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Effect of cigarette smoking on smoking biomarkers, blood pressure and blood lipid levels among Sri Lankan male smokers

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ABSTRACT

Study purpose The aim of this study was to determine the fractional exhaled nitric oxide (FeNO) levels, exhaled breath carbon monoxide (eCO) levels, blood pressure, blood lipid levels between smokers and non-smokers and to determine the association of smoking intensity with the above parameters.

Methods This descriptive study was conducted in selected periurban areas of the Colombo District, Sri Lanka. Adult male current tobacco smokers (n=360), aged between 21 and 60 years were studied and compared with anthropometrically matched male non-smokers (n=180). Data were collected by interviewer-administered questionnaire, clinical assessment and measurement of FeNO by FENO monitor and eCO bySmokerlyser.

Results Smokers had significantly lower mean FeNO levels and higher mean eCO values compared with non-smokers. Presentation of palpitations was higher among the smokers and a significantly positive correlation was identified between palpitations and eCO levels. There was a significantly positive correlation between the systolic blood pressure of smokers with the duration of smoking (DS), Brinkman Index (BI), Body Mass Index (BMI) and there was a significantly negative correlation with FeNO levels. The mean arterial pressure was positively correlated with the DS, BI and BMI. There was a significantly negative correlation between FeNO and the number of cigarettes smoked per day, DS and BI of smokers. Significantly higher total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), very LDL-C, TC: HDL ratio and low high density lipoprotein cholesterol (HDL-C) level was observed among smokers compared with the non-smokers.

Conclusions Tobacco smoking was found to impact blood pressure and serum lipid levels thus enhancing the cardiovascular risk among smokers. The levels of eCO and FeNO are useful biomarkers for determining the intensity of smoking. The results indicate the necessity for urgent measures to stop cigarette smoking in Sri Lanka.

INTRODUCTION

Background

Tobacco smoking is the greatest public health burden in the world.[1 2] It contributes to 8 million deaths globally each year. Among these deaths, 7 million are caused by direct smoking, while another 1.2 million are caused by secondhand smoke.[1] The majority of the world's 1.3 billion smokers (80%) live in low/middle-income countries.[1 3 4] It is responsible for 1.6 million deaths in the WHO South-East Asia Region (SEAR), which is home to the world's largest tobacco manufacturers and users.[5] India and Indonesia are two of the world's top five tobacco producers. Tobacco causes more deaths than AIDS, alcohol, cocaine, homicide, suicide and road traffic accidents.[6] Sri Lanka has an annual 20 000 death rate owing to tobacco use.[7 8] In regard to the cardiovascular diseases (CVD), South Asia saw a 73% rise in mortality attributable to ischaemic heart disease between 1990 and 2010, compared with a global increase of 30%.[9] Additionally, South Asians (those from India, Pakistan, Bangladesh, Nepal and Sri Lanka) have been observed to suffer their first myocardial infarction (MI) about 10 years early than other ethnic groups.[9]

Smoking, hypertension and dyslipidaemia

Cigarette smoking is widely known to be associated with CVDs.[10–14] Hypertension, raises the risk of MI, cerebrovascular accidents, renal failure and other disorders dramatically.[15] Hypertension affects an estimated 1.13 billion individuals globally, with two-thirds of them residing in low-income and middle-income nations.[16] It is well known that cigarette smoking increases blood pressure (BP),[17 18] and is associated with CVDs. However, some studies have concluded that smoking has no impact on hypertension,[19 20] or that the chronic effect of smoking on BP is minor.[21] Another review research found that smoking produces acute hypertension owing to sympathetic nerve activation, but the long-term effect is unclear because quitting smoking does not result in a substantial decrease in BP.[22] However, the effect of smoking on BP needs to be re-evaluated as the current evidence is contradictory. Cigarette smoking has another negative impact on lipid profile (LP) levels of blood. Nicotine has a significantly negative effect on lipid metabolism and regulation.[23 24] Smoking-induced lipid and lipoprotein abnormalities are hypothesised to have an influence on smoking-induced atherosclerosis.[25] Scientists have discovered that smoking produces considerably higher levels of total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and lower levels of high-density lipoprotein cholesterol (HDL-C).[26 27] The alterations mentioned above are linked to an increased risk of CVD.[25] However, the details related to the very LDL-C (VLDL) and TC/HDL ratio are poorly addressed.

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Smoking and biomarkers (fractional exhaled nitric oxide and exhaled breath carbon monoxide) and BP

In both animals and humans, nitric oxide (NO) is increasingly recognised as a biological mediator.[28] The human lung produces NO, which is found in exhaled breath. Exhaled breath NO measurement has been standardised for clinical application.[28] Smoking is a known cause to reduce the fractional exhaled NO (FeNO) levels.[29 30] However, the relationship between FeNO and human BP has not been well investigated.

Exhaled breath carbon monoxide (eCO) is another important biomarker of smoking. When tobacco is burnt CO is produced. Thus, the inhaled breath of burnt tobacco accumulates in the respiratory passages and is exhaled in breath. CO monitors provide an independent diagnostic tool for smoking cessation programmes by providing valuable evidence to identify, educate, evaluate and treat tobacco patients. Monitoring a patient's CO helps determine the level of nicotine addiction and higher readings indicate a greater nicotine dependence.[31 32] However, a single-blind trial study has revealed that there is no effect of eCO on BP levels.[33]

Purpose of the study

Therefore, it is very important to study the effect of smoking on CVD in consideration of the above facts. To the best of the knowledge of the authors, there are no recent published studies on smoking-induced elevated BP, serum cholesterol levels, or biological marker levels in Sri Lanka or other South Asian countries. Further, in South Asian countries, the association between these biological indicators, smoking and the prevalence of CVD is similarly understudied. However, according to existing literature, none of these factors have been studied collectively elsewhere in the world. In terms of Asian populations, our study adds new information about a South Asian group that does not smoke heavily, as much as the people of Far-Eastern Asian communities while it has higher mortality associated with CVDs.[34]

Sri Lanka currently lacks baseline data on the aforementioned characteristics in the smoking population. Additionally, Sri Lanka has a lower rate of personal cigarette usage than the rest of Asia.[34] More research into the cardiovascular response to this low-intensity tobacco use is essential as the burden of CVD is high in the region.

In this study, we investigated the severity of smoking and its relationship to biological indicators, as well as the influence of smoking on hypertension and dyslipidaemia. The purpose was to determine the frequency of smoking, the level of biological markers (FeNO and eCO), and the relationship of these biological markers with BP and dyslipidaemia. To the best of the authors' knowledge, this is a pioneer study conducted on exhaled breath biomarkers, serum LP levels and BP variables among smokers in South Asia. Furthermore, it is important to investigate dyslipidaemia induced by smoking since it may vary due to ethnicity, socioeconomic status, cultural habits and lifestyle factors between communities; and data on Asian communities are sparse in the literature.[35]

METHODS

Study design and setting

A descriptive study was conducted with adult male daily tobacco smokers, (n=360) aged between 21 and 60 years with a history of smoking over 5 years. They were randomly recruited for the study from periurban areas of Colombo district Sri Lanka. A comparison sample of 180 non-smokers matched for age, height and weight was randomly selected from the same area. Non-smokers were respondents who, at the time of their enrolment, confirmed that they had never smoked or not smoked during the last 5 years as well as not smoked a total of 100 cigarettes in their lifetime.[25 35] Smokers and non-smokers with a history of alcohol dependence, lipid-lowering medications and diagnosed psychiatric illnesses were excluded.

Five periurban Ministry of Health divisions named Boralesgamuwa, Homagama, Piliyandala, Maharagama and Ratmalana located in the Colombo district were randomly selected. These periurban divisions comprise the majority of the total district population with a mixture of both rural and urban populations.

Data collection

A pretested interviewer-administered questionnaire was used to obtain information on participants' baseline data, such as occupation, age, smoking frequency, type of tobacco smoking and the number of years of smoking. The anthropometric measurements of height and weight were obtained using standardised measurement techniques. Height and weight were obtained using a stadiometer (KT-GFO6A-Kindcare-China) and a portable electronic bathroom scale (Omron HN-283-Japan). The WHO Guide to Physical Measurements[36] was used for this purpose. The body mass index (BMI) was calculated using the following formula: BMI (kg/m^2)=weight (kg)/ [height (m)]^2. The BP of each participant was measured in a seated position with a standard mercury sphygmomanometer with an appropriately sized cuff and a standard Littman stethoscope. The brachial artery was occluded by the cuff placed around the upper arm and inflated to above systolic pressure. The first audible Korotkoff sound was considered as the systolic measurement and the disappearance of audible Korotkoff sounds was recorded as the diastolic pressure, respectively. Measurements were taken to the nearest 2 mm Hg.[37] Participants who had eaten, drunk alcohol or smoked in the 30 min before the measurement was considered, and BP was assessed after an appropriate time lag.[21] eCO concentration was measured using a standardised calibrated Bedfont Micro+ Smokerlyzer (Bedfont Scientific, UK). The measuring concentration range of the device is 0–500ppm (parts per million) and enabled a large full colour display with a familiar traffic light system to indicate the smoking severity. Further, this can be used in the temperatures of 15°C–40°C temperature and is ideal for the environmental conditions of Sri Lanka. To standardise the breath being analysed by the process the subjects were asked to exhale completely, inhale fully, and then hold their breath for 15 s before exhaling rapidly into the disposable mouthpiece. Ambient CO levels weree recorded before each breath. CO levels were detected as CO molecules in a million parts of the air. The FeNO was measured using NObreath FeNO monitor (Bedfont Scientific; Kent, UK) according to the present American Thoracic Society guidelines.[28] The FeNO monitor measures the concentration range of 5–300 ppb (parts per billion) with an accuracy of 10% for FeNO ≤50 ppb and 10% for FeNO >50 ppb. The sensor has a sensitivity of 5 ppb and the breath test time is 12 s. Its operating temperature range is 10°C–30°C. The monitor is enabled with a screen guide to the patient through a breath test from the icons on the screen. Subjects were asked not to hold their breath before exhalation; they were advised to take a deep breath in and then a long slow exhalation. Ambient NO was recorded. Above two biological markers were analysed for all participants of the study.

The smoking severity was estimated based on the Brinkman Index (BI), which is calculated by multiplying the duration of smoking (in years) by the number of cigarettes smoked

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per day (CD).[38] A 3 mL of blood collected into a sterile plain tube for LP analysis from selected 180 smokers and 180 non-smokers. These smokers were systematically selected based on the smoking severity for representing mild smokers (<2 cigarettes/day), moderate smokers (>2 and <10 cigarettes/day) and severe smokers (>10 cigarettes/day) based on the available literature.[39 40] Analysis was done with the fully automated biochemistry analyser, Thermo Scientific Indiko. Friedewald estimation was used to measure serum LDL-C levels.[25] Hypertension was defined when an individual had a systolic BP (SBP) ≥140 mm Hg and/or diastolic BP (DBP) ≥90 mm Hg, prehypertension was defined as SBP 120–139 mm Hg and DBP 80–89 mm Hg.[41 42]

Statistical analysis

Statistical analysis was performed with IBM SPSS for Windows V.23.0 (IBM). Descriptive statistics were used for smoking details. The normal distribution and the similarity of the variances were tested with the Kolmogorov-Smirnov test before statistical analysis. Categorical data were compared with χ^2 tests for significance between groups. Groups were compared for the parameters with a skewed distribution using the Mann-Whitney test. Smokers and non-smokers were compared with the Mann-Whitney U test. Data are expressed as medians (IQR). The level of significance was set at $p<0.05$.

RESULTS

Basic characteristics of smokers and non-smokers

Data from 360 smokers and 180 non-smokers were analysed. LPs were evaluated in 180 smokers selected from the recruited sample and 180 non-smokers. Accordingly, there was no statistical difference ($p>0.05$) between age, anthropometric measurements between smokers and non-smokers ($p>0.05$). The mean daily consumption of cigarettes by smokers was 5.73±4.88 (SD) sticks, median smoking duration (SD) was 21.0±17.0 (IQR) years and BI was 80.0±135.0 (IQR). The median smoking-initiated age was 18.0±4.0 years (table 1).

Frequency of palpitations, hypertension and BP (SBP, DBP, mean arterial pressure) of smokers and non-smokers

The frequency of palpitations and SBP of the smokers and non-smokers were compared. There was a significant increase in the frequency of palpitations and hypertension among smokers when compared with non-smokers ($p<0.001$) (table 2).

The BP parameters of smokers were compared with those of non-smokers (table 3). Smokers had significantly higher SBP and mean arterial pressure (MAP) than non-smokers (SBP; U=22 219, $p<0.001$, MAP; 23777.5, $p=0.004$). However, there were no significant differences in DBP ($p>0.05$). Smokers had significantly higher eCO levels compared with the non-smokers (CO; U=4853.5, $p<0.001$). The FeNO levels of smokers were significantly lower compared with the non-smoking group (U=18 455, $p<0.001$) (table 3).

Table 1 Anthropometric characteristics of smokers and non-smokers

Variable	Smokers (n=360)		Non-smokers (n=180)		P value
	Median	IQR	Median	IQR	
Age (years)	39.0	18.75	43.0	21.5	0.242
Weight (kg)	65.0	18.97	66.0	14.5	0.652
Height (cm)	166.5	8.00	166.0	10.3	0.412
BMI	23.24	5.92	23.50	3.67	0.738

Mann Whiteney U test.
BMI, body mass index.

Table 2 Palpitations and systolic blood pressure of smokers and non-smokers

Variable	Smokers (n=360)	Non-smokers (n=180)	χ^2	P value
Palpitations				
Yes	50 (13.8%)	0 (0%)	26.51	<0.001*
No	310 (86.2%)	160 (100%)		
Blood pressure				
Normal	146 (42.9%)	108 (65.1%)	22.59	<0.001*
Prehypertension	103 (30.3%)	35 (21.1%)		
Hypertension	91 (26.8%)	23 (13.9%)		

(Pearson χ^2 test), *p<0.001.

Correlation of smoking biomarkers with the prevalence palpitations

There was a significantly positive correlation between the prevalence of palpitations among the smokers with the eCO levels ($r=0.214$, $p<0.001$) However, there was no significant correlation between the presence of palpitations with the FeNO

Correlation of smoking variables with the BP of smokers

There was a significantly positive correlation between the smokers' SBP with the duration of smoking, BI, and BMI and there was a negative correlation with FeNO levels. Furthermore, there was a significantly positive correlation between the smokers' DBP with the duration of smoking, BI, and BMI. MAP was also positively correlated with the duration of smoking, BI and BMI (table 4).

Correlation of FeNO with observed smoking variables and eCO

Table 5 depicts the correlation of smoking variables with FeNO. There was a significantly negative correlation between FeNO and the number of CD, SD, BI and eCO of smokers.

LP values of smokers and non-smokers

Statistically significant LP parameters were identified in all the lipid fractions between age, height, and weight-matched smokers and non-smokers groups (table 6). A significantly higher TC, TG, LDL, VLDL, TC: HDL ratio was observed among smokers

Table 3 Blood pressure (SBP, DBP, MAP) and biological markers (FENO, eCO) of smokers and non-smokers

Variable	Smokers (n=360)		Non-smokers (n=180)		P value
	Median	IQR	Median	IQR	
SBP (Hg mm)	126.00	26.00	120.00	16.00	<0.001*
DBP (Hg mm)	80.00	19.00	80.00	10.00	0.058
MAP (Hg mm)	93.16	12.17	94.0	20.0	0.004†
eCO (ppm)	7.0	8.0	3.0	1.0	<0.001*
FeNO (ppb)	15.0	16.0	24.0	11.0	<0.001*

Mann-Whiteney U test.
*P<0.001.
†P<0 .05.
DBP, diastolic blood pressure; eCO, exhaled breath carbon monoxide; FeNO, fractional exhaled nitric oxide; MAP, mean arterial pressure; SBP, systolic blood pressure.

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Table 4 Correlation of smoking variables with the blood pressure of smokers (SBP, DBP, MAP)

	SBP		DBP		MAP	
Parameters	**R value**	**P value**	**R value**	**P value**	**R value**	**P value**
Smoking duration (years)	0.251	<0.001†	0.234	<0.001†	0.216	<0.001†
Brinkman Index	0.175	0.001*	0.139	0.011*	0.146	0.007*
BMI (kg/m^2)	0.188	0.001*	0.369	<0.001†	0.324	<0.001†
FeNO (ppb)	−0.133	0.015*	−0.37	0.498	−0.075	0.173
eCO ppm	0.043	0.432	−0.03	0.504	0.001	0.989

Spearman correlation.
*p<0.05.
†p<*0.001*.
BMI, body mass index; DBP, diastolic blood pressure; eCO, exhaled breath carbon monoxide; FeNO, fractional exhaled nitric oxide; MAP, mean arterial pressure; SBP, systolic blood pressure.

when compared with non-smokers (TC; U=11 209.0, p<0.001, TG; U=8900, p<0.001, LDL; U=12 895.0, p=0.009, VLDL; U=8916.0, p<0.001, TC: HDL ratio; U=11 209.5, p<0.001) while smokers have significantly low HDL level compared with the non-smokers (U=13 155.0, p<0.001) (table 6).

DISCUSSION

The SEAR is the home to more than 22% of the world's adult smokers aged 15 years and older. Over one-third of the world's youngsters aged 13–15 years (34% or 14.8 million), who use tobacco in diverse forms, are from SEAR.[5] However, tobacco control measures are superior to those in other WHO regions, and despite the high incidence, there is a downward trend in tobacco smoking.[5 43]

Smoking is also a major public health problem in Sri Lanka, with over 20 000 people dying every year as a result.[7] To the best of our knowledge, this is the first study conducted to assess the exhaled breath biomarkers and their association with BP, and LP assessment of cigarette smokers in a community setting in South Asia. The goals of this study were to measure FeNO, BP and LP of smokers and non-smokers. Further, the study attempted to determine the association of cigarette smoking with biological markers, BP and LP abnormalities. Several studies have individually considered these aspects. However, to the best of our knowledge, this study is unique in considering exhaled breath biomarkers in relation to smoking status, BP and LP variations among Sri Lankan smokers.

There was no statistically significant difference in age, height, weight or BMI between smokers and non-smokers (p>0.05) (table 1). Smokers' average daily cigarette intake was not high and was 5.73±4.88 (SD). The observed median values of increase in BP among smokers remain within the normal ranges of BP. Prehypertension was observed in 30.3% of smokers and hypertension was observed among 26.8% of smokers. According to Zheng *et al* daily cigarette usage (cigarettes /day) among Asian nations is low when compared with the rest of the globe.[44] This is in accordance with the data from Sri Lanka as well. This might be owing to societal constraints in Sri Lanka. Further, the inability to afford the cost of cigarettes due to the low economic status may further contribute. Furthermore, Sri Lankan government has taken several initiatives to limit smoking, including raising taxes, prohibiting smoking in public places and banning advertising. However, despite these restrictions smoking continues.

According to the findings, eCO levels were significantly higher in smokers than in non-smokers (p<0.001),[45] whereas FeNO levels were significantly lower (p<0.001). A number of CD, SD and the BI are all inversely linked with FeNO levels (table 5). The inverse association of FeNO with CO is in accordance with those of another study.[24]

Hypertension is the leading risk factor for CVD. Thus, with each 20 mm Hg increase in SBP and 10 mm Hg increase in DBP, the risk of CVD doubles.[46] Further studies reveal that even past smokers had higher BP than never smokers.[17] According to our findings, smokers had a significantly higher rate of palpitations and hypertension than non-smokers. Additionally, we observed a statistically significant positive correlation between palpitations and smoking biomarkers. The eCO level was positively associated with palpitations, which is a novel finding for the South Asian population. Palpitations are the sensations associated with a fast or irregular heartbeat and are most frequently brought on by cardiac arrhythmias or anxiety.[47] Palpitations are reported in patients with arrhythmias, however these can be

Table 5 Correlation of FeNO with observed smoking variables and eCO ppm

	FeNO (ppb)	
Parameters	**R value**	**P value**
Smoking duration (years)	−0.138	<0.001*
No of cigarettes/days	−0.132	0.014†
Brinkman Index	−0.243	<0.001*
eCO ppm	−0.281	<0.001*

(Spearman correlation)
*p<0.001.
†*p<0.05.
eCO, exhaled breath carbon monoxide; FeNO, fractional exhaled nitric oxide.

Table 6 Lipid profile values of smokers and non-smokers

Lipid profile parameters	Smokers (n=180)		Non-smokers (n=180)		
	Median (Mean)	**IQR (SD)**	**Median (Mean)**	**IQR (SD)**	**P value**
TC mg/dL*	210.0	41.6	192.0	43.6	<0.001†
TG mg/dL	137.5	57.0	102.0	61.0	<0.001†
HDL mg/dL	38.5	15.0	40.0	14.0	0.016‡
LDL mg/dL	134.0	55.63	121.8	57.0	0.009‡
VLDL mg/dL	27.6	22.2	20.3	12.70	<0.001†
TC:HDL ratio	5.3	2.40	4.6	1.90	<0.001†

*Independent Student's t-test and Mann-Whiteney U test
†P<0.001.
‡P<0.05.
HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride; VLDL, very low-density lipoprotein cholesterol.

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caused by any arrhythmia, including sinus tachycardia, atrial fibrillation, premature ventricular contractions or ventricular tachycardia.[47] Scientists have shown that CO-poisoned patients have an increased risk of developing cardiac arrhythmias such as paroxysmal tachycardia, ventricular fibrillation/flutter and paroxysmal supraventricular tachycardia.[48] As a result of the continual exposure to CO associated with smoking, we can assume that palpitations may occur frequently among smokers. However, numerous investigations have indicated that the cause of smokers' ventricular arrhythmias is nicotine absorption through cigarette smoking.[49] Nicotine that is released into the circulation during smoking is clearly known to increase the plasma catecholamines, thus affecting the heart rate, and arterial BP and as a result of all those alterations augmented myocardial work and oxygen demand may contribute to the generation of cardiac arrhythmias.[50] However, additional research is necessary to determine the relationship between smoking and palpitations as the causes may be multifactorial.

Furthermore, smokers had a statistically significant higher SBP level than non-smokers besides no significant difference in DBP level between the two groups. Several studies are in accordance with these results.[51–53] In addition, similar to the findings of Talukdar *et al*, a substantial rise in MAP among smokers was a significant finding of this study.[17] Another animal study, similar to the one described above, found that cigarette smoke causes increased BP, which can be reversed if the exposure duration is less than 6 weeks.[54] However, studies reveal this is not valid for prolonged cigarette exposure of more than 16 weeks.[46] SBP is a more common cause of CVD than DBP and has a larger influence on BP grading, however, this varies by age, gender and region.[55]

Furthermore, the SD, BI and BMI were all positively correlated with SBP, DBP and MAP. Similarly, Talukdar *et al* have established a positive correlation between increased BP and SD in a well-designed animal model research, while Tan *et al* have confirmed continued smoking exposure is strongly linked with higher BP.[56] Moreover, there was a significant difference in smokers' percentage for feeling palpitations and presence of hypertension compared with the non-smokers. There was a significant difference in the percentages of normal, prehypertension and hypertension BP categories, while there was a significant correlation of SBP with SD and BI. Smokers are thus more vulnerable to heading to the next level of hypertension category with more disastrous events. Moreover, we could not find a positive relationship between the number of CD day and SBP, as the SBP rise may be multifactorial.[17] According to Orth, the duration of smoking is a cause of increased BP, while another study found the number of CD also has a positive correlation with increased BP.[18] A few processes can be used to explain this. Endothelial NO generation is essential for maintaining the tone of arteries vasodilation. Smoking-induced endothelial dysfunction and reduces NO production, which can impede the relaxation of arterioles.[57 58] According to Salonen *et al*, smoking-related atherosclerotic diseases produce endothelial dysfunction, which reduces NO production.[57] Well-designed animal studies have indicated that smoking reduces NO production, which can lead to a rise in BP.[54 59] Further, NO is not dependant on BMI except for children less than 12 years.[60] According to the findings of the current study smokers' FeNO levels are considerably lower ($p<0.001$) compared with the non-smokers and there was a significant inverse correlation of FeNO with the SBP ($p<0.05$). FeNO levels correlate to the NO produced by the airway epithelium of the lungs.[28] Further, decreased levels of FeNO is an indicator of pulmonary artery hypertension.[30 61] Moreover, we discovered a significantly negative correlation between FeNO and SBP. However, the relationship of FeNO with general hypertension has not been investigated and thus, needs to be assessed before conclusions can be drawn.

According to Dunga *et al*, smoking raises BP mostly by activation of the sympathetic nervous system, and hypertensive smokers have a higher risk of developing severe hypertension.[62] CO does not cause sympathetic nerve stimulation.[63] The impact of CO on sympathetic stimulation was studied in a 7-day single-blind experiment with three intervention groups with administering CO, cigarette smoke and air. This study found that there was no difference of BP among the groups. Urine epinephrine and norepinephrine levels were greater in the cigarette smoking group with no impact of CO compared with air.[33] According to the results of this study, we also found that there was no significant relationship observed between BP and CO levels (table 3). However, BP is correlated with SD and the cumulative smoke exposure (BI), but no association was observed between BP and the number of CD.

Blood lipids play an important role in the human body, contributing to various biochemical functions and acting as a structural component but unstable lipid fractions are hazardous to human health.[64] This study also confirmed that continued smoking is significantly associated with dyslipidaemia. Smoking-related dyslipidaemia can be explained by a variety of processes. Our findings revealed that smokers had considerably higher TC levels than non-smokers in accordance with previous investigations.[65–67] TG, LDL and VLDL of smokers were also high compared with the non-smokers ($p<0.001$) and our findings are compatible with several studies.[3 66–68] Furthermore, smokers had lower HDL values ($p=0.016$) than anthropometrically matched non-smokers and the finding is consistent with those of other studies.[3 52 66–68] Additionally, the ratio of TC:HDL is significantly greater in smokers than in non-smokers ($p<0.001$). However, a large Japanese cohort found no difference in TC and LDL-C of smokers despite increasing TG and decreasing HDL.[35 69] This might be because of various conflicting variables related to lipid metabolism, dietary lipid intake, ethnicity or other factors such as the exercises.

The results of the this study revealed that smokers' HDL-C levels are significantly low compared with non-smokers ($p<0.001$), consistent with other studies.[66 70] Decreasing the HDL-C and increasing the LDL-C and VLDL-C is mostly associated with CVDs. One of the reasons for atheroma and coronary artery disease is an imbalance between good and bad cholesterol. Serum lipid levels in smokers might rise for a variety of reasons. During smoking, high concentrations of nicotine are taken into the circulation via the lungs. Consistent nicotine exposure induces the release of catecholamines from the body, which is caused by the activation of adenyl cyclase in adipose tissue and increase in lipolysis, and the release of free fatty acids into the circulation. Increased amounts of free fatty acids in the liver boost TG and VLDL-C production, resulting in higher levels of TG and VLDL-C in the blood.[3] Increased LDL-C and VLDL-C levels in the blood contribute to a decrease in HDL-C levels.[71] In addition to nicotine-mediated catecholamine release, researchers have found another mechanism that contributes to smokers' lower HDL-C levels. Smokers have higher levels of homocysteine than non-smokers. Increased homocysteine is known to have a negative impact on HDL-C levels and reduces HDL-C levels in smokers.[72]

CONCLUSIONS

Cigarette smoking caused decreased FeNO levels and increased SBP, MAP compared with the non-smokers. Moreover, chronic smoking exposure resulted in increased TC, LDL, VLDL, TG and decreased HDL-C levels. The risk of a rise in serum cholesterol

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with an increase in LDL-C and a lowering in HDL-C in daily smokers is very important since this pattern is associated with coronary heart disease. The results highlight the need for active smoking cessation interventions in primary care in a middle-income country. The data indicate that, despite a lower intensity of smoking than in western populations, the devastating health effects are obviously manifest in this smoking population. CO and FeNO monitors can be used to identify the smoking status of individual smokers and can effectively monitor smoking cessation.

Limitations

We did not do a subgroup analysis depending on the intensity of the smoking. We did, however, use a consistent method for selecting participants. Smoking history was estimated based on the verbal responses of smokers.

Main messages

- Even at low intensity of smoking, smokers' systolic blood pressure and mean arterial pressure were both elevated.
- Chronic smoking increased total cholesterol (TC), low-density lipoprotein (LDL), very LDL, triglyceride and TC: high-density lipoprotein (HDL) ratio while decreasing HDL-cholesterol levels.
- Carbon monoxide and fractional exhaled nitric oxide monitors are suitable to use as independent diagnostic and monitoring tools in smoking cessation programmes, as an aid in determining the severity of smoking.

Current research questions

- What are the best smoking cessation interventions for a middle-income country in primary care?
- What is the effectiveness of practical smoking cessation interventions in reducing cardiovascular disease (CVD) risk of smokers in developing countries?
- Can fractional exhaled nitric oxide monitoring use to predict the CVD risk of smokers?

What is already known on the subjects

- Smoking increases cardiovascular disease risk, exhaled breath carbon monoxide level and decreases fractional exhaled nitric oxide levels.
- Cigarette smoking has a detrimental effect on blood lipid profiles.
- A rise in blood cholesterol with an increase in low-density lipoprotein-cholesterol and a decrease in high-density lipoprotein-cholesterol is linked to an increased risk of coronary heart disease.

Correction notice This article has been corrected since it first published. Affiliation 1 has been updated.

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Contributors PH, SW, TA, MF and ST conceived and designed the study. PH performed the study. PH, SW, TA and MF were involved in data interpretation and statistical analysis. PH wrote the first draft of the manuscript. SW, TA, MF and ST critically revised the manuscript for intellectual content. All authors read and approved the final manuscript. All authors are responsible for the academic content of the paper. SW acted as guarantor

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