LIPID PROFILE AND LIPID PEROXIDATION IN BRONCHIAL ASTHMA

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ABSTRACT

Background: Bronchial asthma, a chronic inflammatory condition, often triggered by allergy & oxidative stress, initiate lipid peroxidation& enhanced release of arachidonic acid from cell membrane. Regarding lipid profile in bronchial asthma patients many conflicting data were reported. Therefore we have conducted this study. **Methodology:** 50 clinically diagnosed bronchial asthma cases for lipid profile and lipid peroxidation levels were compared with 50 healthy controls. **Results:** In our study fasting serum HDL and LDL cholesterol level of cases respectively (52.32mg/dl ±3.58), (99.21mg/dl ±12.49) were found to be significantly higher when compared to controls (44.58mg/dl ±2.58), (103.44mg/dl ±10.55) (*p*-value <0.05). Mean plasma SOD level of cases (3.42 U/mL±0.74) was significantly lowered than controls (7.16 U/mL±0.52). Serum MDA level of cases (5.91nmol/L±0.88) was higher as compared to controls (3.00nmol/L±0.40). (*p*-value <0.001) **Conclusion:** Lipid profile in bronchial asthma patients (raised HDL& decreased LDL) provides some degree of protection to this patients against ischemic heart disease (IHD). But increased in lipid peroxidation as evidenced by decrease plasma SOD & raised serum MDA aggravate airway inflammation, smooth muscle contraction & increased vascular permeability

KEYWORDS: Asthma; Oxidative stress; Lipid peroxidation; Lipid profile.

INTRODUCTION

Asthma is a common problem encountered in routine clinical practice. Asthma is an episodic, chronic inflammatory disease of airways characterized by recurrent episodes of dyspnea, cough, wheezing and tightness of chest. It occurs in all ages but mostly in early ages of life. In India, estimated deaths of 57000 were attributed to asthma in 2004 [1] and 2.28% in rural and 1.64% in urban areas as per ICMR data of 2010 [2]. The prevalence of bronchial asthma is comparatively much more in the region of Nellimarla, Vizianagaram where the study has been conducted. The area is surrounded by several industries like jute industries, pharmaceutical industries and ferro- alloys industries. Individuals employed in these industries are exposed to a host of allergens and dust which irritate the respiratory track and provoke oxidative stress which induce bronchospasm and culminate in many respiratory disorders including Bronchial asthma.

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Bronchial asthma is a chronic, inflammatory condition often triggered by allergy & oxidative stress. Oxidative stress, developed from imbalance between oxidants and antioxidants, may contribute to origin & development of several diseases including bronchial asthma. Lungs have the highest exposure to atmospheric oxygen and vulnerable to oxidative damage by oxidants and pollutants. The large endothelial surface makes it the major target site for circulating oxidants xenobiotics. Oxidative damage play one of the essential roles in development & persistent of bronchial asthma [3,4,].

Reactive oxygen species (ROS) can adversely affect airway cells and initiate lipid peroxidation , protein oxidation, DNA modification resulting in enhanced release of arachidonic acid from cell membranes, contraction of airway smooth muscle, increasing vascular permeability, increasing airway reactivity and airway secretion, synthesis and release of chemo attractants [5-7]. Cholesterol is the second most abundant lipid component of pulmonary surfactant, composing of 10-25% of total surfactant lipid. At least 80% of lung cholesterol appears to be derived from plasma lipoproteins [8, 9].

HDL particles of total cholesterol have various anti-inflammatory and antioxidative properties. HDL improves endothelial function by stimulating endothelial nitric oxide production [10]. HDL directly neutralizes

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lipopolysaccharides derived from Gram negative bacteria and inhibits subsequent production of inflammatory cytokines in lungs [11, 12]. Synthesis of alveolar surfactant is also promoted by HDL. Thus HDL-c serves as anti -inflammatory and antioxidative agent in bronchial asthma [13].

The levels of serum LDL-c have been implicated in the inflammatory cascade in murine model of asthma. Recent finding suggest that LDL-c may modulate the inflammatory state of asthmatic airways in humans [14].

Existing literatures shows that any abnormal lipid profile & lipid peroxidation can affect the course prognosis of bronchial asthma in patients. There are many conflicting report regarding the alteration of lipid profile in bronchial asthma. Some author's report that serum HDL-c is raised & total cholesterol is increased [15-17]. Other that LDL-c registers a decrease in bronchial asthma [18].

Therefore we have conducted this study to look for lipid profile and lipid peroxidation status in bronchial asthma patients of this area. Keeping this in view we have measured serum total cholesterol, triglyceride, LDL-c, HDL-c & VLDL-c along with plasma superoxide dismutase activity & serum MDA level in bronchial asthma patients &compared with normal healthy individuals observe any oxidative stress & dislipidemia in bronchial asthma which may affect the disease.

MATERIALS AND METHODS

Study design: Case control analytical study

Ethics approval: Our study was approved by Institutional Ethical Committee (IEC) of our institution

Study location: Department of Biochemistry

Inclusion criteria: **Case**s: The study subjects were comprised of 50 cases (27 male and 23 female patients) of chronic bronchial asthma in between 40years to 60 years who had attended the OPD of TB and Chest department and diagnosed by history and clinical examination. **Control:** 50 participants, age and sex matched healthy individuals (29 male and 21 females) were considered as control group in this study.

Exclusion criteria: Smokers, steroid dependent patients and those suffering from chronic diseases which are likely to affect the lipid profile and oxidative stress were excluded from the study.

Grouping: Group 1: Control, Group 2: Case

Methodology:

The cases were assayed for serum lipid profile, plasma superoxide dismutase (SOD) and serum Malondialdehyde (MDA). Fasting blood sample from each patient and control were collected and analyzed for serum total cholesterol, triglyceride, HDL-c and LDL-c, VLDL- c, MDA and plasma SOD.

The assays of various parameters in this study were as follows:- The lipid profile estimation was done by random access fully automated analyzer. Principles of measurement of different component of lipid profile measured in the study are as follows [19].

Serum triglyceride	**GPO –Trinder method**
Serum total cholesterol	CHOD-PAP method
Serum HDL cholesterol	Phosphotungstic Acid method
Serum LDL cholesterol & VLDL cholesterol	Friedwald formula

Plasma SOD activity was estimated by a modified spectrophotometric method as described by Kakkar et al [20]. Serum MDA level was assessed by colorimetric method with Thiobarbituric acid (TBA) [21].

Statistical analysis: All the parameter between two study groups was compared by chi-square test, *p*-value < 0.05 was considered as statistical significant.

RESULTS

Gender distribution between two studies groups are shown in table no 1.

Table 1. Distribution of Groups–Gender wise

Group	**Total**	**Male**	**Female**
		Number	**Number**
Control (N=50)	**50**	**29 (58%)**	**21 (42%)**
Cases (N=50)	**50**	**27 (54%)**	**23 (46%)**

Table 2. Biochemical analysis (lipid profile and Lipid peroxidation levels) of two study groups

Parameters		**Case**	**Control**
		Mean ± SD	**Mean ± SD**
Lipid profile parameters (mg/dl)	**TG**	93.42±6.98	95.48 ± 7.97
	LDL	99.21±12.49	103.44±10.55*
	VLDL	18.68 ± 1.39	19.09 ± 1.59
	HDL	52.32 ± 3.58	44.58 ± 2.58**
	TC	170.2±12.17	167.12 ± 9.67
Lipid peroxidation marker	**SOD** (U/ml)	3.42 ± 0.74	7.16 ± 0.52**
	MDA (nmol/L)	5.91 ± 0.88	3.00 ± 0.40**

(Statistical significance: * = *p-value* <0.05, ** = *p*- value <0.001)

Above table shows that mean fasting serum triglycerides value of cases (93.42±6.98mg/dl) were slightly lower as compared to controls (95.48 ±7.97mg/dl).

Mean fasting serum total cholesterol of cases (170.22±12.17mg/dl) was slightly higher as compared to controls (167.12±9.67mg/dl).

Fasting serum HDL and LDL cholesterol level of cases respectively (52.32±3.58mg/dl), (99.21±12.49mg/dl) were found to be significantly higher when compared to controls (44.58±2.58mg/dl), (103.44±10.55mg/dl).

Mean fasting serum VLDL cholesterol of cases (18.68±1.39mg/dl) was lower as compared to controls (19.09±1.59mg/dl), but statistically not significant.

On comparison of lipid peroxidation status, we found that mean plasma SOD level of cases (3.42 ±0.74U/mL) was significantly lowered than controls (7.16±0.52U/mL). Serum MDA level of cases (5.91±0.88nmol/L) was higher as compared to controls (3±0.4nmol/L). This increase was statistically highly significant.

DISCUSSION

In this comparative study 50 patients of bronchial asthma were taken up as cases and 50 healthy individuals were considered as controls. To determine their lipid profile and lipid peroxidation status, we carried out estimation of serum total cholesterol, VLDL-c, HDL-c, LDL-c, TG, SOD & MDA level. All the data were tabulated & compared by suitable statistical test (chi-square).

On analysis of demographic data of two study group, we found that number of male cases were more as compared to females. It may be due to more exposure of males to environmental factors such as dust, allergen and other air pollutants. Many of the males' participants were industrial workers, employed in nearby jute industry.

FEV (in 1st min, FEV1) of bronchial asthma cases were found to be significantly lowered ($p< 0.001$) in comparison to controls. Asthma is a chronic inflammatory disease in which ongoing tissue injury and repair may result in irreversible fibrotic changes in the pulmonary airways leading to decline in lung function [22, 23]. Our study finding also corroborated with pathophysiology of asthma & previous studies.

On comparison of lipid parameters we found that serum Tg & VLDL-c level in bronchial asthma cases were lower & serum total cholesterol was little higher than that of controls. Both the findings were statistically not significant. Our observations were in concurrence with Bahar et. al [17] & Sahu et al [15].

Serum HDL-c level was found significantly higher than controls. Similar findings were reported earlier by different study groups. Increase in serum HDL-c level may be attributed to an increase activity of lecithin cholesterol acyl transferase (LCAT) enzyme and its activator. LCAT catalyses the conversion of surface phospholipids and free cholesterol into lysolecithin and cholesteryl ester. Movement of free cholesterol from cell membrane to nascent HDL is also promoted by LCAT. The esterified cholesterol is transferred from HDL to other lipoproteins with the help of cholesteryl ester transport protein (CEAP). Thus cholesteryl esters of HDL are transported to liver via chylomicron remnants and LDL. The LCAT system in this way involved in the removal of excess cholesterol from lipoprotein and its excretion through liver. Thus it appears that the rise in HDL-c in asthma patients may provide a protection from Ischemic heart disease (IHD) and it considered as anti-atherogenic. HDL particles have various anti-inflammatory and anti-oxidative properties. HDL improves endothelial function by stimulating endothelial nitric oxide production. Synthesis of alveolar surfactant is also promoted by HDL [, 15, 17, 22-24].

Serum LDL was found to be significantly lowered in our study. Earlier Nakazawa et. al also reported lowering of serum LDL in bronchial asthma & hypothesized that LDL receptors participate in the delivery of Cholesterol in to cells. Therefore with increased LDL receptors acting on cell membrane, there may be a resultant decline in serum LDL in bronchial asthma patients. This LDL inside the cell is necessary for synthesis of pulmonary surfactant [18].

In bronchial asthma cases oxidative damage happens because of growing production of reactive oxygen species (ROS). Increased oxidative stress occurs in the airways of bronchial asthma patients. Inflammatory and immune cells in the airways, such as macrophages, neutrophill and eosinophills release increased amounts of reactive oxygen species through Interleukins. These ROS can result in lung injury as a result of direct oxidative damage to epithelial cells and cells shedding. Action of ROS can produce many pathological features including changes in biochemical microenvironment with enhanced arachidonic acid release, increase synthesis of chemo attractant, glucocorticoids, resistance and impaired β-adrenergic responsiveness. This effect lead to airways smooth muscle contraction, increase airways reactivity, secretions and increased vascular permeability. Plenty of mediators including lipid mediators, chemokines, adhesion molecules and esinophil granule proteins (EPO) are promoters of ROS in patients of asthma. To neutralize this increased production of ROS, especially $O_2^{\bullet -}$ free radicals, SOD are increasingly utilized. Thus a decline in plasma SOD level in bronchial asthma patients is anticipated. Similar finding of significant decrease of SOD level in bronchial asthma cases was observed in comparison to healthy controls in our study [25].

We observed that serum MDA level in bronchial asthma cases is significantly raised as compared to the con-

trol. Increased in MDA is expected in situations of increased oxidative stress. As described earlier increased oxidative stress in bronchial asthma also initiates lipid peroxidation. Once lipid peroxidation is initiated, a propagation of chain reactions will take place until termination products are produced. The main primary products of lipid peroxidation are lipid hydro peroxides. Among the many different aldehydes which can be formed as secondary products during lipid peroxidation are Malondialdehydes (MDA), propanal, hexanal and 4-Hydroxynonenal (4-HNE). MDA appears to be most mutagenic product and 4-HNE is the most toxic. Arachidonic acid is increased in airway inflammatory cells of bronchial asthmatic patients. This arachidonic acid may undergo oxidation to produce end product of lipid peroxidation. So MDA is increased in bronchial asthma due to generation by decomposition of arachidonic acid and larger PUFA through enzymatic and nonenzymatic processes. It is more chemically stable and membrane permeable than ROS and less toxic than 4-HNE. Once formed MDA can be enzymatically metabolized or can react on cellular and tissue proteins or DNA to form adducts resulting in bimolecular damage [26-29].

CONCLUSION

In conclusion lipid profile in bronchial asthma patients (raised HDL& decreased LDL) provides some degree of protection to this patients against ischemic heart disease (IHD). But increase in lipid peroxidation as evidenced by decreased plasma SOD & raised serum MDA aggravate airway inflammation, smooth muscle contraction & increased vascular permeability.

Conflict of interest: There is no conflict of interest of authors.

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