metabolic control. Studies have shown that nicotine not only has a direct toxic effect on the pancreatic β cells but is also associated with the development of insulin resistance by inducing a reduction of insulin resistance and negatively affecting insulin action [48- 52]. Thus, in diabetes care, smoking cessation is important for glycemic control

and limiting the development of diabetic complications. However, smoking prevention and smoking cessation may not be emphasized enough in diabetic clinics. Thus, educating patients on the importance of not smoking and engaging in smoking cessation programs are important strategies for the management of diabetes.

In conditions of sustained hyperglycemia, such as in diabetes mellitus, the proportions hemoglobin that is glycosylated increases substantially. Hyperglycemia causes increased activity of hepatic lipase that leads to increased clearance of HDL while impaired catabolism of VLDL causes decreased formation of HDL. Thus the HDL levels decrease in type 2 diabetes. Severity of dyslipidemia increases in patients with higher HbA1c value. As elevated HbA1c and dyslipidemia are independent risk factors of CVD, diabetic patients with elevated HbA1c and dyslipidemia can be considered as very high risk group for CVD. Improving glycemic control can substantially reduce the risk of cardiovascular events in diabetics. It has been estimated that reducing the HbA1c level by 0.2% could lower the mortality by 10% [53].

In our study lipid profile abnormalities were more severe in smokers compared to nonsmokers. The mechanisms responsible are not clearly elucidated; the triglyceride/ high-density lipoprotein abnormalities have recently been suggested to be related to insulin resistance [8,42]. In fact, it has been proposed that insulin resistance is a potential key link between cigarette smoke and cardiovascular disease. In diabetic smokers, cigarette smoke contains many oxidizing substances which enhance the free radical levels and also free radical induced oxidation of LDL[54,55]. Cigarette smoke extract exposure may also decrease the plasma activity of paraoxonase, an enzyme that protects against LDL oxidation[8,56,57]. Thus smoking has added effect in the development of atherosclersosis in diabetic smokers, when compared to diabetic nonsmokers. Different experimental and clinical studies suggest that smoking decreases insulin sensitivity, and consequently results in the disorders of glucose and lipid metabolism such as hyperglycemia and dyslipidemia including low HDL-c and postprandial lipid intolerance. Particularly in diabetic patients, it is clear that cigarette smoking worsens the metabolic control. A large insulin dose is needed to achieve similar metabolic control in smoking patients as in non-smokers [40,49,58].

Because of the aging of the population and an increasing prevalence of obesity and sedentary life habits in the Kingdom, the prevalence of diabetes is increasing. Obesity is a risk factor for coronary artery disease (CAD) through its effects on glycemia, blood pressure, triglycerides and high-density lipid (HDL) cholesterol levels and inflammatory cytokines. Excess waist circumference (WC) is a simple and widely used indicator of abdominal obesity and the risk of cardiovascular disease (CVD) [59-61]. According to the study of Li *et al*. [62], even a small increase in WC is predictive of a substantial increase in the risk for CVD in East Asian countries. Our data indicates that type 2 diabetes patients who smoke have significantly higher central adiposity, according to WC values, than non-smokers. Larger WC in smokers reflects accumulation of visceral tissue in these patients. In concordance with our finding, it has been published that smokers have a higher tendency for accumulating visceral tissue[43,63]. Shimokata *et al*.[64] previously reported positive association between smoking and abdominal obesity, regardless of whether BMI values were low. Seidell *et al*.[65] state that smoking does not cause BMI increase, but that heavy smoking leads to higher WC. The results of Yun *et al*. [43] showed that current smokers had the highest WC and visceral fat thickness (VFT) values, followed by ex-smokers, and then never-smokers in type 2 diabetic patients. Results of previous investigators[66,67] show that smokers with abdominal obesity are at high absolute risk of CAD. Lifestyle intervention with exercise was reported to reduce abdominal obesity and improve coronary heart disease risk factors [68]. Smoking cessation is a priority in primary and secondary prevention of coronary events. Thus to maximize the absolute risk reduction, smoking cessation should be achieved avoiding an increase in abdominal adiposity. Central obesity is more strongly associated with CVD risk than general obesity[69,70]. The deposition of adipose tissue is associated with systemic inflammation which has a direct effect on CVD risk. Therefore, increments in central obesity have a more detrimental effect on CVD risk compared with increments in general obesity. The measurement of WC should be considered for incorporation into the clinical assessment of CVD risk. Treatments of well-established CVD risk factors coupled with reducing overweight and obesity through lifestyle modifications would be an advisable goal in the primary prevention of CVD. It is equally important to maintain a healthy weight and to prevent central or abdominal obesity concurrently. Previous studies have shown a positive association between lipid levels and measures of adiposity. Furthermore, poor glycemic control is strongly associated with abnormalities in lipid levels. These results, along with high prevalence of overweight and obesity, suggest that diabetic patients should be counselled regarding their diets, physical activity and life habits. These patients also need frequent monitoring to ensure optimal lipid level control. Awareness should be encouraged among the diabetic smokers by giving diabetes self-management sessions and to stress upon the benefits of self-care, regular diabetes screening, especially diabetic patients with a family history of obesity and diabetes. Weight management is a necessary therapeutic task for most obese type 2 diabetic patients, which helps in avoiding complications due to the diabetes mellitus.

Universally, the atherogenic index of plasma (AIP) calculated as log (TG/HDL-c) has been used by some practitioners as a significant predictor of atherosclerosis [32,34]. Clinical studies have shown that AIP predicts cardiovascular risk. AIP is an easily available cardiovascular risk marker and a useful measure of response to treatment: AIP < 0.11 → low risk; AIP 0.11-0.24 → intermediate risks; AIP > 0.24 → increased risk. The AIP of diabetic smokers in this study was observed to be significantly increased (0.68 ±0.058) when compared with the diabetic non-smokers (0.51 ±0.063). Earlier studies have indicated the role of AIP as early predictor of risk for development of atherosclerosis in diabetic patients. In line with earlier studies, we also observed significant increase in AIP in diabetic patients, which is further enhanced in smokers as compared to diabetic non-smokers (Table 1). The results of this study are in

accordance with different authors who observed higher values of AIP in smokers compared to diabetic non-smokers [29,42,43,50]. Different authors concluded that AIP has a better prediction of CAD than triglycerides or high density lipoprotein alone. This is because AIP is positively correlated with fractional esterification rate of HDL (FERHDL), and also inversely correlated with LDL particle size. Because FERHDL predicts particle size in HDL and LDL, which in turn predicts the risk of coronary heart disease, the simultaneous use of TG and HDL-c as AIP is useful in predicting plasma atherogenicity. This ratio has a strong predictor of myocardial infraction. Atherogenic Index of Plasma provides information about the atherogenicity of plasma and quantifies the response of therapeutic intervention. Also AIP correlates inversely with insulin sensitivity measurement[32,34,36]. Diabetic smokers in this study exhibited significant lipid abnormalities with increased AIP. We have observed a significant positive correlation between FSG and AIP ($r=0.29$, $p< 0.01$) and between HbA1c and AIP ($r=0.34$, $p < 0.004$) in diabetic smokers (Table 2). These values are comparable with the results of different investigators [42,50,71]. The results suggest that the AIP could be used as a simple parameter to early assessment of risk for development of atherosclerosis in diabetic smokers. In diabetic smokers, prolonged hyperglycemia and insulin resistance increases the lipogenesis and increases the TG concentrations and decreases the HDL-c and thus may contributing for elevation of AIP levels in diabetic smokers. Previous studies have indicated the role of cigarette smoke in attenuation of insulin resistance and exact mechanism is not clear [8,42,58].Thus in diabetic persons with poor glycemic control and cigarette smoking has got elevated risk for the development of atherosclerosis and coronary artery disease. Published results suggest that association of CHD risk and glycemic control can be reflected by the log (TG/HDL) ratio apart from individual lipid parameters. Recent studies have supported the usefulness of AIP value to predict CVD risk and shown it to be a reliable predictor of CHD [71,72].The presence of lipid abnormalities renders the diabetic patients more prone to cardiovascular risk and cerebrovascular diseases; therefore, it is essential that diabetes patients and caregiver work together to chalk out appropriate interventions for the management of dyslipidemia. In addition, previous studies have provided evidence that the cost of diabetes with complications produces almost double burden compared to the presence of diabetes alone [73]. Better management of dyslipidemia can prove helpful in reducing the healthcare burden.

Among the lifestyle-related factors, smoking makes the largest contribution to the absolute risk of macrovascular complications for people with diabetes. Studies of individuals with diabetes consistently demonstrate that smokers have a heightened risk of cardiovascular disease, premature death and increased rate of microvascular complications of diabetes. Cigarette smoking is a leading risk factor for CVD. Patients with diabetes who are smokers are doubly at risk. Some authors describe cardiovascular disease and diabetes as two sides of the same coin. Unfortunately, many patients continue to smoke despite having diabetes, for these patients, the benefits that can be derived from modifying other risk factors are mitigated.

LAP is based on a combination of two safe and inexpensive measurements, WC and serum triglycerides (TG). LAP is an ideal screening tool derived from a combination of clinical parameter and a biochemical parameter i.e. waist circumference and fasting triglyceride level respectively. Waist circumference itself serves as an independent risk factor for cardiovascular diseases and combining it with TG levels will further increases its reliability. Being the two independent components in the accepted definition of metabolic syndrome; LAP is considered as an upcoming index [74]. LAP can be applied easily on a day to day clinical practice to predict metabolic syndrome (MS).Individuals with higher LAP index had an increased risk of metabolic disorders compared to those with lower LAP. This index may be a strong, reliable and low cost tool for predicting cardiovascular disease and metabolic syndrome risk [24,26,28,30,75,76]. LAP is proved to be better predictor of MS than BMI [28,29,30,75,76]. The LAP has been shown to be a good discriminator of diabetes and cardiovascular disease [24,26,27,76]. In our study, the results revealed that the LAP values were significantly elevated in diabetic smokers than diabetic non-smokers *i.e*., 52.92 ±8.76 cm.mmol/l among diabetic non-smokers to 72.36 ±10.31 cm.mmol/l among diabetic smokers (Table 1), which is of statistical significance ($p<0.001$). In concordance with our findings, it has been published that the LAP is significantly higher in diabetic heavy smokers than diabetic non-smokers [29,43]. Our LAP values are comparable with the results of previous authors [76,77,78,79,80]. The present values of LAP are higher than the values reported by different investigators[29,43,81] while these are lower than the values available in literature [30,82,83].

Diabetic smokers in this study exhibited significant lipid abnormalities with increased LAP. We have observed a significant positive correlation between FSG and LAP ($r=0.40$, $p< 0.001$) and between HbA1c and LAP ($r=0.57$, $p < 0.001$) in diabetic smokers (Table 2). There is a dearth of published value of correlation coefficient (r) between LAP and FSG and HbA1c in diabetic smokers. Mirmiran *et al*.[81] found a significant positive correlation between LAP index and FSG ( $r=0.39$, $p<0.001$) in diabetic non-smokers. Rocha et al. [82] reported that fasting glucose was positively correlated ($r=0.05$) with LAP in obese patients with T2 DM and 32.7% of the patients were smokers (past or current). Klisic *et al*.[79] performed Spearman's correlation analysis to test the association between LAP and glycated hemoglobin (HbA1c) in patients with T2 DM and showed that LAP highly positively correlated with HbA1c ( $\rho =0.272$, $p < 0.001$). In a study from Porto Alegre/Brazil, Vieira et al.[84] reported that LAP (log-transformed) was significantly correlated with fasting blood glucose (log-transformed: $r= 0.20$, $p< 0.05$) in the hospitalized patients aged 18 to 80 years without cardiovascular disease. In the present study, both FSG and HbA1c were significantly correlated with LAP index. However, HbA1c showed stronger correlation than FSG (Table 2). Both these indices (AIP and LAP) are valuable tools to evaluate CVD risk in diabetic smokers.

CVD is a major complication and the leading cause of early death among people with type 2 DM. Clinical trials

has shown that lifestyle interventions help in prevention and reduction of CVD risk. Lifestyle management is an essential part of management of type 2 DM and CVD in diabetic patients. Dietary restriction is recommended to achieve weight loss and reduce the risk factors for CVD in type 2 DM. Calorie restriction and weight loss bring down the blood pressure to normal limits and improves blood lipid profile, especially TG and very low-density lipoprotein cholesterol. Patients with type 2 DM who do not show improvements in blood glucose levels with diet therapy are generally prescribed oral hypoglycemic drugs. These drugs control hyperglycemia by either increasing the release of insulin from the pancreatic beta cells or increasing the sensitivity of peripheral tissues to insulin. Exercise improves glycemic control, reduces certain CV risk factors, and increases psychological wellbeing. In addition, physical training has been shown to reverse insulin resistance by increasing the number of skeletal muscle glucose transporters, which may reduce the need for hypoglycemic agents.

Patients with diabetes who are smokers are doubly at risk. Smoking abstinence could reduce CVD events. The initiators of vasculopathy that ultimately develop into long-term complications can be controlled and avoided by strict glycemic control, maintaining normal lipid profile, regular physical exercise, adopting a healthy lifestyle and pharmacological interventions. Health promotion and patient education should be given priority to combat CV complications in type 2 DM patients. A multidisciplinary approach involving patients, health professionals, researchers, and governments should be undertaken to reduce the incidence and prevalence of type 2 DM and CVD, and improve the quality of life and well-being of patients. Cigarette smoking is a leading risk factor for CVD. Understanding the hazardous effects of smoking on diabetes mellitus may lead to increased emphasis on smoking prevention and smoking cessation as important strategies in the management of this condition. Smoking cessation is one of the important targets for diabetes control and the prevention diabetic complications.

Our study suggests that the assessment of smoking behaviors should be added to the guidelines for diabetes care. However, smoking prevention and smoking cessation may not be emphasized enough in diabetes clinics. Therefore, encouraging all diabetic patients to stop smoking and transferring them to smoking cessation clinics in order to give them an education on the importance of the need to stop smoking and engaging in smoking cessation programs is important for glycemic control and limiting the development of diabetic complications. In addition, further studies that are able to explore the effects of smoking should be conducted in order to further understanding of the differential impact of smoking on glycemic control and diabetic complications.

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