



Research Paper

Elevated Monocyte to HDL Cholesterol Ratio as a new Inflammatory Marker in Smokers

Authors

Dr Tharuni Latha. A¹, Dr Nagesh G.N², Dr Preethi.R.Gandhi³, Dr Anila Jose⁴,
Dr Hilas Salih⁵, Dr Rachitha.S⁶

^{1,3,4,5,6}Postgraduates in Medicine, Kempegowda Institute of Medical Science Vvpuram Bangalore

²Professor of Medicine, Kempegowda Institute of Medical Science, Bangalore

Abstract

Background: Cigarette smoking is described as 'probably the most addictive and dependence-producing form of object-specific self gratification known to man'. It is estimated that about half of all regular cigarette smokers will eventually be killed by their habit^{[1],[2]}. Smoking increases the absolute number of deaths from lung cancer, cancer of other respiratory sites, chronic bronchitis/emphysema and cor pulmonale. Deaths from ischaemic heart disease and cerebrovascular disease are advanced by smoking^[3].

Aims & Objectives: To investigate the relationship between monocyte to high-density lipoprotein cholesterol (HDL-C) ratio (MHR) and cigarette smoking.

Materials & Methods: About 50 participants who smoke and 50 healthy subjects with no history of smoking who presented to the Department of Medicine, Kempegowda Institute of Medical Sciences, Bangalore were enrolled in this study. Complete blood count and lipid profile were analysed in all study participants. Smoking habits were calculated according to number of cigarettes smoked per day, in pack years.

Results: According to Pearson's correlation analysis there was a weak but positive correlation between pack year and MHR in the smokers group, and there was a moderate positive correlation between the number of cigarettes smoked daily and MHR in the group. MHR levels were significantly elevated in smokers 15.71 (12.02-20.00) compared to non-smokers 11.17 (8.50-14.16).

Conclusions: Elevated MHR is a good indicator of a systemic inflammatory response in smokers. Smokers who have high MHR levels can easily be identified and could benefit from preventive treatment.

Keywords: smoking; monocyte to high-density lipoprotein cholesterol.

Introduction

Smoking can cause several diseases, mainly affecting the pulmonary and cardiovascular systems, like cancer, cardiovascular disease and chronic obstructive pulmonary disease^[1]. The World Health Organization has proposed that smoking is the single most important preventable

health risk in the world^[2]. Despite warnings, the prevalence of smoking remains high in most countries, thereby remaining a major public health concern^[3]. The effects of cigarette smoking (CS) on human health have been extensively studied at the organ, cellular, and molecular levels. Cigarette smoking has been linked to perturbations in

oxidative stress and immune response^[4]. Many toxins present in CS have immunomodulatory effects and also contain trace amounts of microbial cell components, like bacterial lipopolysaccharides which can induce chronic inflammation at mucosal surfaces and modify host responses to exogenous antigens^[5].

Monocytes and macrophages are the most abundant cells that secrete proinflammatory and prooxidant cytokines as part of inflammatory reactions^[6]. High-density lipoproteins (HDL) protect endothelial cells against the noxious effects of low-density proteins (LDL) and prevent the oxidation of the LDL molecules. Therefore, it was believed that HDL had both anti-inflammatory and anti-oxidant effects [7]. The ratio of the monocyte count to the HDL cholesterol level (MHR) is an easy calculable cardiovascular prognostic marker indicating the extent of inflammation and oxidative stress^[7-9]. As both inflammation and oxidative stress are related to atherosclerosis caused by smoking, we studied that higher MHR may be associated with the presence of smoking compared to non-smoking. Therefore, we aimed to investigate the relationship between MHR and cigarette smoking.

Materials & Methods

This was an observational study. Conducted in Department of General Medicine, Kempegowda Institute of Medical Sciences and Research Centre, Bengaluru.

Total 100 subjects were included in the study.

Smokers- Participants who smoked one or more cigarettes per day were accepted as smokers. Smoking characteristics - the number of cigarettes smoked daily and the number of pack years of smoking. Pack.years was calculated as number of cigarettes smoked per day × number of years smoked/20.

Hypertensives- The participants having a systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg and those taking antihypertensive drugs

Diabetics- The participants using oral antidiabetic drugs or insulin or having fasting blood glucose level ≥ 126 mg/dL

Inclusion Criteria

- Age group of all participants were between 18 and 75 years old who had no cardiac disease or atherosclerotic risk factors (except from hyperlipidaemia).

Exclusion Criteria

- Patients with the presence of chronic diseases, such as diabetes mellitus, hypertension, coronary artery disease, heart failure, chronic lung disease, connective tissue disease, chronic kidney disease, metabolic syndrome, thyroid dysfunction
- Use of non-steroidal anti-inflammatory drugs (nsaids) in the previous week
- Steroid use in the previous 6 months (including steroid creams)
- Upper respiratory tract infection within the last 3 weeks
- Pregnant women,
- Anaemia, leucocytosis, leukopenia or any other haematological, biochemical or serological abnormalities
- Routine alcohol intake, marijuana, and use other tobacco products, and ex-smokers

The patients underwent general physical examination, systemic examination and a group of tests that included:

- Complete blood count
- Lipid profile
- Exercise stress test
- 2D Echocardiography

All blood samples (6 mL for full biochemistry, 5 mL for complete blood count) were obtained from the ante-cubital vein after 12 h of fasting.

Results

A total of 100 patients were included in the study out of which 97 were males and 3 were female patients. Minimum age was 18 years and maximum age was 75 years. We observed that MHR values for the smoker group were significantly elevated than those of the non-

smoker group (respectively, 15.71 (12.02–20) and 11.17 (8.50–14.16), $p < 0.0001$). Triglycerides, high-density lipoprotein cholesterol (HDL-C), WBC (white blood cell), monocytes, haematocrit and haemoglobin values for the smoker group were significantly higher than those of the non-smoker group. BMI (body mass index) was significantly lower in the smoker group than the non-smoker group.

According to Pearson’s correlation, there was a weak positive correlation between pack year and MHR, there was a moderate positive correlation between the number of cigarettes smoked daily

and MHR in the smoker group (Tables 1 and 2). Although there were no statistically significant differences between the two groups regarding total cholesterol, for low-density lipoprotein cholesterol (LDL-C), there were positive correlations between these parameters and pack, year—the number of cigarettes smoked daily in smoker group (Tables 1 and 2,).

There were no statistically significant differences between the smoker group and non-smoker group in terms of hyperlipidaemia, age and other investigated laboratory parameters.

Pearson’s correlation analysis between smoking as pack year, MHR and blood lipid levels

Variable	Pack year	
	r	p
MHR	0.273	<0.0001
MONOCYTES (x103/mm3)	0.205	<0.0001
HDL CHOLESTEROL (mg/dl)	-0.155	0.002
TRIGLYCERIDES (mg/dl)	0.242	<0.0001
TOTAL CHOLESTEROL (mg/dl)	0.201	<0.0001
LDL CHOLESTEROL (mg/dl)	0.200	<0.0001

Pearson’s correlation analysis between the numbers of cigarettes smoked daily, MHR and blood lipid levels

Variable	No. of cigarettes smoked per day	
	r	p
MHR	0.379	<0.0001
MONOCYTES (x103 mm3)	0.321	<0.0001
HDL CHOLESTEROL (mg/dl)	-0.229	0.002
TRIGLYCERIDES (mg/dl)	0.203	<0.0001
TOTAL CHOLESTEROL (mg/dl)	0.112	0.025
LDL CHOLESTEROL (mg/dl)	0.146	0.004

Discussion

Smoking usually begins for many reasons such as parental smoking, curiosity, peer pressure, rebelliousness and assertion of independence. Once it becomes regular the pharmacological properties of nicotine are a major influence on the persistence of the habit, which appears to become advantageous to mood and/or life response. Lung cancer is the most notorious of the diseases caused by smoking. Death from lung cancer is 8–25 times more common among cigarette smokers, with a clear dose–response relationship. As smoking has increased among women so have their death rates from lung cancer, leading to a situation in some areas where lung cancer has overtaken breast

cancer as a cause of death. Mortality from chronic bronchitis and emphysema shows a relation to cigarette smoking almost as strong as that for lung cancer. Among those smoking 25 or more cigarettes daily mortality is over 20 times higher than in non smokers.

Smoking also causes ischaemic heart disease, cerebrovascular disease and peripheral vascular disease. A cigarette smoker has two to three times the risk of heart attack compared with a non-smoker and a 30–60% greater chance of death from heart attack, whilst heavy smokers aged 45 years or younger have 10–15 times the risk of fatal heart attack.

Cigarette smoke contains many toxic compounds, including polycyclic aromatic hydrocarbons, tobacco-specific nitrosamines and radioactive polonium as well as radon, all of which are potent carcinogens and mutagens in animals. Cigarette smoke causes release of elastolytic enzymes from lung neutrophils and macrophages, nitrogen oxides contained in the smoke cause emphysema and oxidants in smoke reduce the levels of α -1-antitrypsin in human and animal lungs. Endogenous nitric oxide is an important defense in the respiratory tract against infection and in counteracting bronchoconstriction and vasoconstriction. Cigarette smoking reduces exhaled nitric oxide concentration which contributes to the increased risk of chronic respiratory diseases in smokers.

Increase in permeability of systemic blood vessel walls to lipids has been suggested as contributing to the cardiovascular risks of smoking. Smoking increases atherosclerosis and a tendency to thrombosis.

Nicotine and the increased oxidative stress generated from smoking induce vascular endothelial dysfunction via the inhibition of endothelial nitric oxide synthase and decreasing generation of nitric oxide. Also nicotine increases the expression of adhesion molecules in endothelial cells, such as E-selectin and intracellular adhesion molecular 1, because of enhanced attachment and transmigration of monocytes to the vessel wall.

Monocytes are distinct types of leukocytes which have a key role in inflammation and the atherosclerosis process^[6]. Activated monocytes interact with damaged or activated endothelium, which results in the overexpression of proinflammatory cytokines/adhesion molecules, including monocyte chemotactic protein 1 ligand, vascular cell adhesion molecule 1 and intercellular adhesion molecule 1. Thereafter, monocytes differentiate into the macrophages that ingest oxidized LDL-C and form dangerous foamy cells^[7]. In another study, the count of circulating monocytes was found to be a predictor for new

plaque development. HDL-C can prevent inflammatory responses by acting directly on monocytes. Recent studies indicate the role of HDL-C in modulating monocyte activation, adhesion and in controlling the proliferation of progenitor cells that differentiate to monocytes. HDL-C also prohibits oxidation of LDL-C in addition to inhibition of macrophage migration. It also removes oxidized LDL-C from foamy cells^[7-11]. Therefore, monocytes show a pro-inflammatory effect, but HDL-C functions as a reversal factor during this process.

Hence we can hypothesize that MHR reflected the systemic inflammation and endothelial dysfunction in smokers. In the present study, we found that MHR levels were significantly higher in smokers than in non-smokers, and there was a relationship between MHR and pack year—the number of cigarettes smoked daily. Therefore, MHR may be used as a surrogate marker of inflammation and endothelial dysfunction in smokers.

Conclusion

MHR is a simple, easy, cost-effective tool that should be used for predicting the systemic inflammatory response and possible endothelial dysfunction in smoker cases. Cases with high MHR levels can easily be identified using routine blood investigations like (CBC and lipid profile) and measures to prevent ill effects of smoking can be undertaken at the earliest.

Limitations

Exposure to second and third hand smoking could not be assessed clearly

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