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Asthma and Diabetes: A Review of the Literature.

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ABSTRACT

Asthma and diabetes are the fastest growing disease in India. Both asthma and diabetes are interlinked in many aspects. Asthma, a major problem facing in our polluted environment. It is a reversible and curable disease. Like diabetes the prevalence is increasing day by day so the drug makers earning in millions because of asthma. treatment of asthma includes with the class of drugs from beta blockers (Salbutamol, formoterol) and inhaled corticosteroids (beclomethasone, budesonide). Majorly compare with the oral and I.V's, Inhalation route has more efficacy. On the other hand diabetes mellitus, describes a group of metabolic diseases in which the person has high blood glucose (blood sugar), either because insulin production is inadequate, or because the body's cells do not respond properly to insulin, or both. Most of the Patients with high blood glucose or sugar level will typically experience frequent urination, they will become increasingly thirsty and hungry. the treatment of diabetes includes sulfonylureas (glimepiride, glibenclamide), biguanides (metformin), Alpha-glycosidase inhibitors (acarbose, voglibose), Thiazolidinediones (pioglitazone), Meglitinides (repaglinide) and gliptins (sitagliptin, vildagliptin). in this review article we clearly established the correlation between asthma and diabetes through various studies.

Keywords: Relievers, Controllers, LABA, ICS, Diabetes, Biguanides, Thiazolidones.

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INTRODUCTION

Diabetes is a lifelong disorder, which is markedly affected by day to day variations in diet, exercise, infection and stress. These factors have to be addressed on daily basis while managing diabetes and the patient is the person best equipped to deal with the situation. Hence, a thorough knowledge of the disease and how it alters normal body functions and the awareness of its acute and chronic complications is necessary .it enables the diabetic patient to take better care of him or herself. Awareness of diabetes, its complications and better health care has proved to improve the long term outlook of this disease. The management of diabetes is intimately linked to food therefore; knowledge about food and nutrition and the scientific base of biochemistry, physiology, and pathogenesis go a long way towards the understanding and dealing with the disorder [1]

Asthma, a major problem facing in our polluted environment. It is a reversible and curable disease. Like diabetes the prevalence is increasing day by day so the drug makers earning in millions because of asthma. Still in rural areas most of the people thought that asthma is because of god's curse. In olden days it was recognized in Ancient Egypt and was treated by drinking an incense mixture known as kyphi [2].It was officially named as a specific respiratory problem by Hippocrates circa 450 BC, with the Greek word for "panting" forming the basis of our modern name [3].In 200 BC it was believed to be at least partly related to the emotions [4].

In recent days, Asthma constitutes a heavy medical, social, and economic burden, and its prevalence is steadily increasing worldwide [5]. Indeed, asthma affects over 300 million people around the world, and some epidemiologic projections estimate that this number will increase further during the next few decades [6].

ASTHMA

Definition:

Asthma is a common chronic inflammatory disease of the airways characterized by variable and recurring symptoms, reversible airflow obstruction and bronchospasm [7]. As per the Global Initiative for Asthma (GINA) defined as "a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction within the lung that is often reversible either spontaneously or with treatment"[8, 9].

Symptoms of asthma include [10]:

- Episodic breathlessness or dyspnoea (especially at night or early morning, or after some exertion)
- Wheezing
- Cough (especially at night or early morning, or after some exertion)
- Chest tightness
- In children, often, the only symptom may be coughing at night or early morning, and after physical activity.

Types of asthma:

Asthma may also be classified as atopic (extrinsic) or non-atopic (intrinsic) [11] where atopy refers to a predisposition toward developing type 1 hypersensitivity reactions [12].types of asthma are: child onset asthma (asthma from childhood)[13], adult onset asthma (asthma during adult age or >18 years) [14], exercise induced asthma (experienced asthma during exercises)[15], cough induced asthma, occupational asthma (affected by asthma in occupational sites i.e., industry, polluted environment etc.) [16], nocturnal asthma, steroid resistant asthma and brittle asthma. [17]

Treatment:

Most of the asthma medications are in inhalation routes. The class of drugs used are β_2 agonists [18], inhaled corticosteroids, anti-cholinergic and leukotriene antagonists.

Relievers:

These are basically bronchodilators-they dilate the bronchus. It meant to be used for immediate relief of symptoms. It has a short duration of action. It can be used up to 3-4 times per day. Frequent use of relievers indicates poor control of asthma and probable under use of preventors. Relievers are also used as rescue medicines or SOS treatment in acute cases. These include the class of drugs known as short acting β_2 agonists (salbutamol and levosalbutamol)[19]. In India most of the people using Salbutamol, levosalbutamol and Ipratropium as relievers.

Controllers [20]:

It takes time to act and control airway inflammation, i.e., the root pathology of asthma. Most preventers need to be administered only once or twice daily, since they have a prolonged effect. In controlling asthma inflammation on an ongoing basis, the anti-inflammatory corticosteroids are used to reduce inflammation in moderate to severe asthma. Interaction between corticosteroids and long-acting β_2 -agonists (LABA). Corticosteroids have anti-inflammatory effects but also increase the numbers of β_2 -Receptors, whereas β_2 -agonists, as well as inducing direct bronchodilation, act on Glucocorticoid receptors to increase the anti-inflammatory effects of corticosteroids[20]. Inhaled corticosteroid available in India are budesonide, ciclesonide, mometasone, beclomethasone and fluticasone. In case of LABA formoterol and salmeterol are widely used in India.

DIABETES

Diabetes is a major cause of morbidity [21, 22]. And mortality worldwide [23]. The word diabetes is from the Greek diabane in which means to pass through, in reference to the excessive urine produced as a symptom of these diseases. And the term diabetes, without qualification, usually refers to diabetes mellitus, which roughly translates to excessive sweet urine (known as "glycosuria").

Types of Diabetes:

Majorly diabetes can be classified into three broad classifications, they are type 1, type 2, and gestational diabetes.

Causes of Diabetes:

Diabetes having so many causes they are, In type 1 diabetes is also partly inherited and then triggered by certain infections, with some evidence pointing at Coxsackie B4 virus. In case of type 2 diabetes, it is due to a combination of lifestyle [24]. And genetic factors [25]. Several numbers of changes in life and food habit modifications. The other causes include age, obesity, food habit modification, etc. [26]

Treatment:

Type 1 treatments usually include combinations of regular or NPH insulin, and/or synthetic insulin analogs. And for the treatment of type 2 diabetes mainly people are preferred oral medications the oral drugs[27], classes include sulfonylureas (glimepiride (brands like Glimy), glibenclamide (daonil)[28], biguanides (metformin (glycomet)[29], Alpha-glycosidase inhibitors (acarbose, voglibose (volix)), Thiazolidinediones (pioglitazone (pioz), Meglitinides (repaglinide) and gliptins (sitagliptin, vildagliptin (jalra)). Most of the physicians are prescribing each and every drug from the classes for their patients' satisfaction in diabetes. But some studies say that long term usage of diabetic medications will help the patients to experience the neuropathy, retinopathy and nephropathy.

Correlation of Asthma and Diabetes:

In this review we clearly explained about the correlation of Asthma and diabetes with supporting articles .Asthma is a chronic inflammatory lung disease affecting nearly 300 million people globally, and its prevalence is on the rise in many parts of the world [30]. In addition to being a major cause of morbidity in-and-of itself, asthma may be a potential risk factor for the development of proinflammatory conditions such as type 2 diabetes (T2D) [31]. Possible Mechanisms for the hypothesized link between asthma and increased risk for T2D include genetic pleiotropy [32], effects of lung-related inflammatory cytokines on insulin sensitivity [33], Effects of hypoxia on glucose metabolism [34], and adverse early-life exposures [35] and their effects on organ development [36].

One retrospective and two prospective [37] studies have reported findings on the association between asthma and T2D in adults. In the Nurses' Health Study, asthma was not associated with increased risk of T2D [38]. However, the Women's Health Study reported a 1.5-fold increased

T2D risk for women with asthma, after adjusting for baseline BMI and other potential confounders [39]. A recent population-based retrospective matched case-control study found a greater than 2-fold increased risk of diabetes in asthmatics compared to those without asthma [40].

However, this study did not adjust for important confounders including adiposity, smoking, and other lifestyle factors [41]. There have been no prospective studies to date that have examined whether the asthma-diabetes association exists in both males and females or is specific to women[42], as has been reported in studies of asthma and cardiovascular disease [43], or if the association is present in non-Western populations. Furthermore, whether the asthma-diabetes association differs by asthma age-at-onset was not assessed in previous studies. Asthma is a heterogeneous disease presenting with various immunologic, physiologic, and pathologic phenotypes [44]. Child- and adult-onset asthma differ with respect to asthma triggers [45], sex, and patterns of inflammation[46].

Asthma and COPD are inflammatory lung disorders associated with significant morbidity and mortality worldwide [47]. Their commonly reported co morbidities include cardiovascular disease, diabetes mellitus, hypertension, osteoporosis, and other chronic medical conditions [48]. Respiratory viral and bacterial infections, tobacco smoking, and pollutants are important factors in triggering a plethora of inflammatory pathways that may mediate the relation of chronic lung diseases and their co morbid diseases. Although the inflammatory process in COPD is different from that in asthma in terms of inflammatory cells, mediators, and inflammatory response to therapy [49], there is growing evidence to show a role of several common inflammatory signaling pathways in the pathogenesis of both asthma [50] and COPD [51].

Low-grade inflammation as reflected by elevated levels of many proinflammatory biomarkers such as interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), C-reactive protein (CRP), and adhesion molecules has been recognized as a major contributor to the development of type 2 diabetes [52,53]. It thus seems reasonable to speculate that elevated circulating levels of certain inflammatory cytokines caused by chronic airway inflammation may also contribute to the development of insulin resistance in the liver, skeletal muscle, and vascular endothelium, ultimately leading to the clinical expression of type 2 diabetes.

In epidemiologic studies, several cross-sectional studies have suggested that lung function impairment was associated with high prevalence of the metabolic syndrome [54] and type 2 diabetes, even after adjusting for adiposity. Several prospective studies have shown inverse associations between lung functions and risk for developing insulin resistance or type 2 diabetes in non diabetic individuals' from diverse populations [55-57].

One recent prospective cohort study from the Nurses' Health Study reported increased risk of type 2 diabetes associated with patients with COPD but not among asthma patients. Although the differences in the diabetes risk between patients with COPD and those with asthma may reflect the different underlying inflammatory processes in asthma and COPD, no other independent studies have confirmed this relationship. We therefore prospectively examined the association of asthma and COPD with risk of type 2 diabetes in a large cohort of women with over 12 years of follow-up. In addition, we investigated whether the associations would vary for the presence of asthma and/or COPD when examined separately and whether they would differ

according to levels of potential factors, including age, BMI, smoking status, physical activity, alcohol intake, postmenopausal hormone use, and menopausal Status.

The prevalence of type 1 diabetes [58, 59] and asthma [60,61] has escalated in the industrialized world over recent decades. Due to industrialization most of the companies are shifted to the rural area also. Now a day's people from rural are more prone to get affect from asthma. Extensive research efforts are aiming to uncover the immunological mechanisms behind these diseases in order to reverse this trend with novel immunomodulatory preventative procedures.

An explanatory model has consequently emerged, whereby the predominance of T-helper type 1 (Th1) cells is characteristic of type 1 diabetes and other autoimmune disease, whereas Th2 polarized immunity is attributed to allergy, asthma and other atopic disease [62]. This widely accepted Th1/Th2 paradigm presents the said immunological conditions as antagonistic causes of autoimmune and allergic disease. However, epidemiological studies have shown that type 1 diabetes and asthma tend to simultaneously cluster within populations [63].

In addition, the diseases can clinically coexist in the same individual [64]. These findings are in stark discordance with the traditional Th1/Th2 paradigm. Recently, a unifying hypothesis has been presented that can explain the simultaneous increase of autoimmune and allergic disease [65]. Modern lifestyle with increased hygiene awareness and declined numbers of siblings has led to reduced microbial stimulation in infancy. This reduced exposure to microbes can lead to deficient maturation of regulatory T-cells and antigen-presenting cells. Regulatory-cells have a substantial influence on the development and function of the immune system, guarding against both hyper responsiveness and autoimmunity. Antigen-presenting cells such as the dendritic cell also play a pivotal role in initiation of all immune responses [66], both beneficial and pathogenic, and their functions appear to have important tolerogenic effects. Defects in immune regulatory mechanisms can potentially lead to aberrant immune responses to allergens, as well as to detrimental autoimmunity.

There is a high and rising rate of immune-mediated diseases in the Western world. Immigrants from South Asia have been reported to be at higher risk upon arrival to the West. So to study about the risk of immune-mediated diseases in South Asian and other immigrants to Ontario, Canada, and their Ontario-born children.

Population-based cohorts of patients with asthma, type 1 diabetes (T1DM), type 2 diabetes (T2DM), and inflammatory bowel disease (IBD) were derived from health administrative data. They determined the standardized incidence, and the adjusted risk of these diseases in immigrants from South Asia, immigrants from other regions, compared with non-immigrant residents of Ontario. The risk of these diseases in the Ontario-born children of immigrants were compared to the children of non-immigrants.

Compared to non-immigrants, adults from South Asia had higher risk of asthma (IRR 1.56, 95%CI 1.51-1.61) and T2DM (IRR 2.59, 95%CI 2.53-2.65). Adults from South Asia had lower incidence of IBD than non-immigrants (IRR 0.32, 95%CI 0.22-0.49), as did immigrants from other regions (IRR 0.29, 95%CI 0.20-0.42). Compared to non-immigrant children, the incidence of asthma (IRR 0.66, 95%CI 0.62-0.71) and IBD (IRR 0.47, 95%CI 0.33-0.67) was low amongst immigrant children from South Asia. However, the risk in Ontario-born children of South Asian immigrants relative to the children of non-immigrants was higher for asthma (IRR 1.75, 95%CI 1.69-1.81) and less attenuated for IBD (IRR 0.90, 95%CI 0.65-1.22)[67].

They concluded that Early-life environmental exposures may trigger a genetic predisposition to the development of asthma and IBD in South Asian immigrants and their Canada-born children.

African American women are disproportionately burdened by asthma morbidity and mortality and may be more likely than asthma patients in general to have comorbid health conditions. This study sought to identify the self-management challenges faced by African American women with asthma and comorbidities, how they prioritize their conditions and behaviors perceived as beneficial across conditions. In-depth interviews were conducted with 25 African-American women (mean age 52 years) with persistent asthma and at least one of the following: diabetes, heart disease or arthritis. Information was elicited on women's experiences managing asthma and concurrent health conditions. The constant-comparison analytic method

was used to develop and apply a coding scheme to interview transcripts. Key themes and subthemes were identified.[68]

Participants reported an average of 5.7 comorbidities. Fewer than half of the sample considered asthma their main health problem; these perceptions were influenced by beliefs about the relative controllability, predictability and severity of their health conditions. Participants reported ways in which comorbidities affected asthma management, including that asthma sometimes took a “backseat” to conditions considered more troublesome or worrisome. Mood problems sometimes attributed to pain or functional limitations resulting from comorbidities, reduced motivation for self-management. Women described how asthma affected comorbidity management; e.g. by impeding recommended exercise. Some self-management recommendations, such as physical activity and weight control, were seen as beneficial across conditions.

This study concluded that multiple chronic conditions that include asthma may interact to complicate self-management of each condition. Additional clinical attention and self-management support may help to reduce multimorbidity-related challenges.

Thiazolidinediones are oral diabetes medications that selectively activate peroxisome proliferator activated receptor gamma and have potent anti-inflammatory properties. While a few studies have found improvements in pulmonary function with exposure to Thiazolidinediones, there are no studies of their impact on asthma exacerbations. The objective of this study is to assess whether exposure to Thiazolidinediones was associated with a decreased risk of asthma exacerbation. They performed a cohort study of diabetic Veterans who had a diagnosis of asthma and were taking oral diabetes medications during the period of 10/1/2005 – 9/30/2006. The risk of asthma exacerbations and oral steroid use during 10/1/2006 – 9/30/2007 was compared between patients who were prescribed Thiazolidinediones and patients who were on alternative oral diabetes medications. Multivariable logistic regression and negative binomial regression analyses were used to characterize this risk. A sensitivity analysis was performed, restricting our evaluation to patients who were adherent to diabetes therapy. They identified 2,178 patients who were on Thiazolidinediones and 10,700 who were not. Exposure to Thiazolidinediones was associated with significant reductions in the risk of asthma exacerbation (OR = 0.79, 95% CI, 0.62 – 0.99) and oral steroid prescription (OR = 0.73, 95% CI 0.63 – 0.84). Among patients who were adherent to diabetes medications, there were more substantial reductions in the risks for asthma exacerbation (OR = 0.64, 95% CI 0.47 – 0.85) and oral steroid prescription (OR = 0.68, 95% CI 0.57 – 0.81). At last they concluded that Thiazolidinediones may provide a novel anti-inflammatory approach to asthma management by preventing exacerbations and decreasing the use of oral steroids [69]

Both severe asthma and obesity are growing health problems. Severe asthma leads to a poor quality of life. The relationship among BMI, co morbidities and severe asthma control in adults is still unclear. In this study they discussed about the effect of the co morbidities as atopy, type II diabetes, gastroesophageal reflux, hypertension, cardiovascular diseases, osteoporosis, infections, and psychological factors with BMI on asthma control in a cohort of adult severe asthmatics. One hundred and two patients were enrolled in a cross-sectional study assessing asthma control, treatments, pulmonary function, inflammatory markers, and co morbidities. Patients were divided into 3 classes according to BMI: normal weight, overweight, and obese. We found that the optimal state of asthma control is lower. whereas the score of Asthma Control Questionnaire, the number of asthma exacerbations during last year, the oral corticosteroids requirement during the previous year, and the LABA treatments are higher in obese than in overweight and normal weight severe asthmatics. The number of subjects with type II diabetes is higher among obese and overweight patients than in normal weight asthmatics. Finally they concluded that BMI represents a factor for the deterioration in disease control in severe asthma.[70]One of the study which suggests patients with asthma and diabetes mellitus have an increased incidence of sleep apnea and GERD.in addition ,these patients have higher total cholesterol and triglyceride levels and require higher doses of statin medication to those with type 2 diabetes alone.[71]

CONCLUSION

Asthma and diabetes are one of major problem facing in our country. Because of these diseases, pharmaceutical companies earning their profits in Billions. This is the time to wake up and prevent from both the asthma and diabetes by maintained pollution free environment, balanced diet, controlled food modifications.

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