

The Factor Risk of Obesity to Asthma and Intervention Study of Treatment Technique: A Systemic Review

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Abstract

Asthma has increased by 2.0 and 2.3 times in obese children and adults. Obesity is also associated with inflammation and control of asthma which can be mediated by increased respiratory tract inflammation and hyper responsive respiratory tract. Systematic Review and meta-analysis method by using PRISMA-P 2015 were used in this study. We were collected through searching electronic literature from Scimedirect, Researchgate and Google Scholar. Based on the literature study method conducted in 25 related journals, it can be summarized that there are similar perceptions of the results of analysis where asthma is closely related to obesity due to several main factors. Obesity impact as an important role in the development of respiratory diseases. Asthma and obesity are complex and multifactorial which greatly affects health conditions, where the body's internal factors and environment play an important role in the health and quality of life of the community. Weight loss can improve lung function, reduce the possibility of asthma, and improve overall health status. Appropriate treatment techniques for individuals suffering from acid obesity can be done through simvastatin therapy and increased body adiponectin.

Keywords: *Asthma, obesity, breathing, treatment, exercise*

1. Introduction

In recent years, the mechanism underlying the relationship between obesity and asthma is widely investigated. The prevalence of obesity has increase, about 65% of the population in the US is classified as overweight or obese. Obesity is a known risk factor for causing many diseases in humans, including asthma, cardiovascular disease, diabetes, and certain types of cancer [X. Song, B. Li et al & L. guellimault. 2019].

Asthma is a type of long-term or chronic disease in the respiratory tract that is characterized by inflammation and narrowing of the airways which causes tightness or difficulty breathing. In addition to difficulty breathing, people with asthma can also experience other symptoms such as chest pain, and coughing [L. guellimault. 2019, J.A. Lucas et al 2018].

Based on several studies in Asia, the prevalence of asthma varies from 0.7% - 11.9%. The prevalence of asthma in China is reported 0.7 - 3.8%, Korea 3.6 - 6.8%, Iran 1.4 - 6.1%, India 2.4 - 3.5%, and the prevalence of asthma in South and Southeast Asia, 2.4 - 3.9%. Whereas in Indonesia, an increase in asthma prevalence from 4% in 2007 to 4.5% in 2013. West Java Province has a higher asthma prevalence compared to the national asthma prevalence of 5% [Risksedas, 2013]

The National Health and Nutrition Examination Survey (NHANES) data shows that one in three asthma patients is obese and the prevalence of obesity among current asthma subjects has increased from 21.3% to 32.8% [F. Rusconi, M. Popovic 2017]. An EAACI meta-analysis showed that almost twice as much weight gain triggered the possibility of asthma.

In our analysis of the 2013-2014 National Health and Nutrition Examination Survey (NHANES), a total of 1,375 adult male participants were involved. Among them, 12.65% had asthma [Y. Tomita et al. 2019]. Several studies have shown that asthma is a risk factor for obesity that is positively correlated with BMI. Regarding the BMI threshold for diagnosing an increased risk of asthma, previous studies from Western countries have shown an increase in the prevalence of asthma with a BMI higher than 25 kg / m or 30 kg / m [Y. Tomita et al. 2019, M.To, K. Haruki, 2018, R barros 2017].

Generally the respiratory system of obese people has a high respiratory rate and low tidal volume which increases the risk of asthma and the severity of asthma. In addition, many studies have shown that

obstruction of obesity- induced lipid metabolism and changes in endocrine function of adipose tissue worsen the condition of asthma [L. Zhu, X. Chen 2019].

Cross-sectional studies in children and adults have shown that plasma leptin levels are higher in asthma patients [C.T. Juel, C.S. Ulrik, 2013]. Increased levels of leptin are the physiopathological basis of metabolic disorders and systemic inflammatory reactions [Gibeon D, et al. 2013] Leptin is positively correlated with total body fat mass and may also play an important role in the pathogenesis of asthma. Leptin is a fat originally identified as a hormone released by adipocytes and positively correlated with total body fat mass [Ostrom NK, et al. 2013].

Correlation analysis shows that there is a positive correlation between the percentage of neutrophils and serum leptin / cholesterol levels, which suggests that the efficacy of simvastatin therapy in asthma obesity may be related to an increase in dyslipidemia and a decrease in leptin levels [Abd El-Kader MS, et al. 2013, Chen Z, et al. 2017]. Cumulative studies have shown that the protein hormone adiponectin can produce beneficial anti-inflammatory effects [Westergren T, et al. 2016]. Thus, the findings of this study indicate that adiponectin can be used as a new pharmacological intermediary for treating asthma in obese individuals [Westergren T, et al. 2016]. Based on the description above, the author would like to know a review of obesity with asthma and the collection of research on interventions carried out for cases of obesity against asthma. In the study of obesity with asthma there has been a lot of literature that discusses it for conversion studies in cases of obesity against asthma not yet seen in Indonesia, so this needs to be used as a review journal to obtain benefits and research for the intervention of obesity cases against asthma.

2. Method

Search Strategy

In this study we conduct a writing system using the PRISMA method (Preferred Reporting Items for Systematic Reviews and Meta-analyzers). We search three source databases, namely Scencedirect, Researchgate and Google Shcolar to take peer- reviewed publications from publications relevant to the titles we adopted. Database search based on publications from 2013 to 2019. The search term covers 4 aspects, namely asthma, obesity, breathing, medication and exercise.

Eligibility Criteria

This study reviews the problem of asthma related to obesity. In the first stage, we classified the titles and abstract studies that will be used as the study literature. There are limitations to the reference grouping including the language in which we only refer to the literature with the study of English and Indonesian; then the country of origin of study where we only take from studies in the Asia region and Europe only; and finally the factors associated with asthma are narrowed by only seeing references related to asthma against obesity. The exclusion criteria for the study are outside the boundaries of the above compilation that are irrelevant.

Data Extraction

The literature data is sought and summarized for 2 weeks starting from April 1, 2019 according to the scope of this study. Compilation was carried out independently by two authors. The main section of the review study contains titles, abstracts, and discussions filtered to identify studies that include relevance for reference. Reviewing the contents of reference studies is also done carefully so that it is easy to find the essence of the related study. The criteria for grouping this study will lead us to conclusions. The research data from the literature are summarized in the form of tables and pictures of structured study results and given an explanation according to the results of the study. The conclusion in this study is that we combine it based on the results of the reference conclusions.

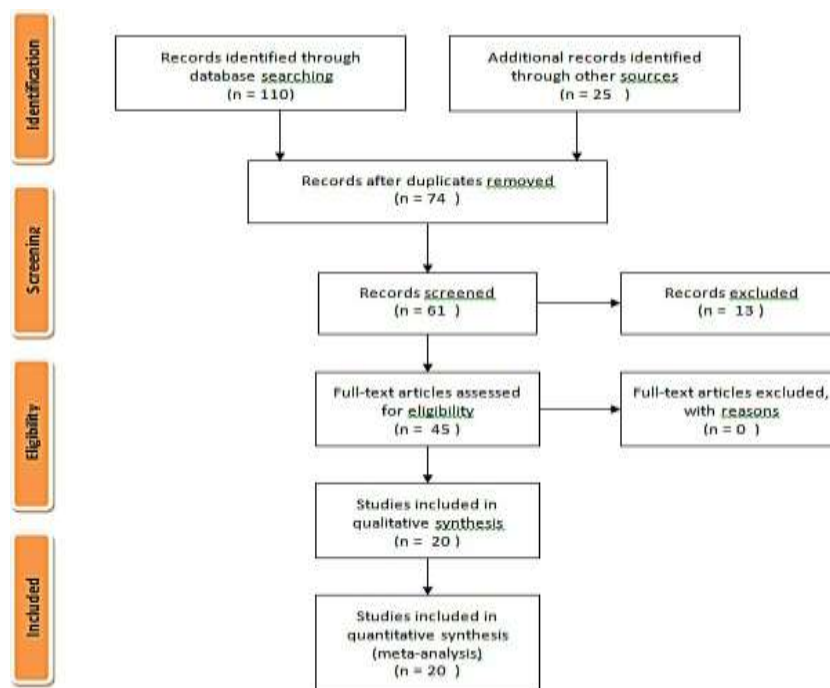


Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) Method

3. Result

Quantity of systematic reviews

Based on the stages of the PRISMA method used, we looked for 135 records identified from 3 bases (Sciencedirect, Researchgate and Google Shcolar) and obtained 74 single quotes, then manually selected for possible entry as a related reference. After filtering 61 literature, 13 literature were released because there was no relevance. Furthermore, there are 45 remaining records / literature assessed for eligibility. The literature reviews the relationship and interrelated factors between obesity and asthma in several regions and the range of sufferers, while also examining matters related to treatment techniques that can be done. From the results of the feasibility of the study, only 20 literature were found that had been observed meeting the topic of the study.

Korelation Between Obesity Against to Asthma

From the 20 literature studies reviewed showed that 10 references mention obesity is a known risk factor for causing many diseases in humans, including asthma. Complications of obesity are very relevant to chronic inflammation (asthma). 5 references state that the respiratory system of obese people has a high respiratory rate and low tidal volume which increases the risk of asthma and the severity of asthma. In addition, 3 study references concluded that impaired obesity-induced lipid metabolism and changes in endocrine function of adipose tissue worsen asthma conditions, can change the efficacy of standard asthma drugs, which make asthma patients respond poorly to treatment. The remaining 2 other references state that Simvastatin and adiponectin treatment can be used as new pharmacological tools to treat asthma in individuals with asthma obesity. 20 These references are summarized in Table 1.

Table 1. Correlation Between Obesity Against to Asthma

No.	Journal Title	Database	Place of Journal	Journal Author	Relation Between Astma and Obesity
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1.	Exercise induced bronchospasm, asthma control, and obesity	Allergy Asthma Proceeding	USA	Ostrom NK et al, 2013	Exercise-related respiratory symptoms occur more commonly in patients with not well and very poorly controlled asthma. Obesity was found more often in adolescents and adults, but not children, with asthma, which was not well and very poorly controlled
2.	Impact On Severity, Asthma Control, And Response To Therapy, Respir	Respire Care	Denmark	C.T. Juel et al, 2013	Overweight and obesity is associated with poorer asthma control and, very importantly, overall poorer response to asthma therapy, compared with normal weight individuals.
3.	Obesity-Associated Severe Asthma Represents a Distinct Clinical Phenotype	Original Research Asthma (CHEST)	England	Gibeon D, 2013	Patients with severe asthma display particular characteristics according to BMI that support the view that obesity-associated severe asthma may represent a distinct clinical phenotype.
4.	Body Mass Index As Predictor For Asthma: A Cohort Study Of 118,723 Males And Females	European Respiratory Journal	Oslo	V. Hjellvik et al, 2014	Asthma incidence, as measured by anti-asthmatic drug use, was positively related to both BMI and change in BMI. For BMI, the association was stronger for never-smokers than for ex-smokers and current smokers.

5.	Linking obesity and asthma	New York Academy of Sciences	New York	E. Rand Sutherland, 2014	Epidemiologic, clinical, and translational studies suggest that obesity increases the risk of developing asthma while also making it more difficult to achieve optimal asthma control
6.	Obesity increases airway hyperresponsiveness via the TNF-alpha pathway and treating obesity induces recovery	Plos One	South Korea	J.Y. Kim et al, 2015	Restoring normal body weight is an appropriate strategy for reducing TNF- α levels, and controlling inflammation may help improve asthma severity and control in obesity-related asthma.
7.	Childhood obesity in relation to poor asthma control and exacerbation: a meta-analysis	European Respiratory Journal	Europe	Ahmadizar F et al, 2016	In asthmatic children, obesity is associated with a minor increased risk of asthma exacerbations but not with poor asthma control.
8.	Heterogeneity of obesity-asthma association disentangled by latent class analysis, the SAPALDIA cohort	Respiratory Medicine	Switzerland and	Ayoung Jeong et al, 2017	Obesity was positively associated with symptom-presenting asthma classes but not with symptom-free ones. Percent body fat showed the strongest association with the persistent multiple symptom-presenting asthma

9.	The Effect of Obesity to the Occurrence of Asthma in Fatimah Islamic Hospital Cilacap, Indonesia	Sainteks	Indonesia	Nurrizky haitamy, et al 2015	Chi square test results also showed significance of 0.002 which means there was effect between obesity and asthma in Fatimah Islamic Hospital Cilacap. Based on this research, conclusion can be drawn that there is an effect of obesity to the occurrence of asthma in Fatimah Islamic Hospital Cilacap (p=0,002)
10.	Obesity increases the prevalence and the incidence of asthma and worsens asthma severity	Clinical Nutrition	Portugal	R. Barros ae al, 2017	Obesity is associated in a dose dependent way with an increase of prevalent and incident asthma, and it seems to increase the odds of a more persistent and severe asthma phenotype independently of socio-demographic determinants, physical activity, and dietary patterns. Study results provide rational for future lifestyle intervention studies for weight reduction in the obesity asthma phenotype.
11.	Treatment of obese asthma in a mouse model by simvastatin is associated with improving dyslipidemia and decreasing leptin level	Biochemical and Biophysical Research Communications	China	W. Han et al, 2017	Simvastatin treatment reduces the levels of glucose, lipid, leptin and neutrophil percentage, and improves airway inflammation and remodeling, which can be as a potential therapeutic target used in the treatment of obese asthma in humans. Correlation analysis shows that there is positive correlation between neutrophil percentage and serum leptin/cholesterol level, which indicates that the

					therapeutic efficacy of simvastatin on obese asthma might be associated with improving dyslipidemia and decreasing leptin level.
12.	Efficacy of an exercise intervention among children with comorbid asthma and obesity	Public Health	USA	J.A. Lucas et al, 2018	The mean age of this population (N=232) was 11 years; 54% were male, 64% were hispanic, and 37% had asthma, study found both beneficial and practical for obese children with asthma for losing weight and improving cardiorespiratory function
13.	Obesity-associated severe asthma in an adult Japanese population	Respiratory investigation	Japan	Masako To et al, 2018	In the female cohort, the annual exacerbation ratio and the percentage of frequent exacerbators were significantly higher in the Obese group compared to the Non-Obese group. A multivariate logistic regression analysis showed that obesity was independently associated with frequent asthma exacerbations in the female cohort.
14.	Obesity and asthma	Journal of Allergy and Clinical immunology	Pittsburgh	U. Peters et al, 2018	Obesity is an important risk factor for asthma and asthma morbidity, both in children and adults This is a reflection of an obese asthma syndrome that is complex and multifactorial. Potential underlying mechanisms include a shared genetic component, dietary and nutritional factors, alterations in the gut microbiome, systemic

					inflammation, metabolic abnormalities, and changes in lung anatomy and function
15.	Asthma alleviates obesity in males through regulating metabolism and energy expenditure	BBA - Molecular Basis of Disease	China	Xiaomin Song et al, 2019	Found that Body Mass Index (BMI) and waist circumference were significantly lower in males suffering asthma and suggest asthma in males decreases obesity by improving the metabolism function of brown and subcutaneous adipose tissue, and decreasing insulin resistant in the liver
16.	Chronic cough and obesity	Pulmonary Pharmacology & Therapeutics	France	Laurent Guilleminault, 2019	The crucial role of obesity has been highlighted in the development and progression of many respiratory diseases, obesity, particularly abdominal obesity, may also be associated with chronic cough (CC)
17.	Obesity, but not metabolic syndrome, as a risk factor for late-onset asthma in Japanese women	Allergology International	Japan	Yasuhiro Tomita et al, 2019	Only the obesity measures, not metabolic syndrome, were shown to be significant risk factors for the incidence of late-onset asthma but only in middle-aged Japanese women, and not in men
18.	Severe asthma in Japan	Allergology International	Japan	Hiroyuki Nagase, 2019	The characteristic phenotype of severe asthma in Japan seems to be distilled into the following two features: low incidence of obesity and high prevalence of patients with type 2 inflammation. Only 5e7% of Japanese severe asthma patients had a body mass index (BMI) 30 kg/m and more than 80% of patients

					with severe asthma exhibited type 2 inflammation. Although the relationship between obesity and non-type 2 inflammation is complex, the low incidence of obesity might explain the prevalence of type 2 inflammation.
19.	Obesity and severe asthma	Allergology International	USA	H Tashiro et al, 2019	there is increasing evidence that obesity is causally related to asthma. Evidence of a role for the microbiome in obese asthma also suggests that greater attention to components of diet and their impact on the gut microbiome may ultimately prove useful for the obese asthmatic patient
20	Adiponectin alleviates exacerbation of airway inflammation and oxidative stress in obesity-related asthma mice partly through AMPK signaling pathway	International Immunopharmacology	China	Lili Zhu et al, 2019	Study was conclude that adiponectin alleviates exacerbation of airway inflammation and oxidative stress in a murine model of obesityrelated asthma partly through AMPK signaling pathway.

4. Discussion

Asthma is a chronic respiratory disease that affects around 235 million people worldwide. Asthma is chronic airway inflammation and is accompanied by other allergic diseases in some cases, which have a high incidence among children. An increasing number of epidemiological studies focus on obesity and asthma. The majority of them showed that asthma was positively associated with obesity [X. Song et al 2019].

Obesity is defined as a weight more than 20% above the ideal. Obesity can worsen asthma conditions, and change the efficacy of standard asthma drugs, which make asthma patients respond poorly to glucocorticoid treatment [L. Zhu, X. Chen et al, 2019]. At present, a large number of epidemiological results indicate a link between asthma and obesity. The effect of leptin levels due to obesity, lack of

adiponectin levels in the body, and improper treatment techniques can be a major source of obesity-related asthma.

Effect of Leptin Levels on Asthma Severity and the Role of the Technique for Treatment of Simvastatin

Obesity and induced asthma affect lung function. Generally the respiratory system of obese people has a high respiratory rate and low tidal volume which increases the risk of asthma and the severity of asthma. In addition, many studies have shown that obesity-induced lipid metabolism (high levels of leptin) induced and changes in endocrine function of adipose tissue worsen asthma conditions [F. Rusconi, et al, Y. Tomita 2019]. Moreover, an inappropriate asthma treatment system can aggravate asthma, especially in people with obesity. The study found that the weight of the obesity asthma group was 20% greater than ordinary mice but suffered from asthma. Asthma-obese mice have higher glucose, lipid and leptin levels. Symptoms of the obese asthma group are more severe than the normal asthma the obesity in asthma has more severe airway inflammation and structural changes, this clearly shows that obesity increases the severity of asthma. In addition, the obese asthma group has a higher percentage of neutrophils and the percentage of macrophages is lower than the asthma group. These results are influenced by higher levels of leptin levels [F. Rusconi, Tomita. 2019] Leptin is a pleiotropic hormone and also has proinflammatory effects involved in regulating the immune response. Recent studies have shown that leptin is involved in the severity of asthma [J.Y. Kim, J.H et al 2014].

Leptin is positively correlated with total body fat mass and may also play an important role in the pathogenesis of asthma. Leptin, a fat originally identified as a hormone released by adipocytes and positively correlated with total body fat mass [Westergren T 2014]. As an adipose signal, an increase in leptin levels means excess lipid storage, which is involved in modulating energy balance and limiting excess fat accumulation [L. Zhu, X. Chen et al, 2019]. Dill reported that leptin can increase leukotriene synthesis in alveolar macrophages, and leukotrienes play a central role in the pathophysiology of asthma, which implies that leptin may be involved in the occurrence and development of asthma. This finding suggests that leptin is associated with asthma, and can serve as a link between obesity and asthma [Abd El-Kader MS, et al. 2013, Chen Z, et al. 2017, Westergren T 2014] Treatment in obese asthmatics should pay attention to related causes such as excessive levels of leptin. A study shows that obesity increases asthma severity, and asthma obesity is a phenotype of refractory asthma [Gibeon D, et al 2013 & V. Hjellvik, A. Tverdal 2014] Refractory asthma patients are usually treated with systemic glucocorticoids or dexamethasone in clinical applications. But in obese asthma individuals, the study found that dexamethasone only suppressed airway inflammation, and did not have an effect on airway repair. In addition, obese asthmatics treated with dexamethasone will increase glucose, lipid and neutrophil levels so that they will worsen metabolic disorders and cause bad side effects. These findings suggest that obesity asthma may be an SR asthma subtype and responds poorly to these two treatments [Ostrom NK, et al 2019] Conversely, simvastatin can increase metabolic disorders, and suppress inflammatory airways and reformation. In addition, compared with dexamethasone, simvastatin treatment reduces the percentage of leptin. These results indicate that simvastatin is effective in the treatment of obesity asthma. Correlation analysis showed that there was a positive correlation between the percentage of neutrophils and serum statin levels which showed that the efficacy of the therapy of simvastatin in obesity asthma with decreased levels of leptin [Van Leeuwen JC et al, 2014]

5. Conclusion

Obesity causes an increased risk of asthma and the severity of respiratory symptoms by reduced lung function or airway hyperreactivity (AHR), although it contributes to the more difficult to control asthma individuals it is important to consider that in clinical management, obese individuals are encouraged to lose weight. Weight loss can improve lung function, reduce the possibility of asthma, and improve overall health status. For this reason, in order to reduce the number of obese asthma, it is recommended to control quality of life such as diet, food intake and increase physical activity. Appropriate treatment techniques for individuals suffering from acid obesity can be done through simvastatin therapy and increased body adiponectin.

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