Gender aspects, overnutrition, and air pollution in relation to asthma severity in adolescents

L A Garina1,*, F A F Mansoer2, M R Grahadinta3 and I Puspitasari3

1 Pediatric Department, Universitas Islam Bandung Medical School, Bandung 40116, Indonesia
2 Obstetric and Gynaecology Department, RSUD Al-Ihsan, West Java Province, Indonesia
3 Medical Education Program, Universitas Islam Bandung Medical School, Bandung 40116, Indonesia

* lisa.adhia@unisba.ac.id

Abstract. The prevalence of obesity in asthmatic patient has increased, and associated with worse asthma severity and quality of life. This study investigates the effect of gender and overnutrition on asthma severity. Observational study on 41 overnutrition (overweight and obese), and 41 normweight asthmatic adolescents in two primary high schools. Diagnosis and asthma severity based on GINA, ISAAC and Indonesian Paediatrician Association (IDAI). The BMI was converted to z score from WHO, and lung function was measured by spirometer. The statistical analysis was performed with the software SPSS v.20. The mean BMI in female was higher than male. The mean FEV1; FVC; FEV1/FVC in female was lower than male. The mean FEV1; FVC; FEV1/FVC in overnutrition was lower than normweight. Based on asthma severity: 39% intermittent, 39% mild persistent, 17% moderate persistent, and 5% severe persistent. As many as 77% of 47 females had persistent, of 41 overnutrition asthmatic adolescents 85% had persistent asthma. There are an impact of gender and overnutrition on asthma severity (OR: 4.4; 95% CI: 1.7-11.3; p=0.002 and OR: 9.1; 95% CI: 3.1-26.5; p<0.001). Among asthmatic adolescents the risk for persistent asthma was greater in females with overnutrition compare to males.

1. Introduction
Asthma is chronic inflammation disease involving the airways in the lung which results in hyperactivity and varying degrees of airway obstruction [1]. The history symptoms include episodes of wheezing, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation [2].

Asthma is a serious global health problem affecting all age group. Asthma affects an estimated 334 million individuals worldwide, with increasing prevalence in many developing countries [3].

Although not the highest cause of morbidity or mortality in children, asthma is an important health problem. If not manage properly, asthma can reduce the quality of life of children, limit daily activities, interfere with sleep, increase school attendance rates, and decrease academic achievement in school. For families and health care providers, uncontrolled asthma will increase health costs [1].

The international study of asthma and allergies in childhood (ISAAC) research shows that 14% of the child population has asthma symptoms and their prevalence varies between countries and study centers [3,4]. Research in several cities in Indonesia using the ISAAC questionnaire has varied results.
Prevalence ranged from 3% in Bandung (Kartasasmita CB) to 8% in Palembang (Tanjung) in the age group of 6—7 years, while in the age group of 13—14 years the range was between 2.6% in Bandung (Rosalina I) and the highest in Subang 24.4% (Sundaru) [1].

Asthma prevalence persists or decreases in some developed countries but increases rapidly in developing countries because of the westernized lifestyle [5]. The prevalence of asthma and obesity has increased in the last few decades in many countries. Based on surveys in the United States (USA) in children aged 0—17 years found 13% of obese children diagnosed with asthma [6].

The prevalence of overweight in West Java-Indonesia is 10.7%, and obesity is 7.9% in the 5—12 year age group, prevalence of overweight is 7.5% and obesity is 2.2% in the 13—15 year age group [7].

Asthma is difficult to control in patients with obesity. Factors influencing include gastroesophageal reflux, effects of obstructive sleep apnoea (OSA), mechanical factors, and other factors. Weight loss in obese patients will improve the degree of asthma control, pulmonary function and reduce the need for treatment [1]. Obesity causes inflammation and abnormal oxidative stress in the circulation, chest cavity restriction with narrowing of the airway and other comorbidities associated with obesity [8]. Obesity also causes respiratory air flow resistance by decreasing forced expiratory volume in 1 minute (FEV1) and forced vital capacity (FVC) [9].

There are gender differences in the incidence of asthma, the prevalence, and frequency of symptoms. After puberty, the prevalence of asthma is increase and more severe in female [10].

Asthma is 5—7 times more common in obese female children than in normal weight over the age of eleven [11]. Obese female have an increased risk of suffering from asthma symptoms (episodes of wheezing, asthma, asthma recurrence, frequency of asthma symptoms, and asthma triggered by exercise) [12].

The impact of obesity on asthma has more clinical manifestations in female than in male. A gender difference in the epidemiology of obesity and its impact on asthma shows that female sex hormones may contribute to an increased risk of asthma in obesity [13]. This study investigates the effect of gender and overnutrition on asthma severity.

2. Methods

There were 105 (4.1%) asthmatic adolescents from 2579 students. An observational study in 41 overnutrition (overweight and obese), and 41 normweight asthmatic adolescents in two public junior high schools (SMPN 1 and SMPN 9) in Bandung City from February to June 2018. The inclusion criteria in this study were adolescent with asthma age 11-14 years, not in acute attacks or exacerbations, fever, cough, runny nose, present in the study and agreed to participate. Exclusion criteria in this study were asthmatic children with under nutrition (wasted and severely wasted). Based on the inclusion and exclusion criteria, the study was conducted on 82 subjects consisting of 41 overnutrition and 41 normweight asthmatic adolescents by consecutive sampling.

Diagnosis and history of asthma based on the global initiative for asthma (GINA) and the international study of asthma and allergies in childhood (ISAAC) questionnaire. Severity of asthma classification based on national paediatric asthma guidelines from the Indonesian paediatric association (IDAI), consisting of:

- intermittent (episode of asthma symptoms <6x/year or period of symptom ≥6 weeks)
- mild persistent (episode of asthma symptoms >1x/month, <1x/week)
- moderate persistent (episode of asthma symptoms >1x/week, but not daily)
- severe persistent (episodes of asthma symptoms occur almost every day)

Body weight was measured by seca scales and height measured by microtoa, carried out 3 times and the mean value was taken to determine the value of Body Mass Index (BMI) in kg/m², then converted to z score curve based on WHO Child Growth Standard (WCGS) for each group by age and sex. Based on the classification of BMI indicators for age, divided into:
- severely wasted, z score below -3
- wasted, z score below -2
- normal, z score 0 to below -1
- possible risk of overweight, z score above 1
- overweight, z score above 2
- obese, z score above 3

Pulmonary function test (PFT) using a spirometer and determined the FEV1 (force expiratory volume in one second), FVC (forced vital capacity) and FEV1/FVC ratio. Percent predicted PFT values were computed for each individual.

The statistical analysis was performed with the software SPSS v.20. Significance test between variables using Pearson’s Chi-square test and also determined the value of Odd Ratio (OR).

The study was approved by the ethical committee of the Faculty of Medicine, Universitas Islam Bandung, West Java, Indonesia.

3. Results
The study included 82 asthmatic children, 41 overnutrition (overweight and obese), 41 normweight asthmatic adolescents, consisting of 35 males and 47 females. As many as 54.3% of males are of normweight, 53.2% of females are of overnutrition (overweight and obese).

The mean weight, height, body mass index (BMI), and results of lung function test based on gender as shown in Table 1.

| Variable     | Males       | Females      |
|--------------|-------------|--------------|
| Body weight  | 51.3 (11.8) | 50.8 (9.1)   |
| Height       | 153.7 (8.7) | 148.3 (6.3)  |
| BMI          | 21.6 (3.9)  | 23.1 (3.8)   |

Based on Table 2, obtained mean weight, height, body mass index (BMI), and lung function test results based on nutritional status.

| Variable     | Overnutrition (overweight and obese) | Normweight |
|--------------|---------------------------------------|------------|
| Body weight  | 57.5 (9.5)                            | 44.5 (6.0) |
| Height       | 150.4 (7.9)                           | 150.8 (7.8)|
| BMI          | 25.4 (3.4)                            | 19.6 (1.7) |

Based on asthma severity classification: 39% intermittent, 39% mild persistent, 17% moderate persistent, and 5% severe persistent (39% intermittent and 61% persistent asthma). As many as 77% of
47 females experience persistent asthma, from 41 overnutrition (overweight and obese) 85% have persistent asthma.

The results of the study showed that asthmatic adolescent with overnutrition and gender had an effect on the asthma severity, according to Table 3.

**Table 3.** Influence of gender and overnutrition on the asthma severity.

| Variable                        | Intermittent | Persistent | p       | OR (95% CI)          |
|---------------------------------|--------------|------------|---------|----------------------|
| Gender (n)                      |              |            |         |                      |
| Males                           | 20           | 15         | 0.002*  | 4.4 (1.7—11.3)       |
| Females                         | 11           | 36         |         |                      |
| Nutritional status (n)          |              |            |         |                      |
| Normweight                      | 25           | 16         | <0.0001*| 9.1 (3.1—26.5)       |
| Overweight and obese            | 6            | 35         |         |                      |

*Pearson’s Chi-square test

4. **Discussion**

The results of the present study found that the body mass index (BMI) of adolescent females with asthma was higher than males. Similar results were observed in previous study shows among adolescents with undiagnosed asthmatic symptoms at baseline, the risk of developing physician-diagnosed asthma one year later increased significantly for females with higher starting BMI, but not so for males. At the beginning of the study 23.9% of adolescent males and 23.9% of females had overnutrition and one year later, overweight and obesity increased in females to 34.8% [14].

Suh M et al obtained results among females, higher BMI was also significantly associated with higher prevalence of wheeze. However, one possible explanation is that because the prevalence of asthma or asthma symptoms in childhood is more common in males with a switch to increased prevalence in females by adolescent [15,16].

Female adolescents who were overweight or obese to start were respectively at a 12% and 75%, greater risk of developing asthma than those with normal weight. This pattern, however, was not observed in males.14 Females who developed overweight or obese at 11 years, were more likely to show new symptoms of asthma between ages of 11 or 13 years than no overweight group. The same study also found that the association between overweight or obesity and asthma was stronger in females who started puberty before 11 years of aged [17].

This study shows pulmonary function test (FEV1 and FVC) in females were lower than males. Similar result in previous study shows male adolescents generally had 20-25% larger lung capacity than their female counterparts. Small but statistically significant differences in the FEV1, FVC, and FEV1/FVC ratio were observed between the baseline and follow-up exams for both genders. Furthermore, both males and females diagnosed with asthma had lower than predicted pulmonary function tests at follow up.14 Circulating sex hormones changed with puberty; in males greater androgen levels associated with better lung function, while in females greater circulating oestrogen had a weak but significant negative association with lung function [18].

Similar to our study they found that percent predicted FEV1, FVC, and FEF25–75 were reduced in children with obesity; however, unlike our findings, they reported lower FEV1/FVC ratio in overweight and obese children compare to normal weight [19]. Other study found a negative linear relationship was found between BMI z-score and percent predicted FRC, ERV, RV, and absolute FEV1/FVC [20].

The studies show consistent data and evidence of association between decreased spirometer values of forced vital and capacity and forced expiratory volume on the first second with obesity in children and adolescents [21].

These differences results could be explained by the sample size, inclusion and exclusion criteria, and the variation in the degree of obesity in each study.
There was any relationship between overnutrition (overweight and obese) and asthma severity classification in female adolescents in this study. In females, the association remained after adjustment for confounders. Furthermore, the association between BMI and asthma severity was stronger in females with early menarche than in females without early menarche. Results support the role of hormonal factors in the severity of asthma. It is well known that increased BMI is related to rapid sexual maturation, increases oestrogen, and leads to early menarche [22]. Female sex hormones and their receptors favour asthma development, male sex hormones and their receptors have a protective effect. However, the role of male and female sex hormones in asthma pathogenesis is not entirely elucidated [11].

Obese respondents were less likely to be in asthma remission, and were more likely to have severe persistent asthma [23]. The mechanisms by which obesity adversely influences asthma prevalence and morbidity are not well understood, but several theories have been proposed. These include the mechanical effects of obesity on airway physiology, chronic systemic inflammation and oxidative stress, alterations in adipokines that are also important in immune regulation, and shared comorbidities, including SDB and gastroesophageal reflux disease [24].

Our study has several limitations. This study included small sample size, no include assessments of pubertal status, lack of distinction between overweight and obese categories, and persistent asthma classification (mild persistent, moderate persistent, and severe persistent).

Additional research will be required to determine whether the increased asthma risk results from asthma phenotypes differences based on bio molecular and hormonal aspects.

5. Conclusion
Among asthmatic adolescents the risk for persistent asthma was greater in females compare to males, and overnutrition (overweight and obese) more likely persistent asthma than normweight. These gender differences and overnutrition in asthma indicates the presence of different asthma phenotypes is a complex process.

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