Risk Factors of Asthma among Adolescent and Adults: A Systematic Review Study and Meta-Analysis

Sri Iswahyuni[1], Rejo[1], Sri Sayekti Heni Sunaryanti[1], Asruria Sani Fajriah[2], Tri Yuniarti[1], Isnani Nurhayati[1]

[1]School of Health Sciences Mamba'ul Ulum Surakarta, Central java, Indonesia
[2]Institute of Health Sciences Strada Indonesia Kediri, East Java, Indonesia

ABSTRACT

Background: Asthma is a global public health problem that affects the quality of life of patients and is associated with the number of deaths each year. Factors such as genetics, environment and behavior are believed to have a significant relationship to the development of asthma. This study aimed to identify risk factors for asthma in adolescents and adults.

Subjects and Method: This was a systematic review and meta-analysis with a search for articles published by the online database PubMed in 2016 to 2021. The dependent variable was asthma. The independent variables were several risk factors that influence diseases such as smoking, age, and others. Data were analyzed using RevMan software version 5.3.

Results: A subgroup analysis was conducted from 4 articles which stated that cardiovascular related There were a total of 12 articles analyzed in this study. Subjects who had allergic rhinitis (OR= 3.80; 95% CI= 1.65 to 8.77; p= 0.001) had a greater risk of developing asthma than those who did not. This also applies to subjects who smoke (OR= 1.53; 95% CI= 1.32 to 1.78; p= 0.001), live in urban areas (OR= 1.46; 95% CI= 1.13 to 1.89; p= 0.03), are female. (OR= 1.19; 95% CI= 0.91 to 1.55; p= 0.001).

Conclusion: Asthma is more susceptible to people who have allergic rhinitis, smoke, live in urban areas, are female.

Keywords: asthma, prevalence, risk factors.

Correspondence:
Sri Iswahyuni. School of Health Sciences Mamba'ul Ulum Surakarta, Central java, Indonesia. Email: iswahyunisri@yahoo.co.id. Mobile: +62 815-6720-715.

BACKGROUND

Chronic respiratory disease accounts for 4.7% of disability-adjusted life years (DALYs) globally, of which asthma accounts for one-fifth of the total (Murray et al., 2012). Asthma is a chronic inflammatory disease of the respiratory tract characterized by the sensitivity of the airways to environmental and biological factors such as dust, chemicals, smoke, allergens, and viruses (Barnes et al., 2012; Bousquet et al., 2010; Lötvall et al., 2011; Martinez and Vercelli, 2013). According to World Health Organization (WHO) estimates, 300 million people had asthma and 255,000 died of asthma in 2005 (WHO, 2008). As per the 2014 global asthma report estimates, asthma is the 14th most important disorder in terms of degree and duration of disability, and currently affects approximately 334

million people. (The International Union Against Tuberculosis and Lung disease, The International Study of Asthma and Allergies in Childhood (ISAAC), 2014). By 2025, it is estimated that there will be an additional 100 million cases of asthma globally (GA Network, 2014).

Asthma is a complex disease with various potential risk factors of genetic, environmental and behavioral nature, such as solid fuel use, tobacco smoking, alcohol, and body mass index (BMI) (Beasley et al., 2015). Atopy is an important risk factor for asthma, rhinitis, and eczema, due to the allergic component of these diseases (Aït-Khaled et al., 2009; Cohen et al., 2003; Mallol et al., 2013). The exact cause of the increased prevalence of asthma is still poorly understood but several hypotheses have begun to explain (Nyembue et al., 2012). Many of these refer to the role of environmental risk factors in increasing disease prevalence worldwide (Beasley et al., 2003). Environmental factors such as exposure to various allergens, irritants, industrial pollutants, and particulate matter (such as from road traffic) are associated with asthma in developing countries (Obel et al., 2017).

A better understanding of the causative factors of asthma is urgently needed, and this knowledge can be used to develop public health and pharmacologically effecttive primary prevention measures in reducing the prevalence of asthma worldwide (Beasley et al., 2015). Therefore, this study aims to identify risk factors associated with asthma in adolescents and adults.

SUBJECTS AND METHOD

1. Research design
The design of this study was a systematic review and meta-analysis. Search articles using the PubMed online database. The articles used in this review are articles pub-

lished in 2016 to 2021. In the article search process, researchers used the keywords "asthma", "risk factors", and "prevalence".

2. Inclusion Criteria
The inclusion criteria of this study were: 1) primary articles describing risk factors for asthma in adolescents; 2) original research papers; 3) there is relationship data indicated by the effect size odd ratio. The exclusion criteria for this study were: 1) articles in languages other than English and Indonesian; 2) review papers; 3) research data is incomplete or not available.

3. Variable Study
The dependent variable was asthma. The independent variables were several risk factors that influence diseases such as smoking, age, and others.

4. Operational Definition of Variables
Smoking variables were categorized as people who currently or have smoked. The variable is people living in urban areas compared to people living in rural areas. Gender was divided into two categories with men as a comparison. People who had never been diagnosed with allergic rhinitis were compared for the variable allergic rhinitis.

5. Instruments Study
Search articles using an online database (PubMed). The process of searching and filtering articles using a Prism diagram (chart 1). Articles included in this study must meet the inclusion criteria and have been reviewed using a critical appraisal in accordance with the research design of each article.

RESULTS

1.Characteristics of Research Articles
There are a total of 630 articles searched from the PubMed online database using the keywords "asthma", "risk factors", and "prevalence" by selecting the year of publication between 2016-2021. There were a total of 12 articles that met the inclusion

criteria and were processed in a qualitative and quantitative synthesis (Chart 1). Articles come from several countries in the world, namely China, Sweden, Canada, Uganda, Nigeria, Iran, and there is 1 article from multiethnic namely Dutch, South-Asian Surinamese, African Surinamese, Moroccan, Turkish and Ghanaian. The characteristics of each article are described in full in table 1.

The author extracted OR and AOR data for each article. OR and AOR values were analyzed separately. Data extraction results of each article can be seen in table 2.

The articles that were analyzed quantitatively in this study were taken from several journals available online using the Pubmed database. The number of references can be seen in table 3.

2.Risk Factor

Researchers got 6 independent variables related to asthma. These variables were smoking status, living in urban areas, gender, and comorbid allergic rhinitis.

2.1 Allergic Rhinitis

Subjects with allergic rhinitis had a 3.80 higher risk of developing asthma than those who did not. This result was statistically significant. The author uses a random effect because the heterogeneity value is 98%.

2.2 Smoke

Subjects who smoked had a 1.53 higher risk of developing asthma than those who did not. This result was statistically significant. The author uses a random effect because the heterogeneity value is 71%.

2.3 Living in an Urban Area

Subjects who live in urban areas have a 1.46 higher risk of developing asthma than those who do not. This result was statistically significant. The author uses a random effect because the heterogeneity value is 66%.

2.4 Gender

Subjects with female sex had a 1.19 higher risk of developing asthma than those without. This result is not statistically significant. The author uses a random effect because the heterogeneity value is 91%.
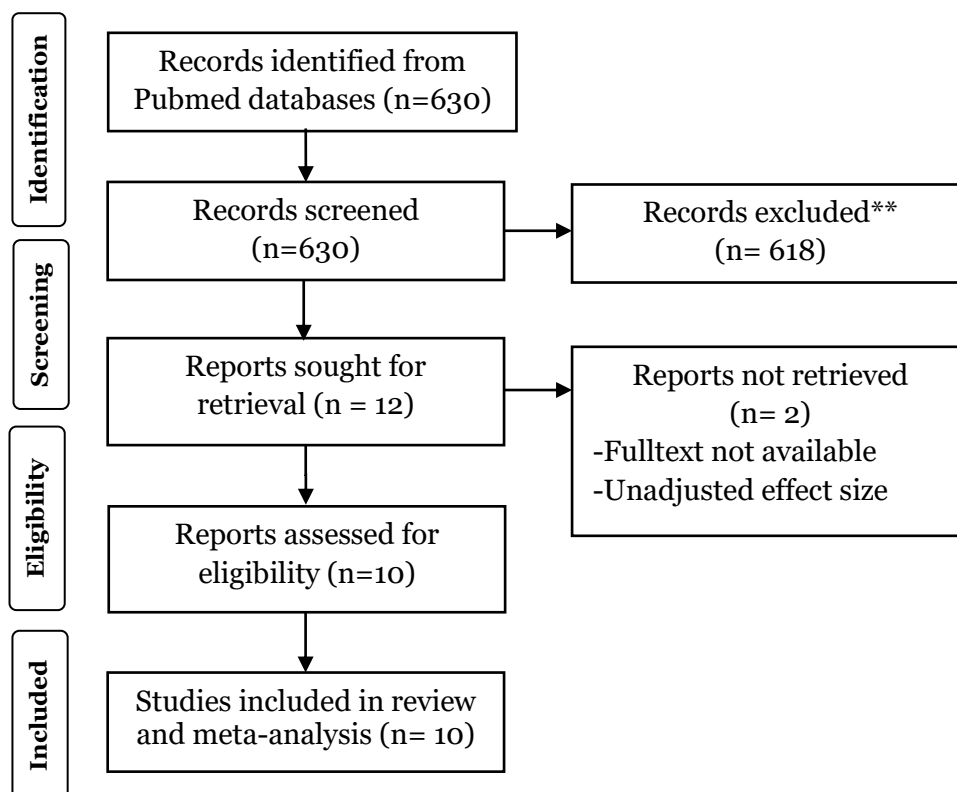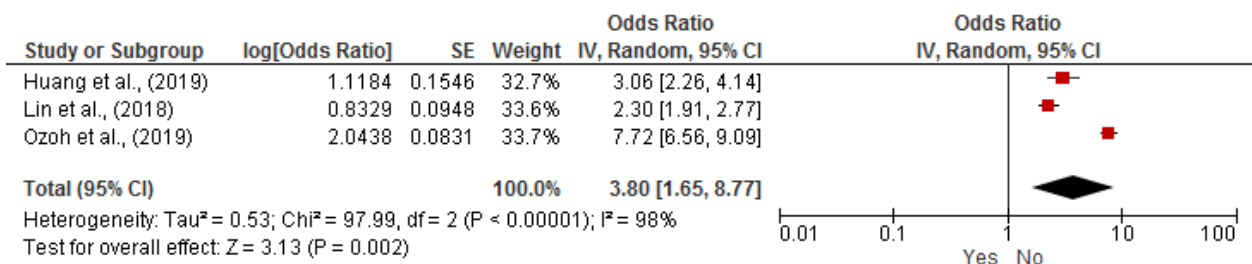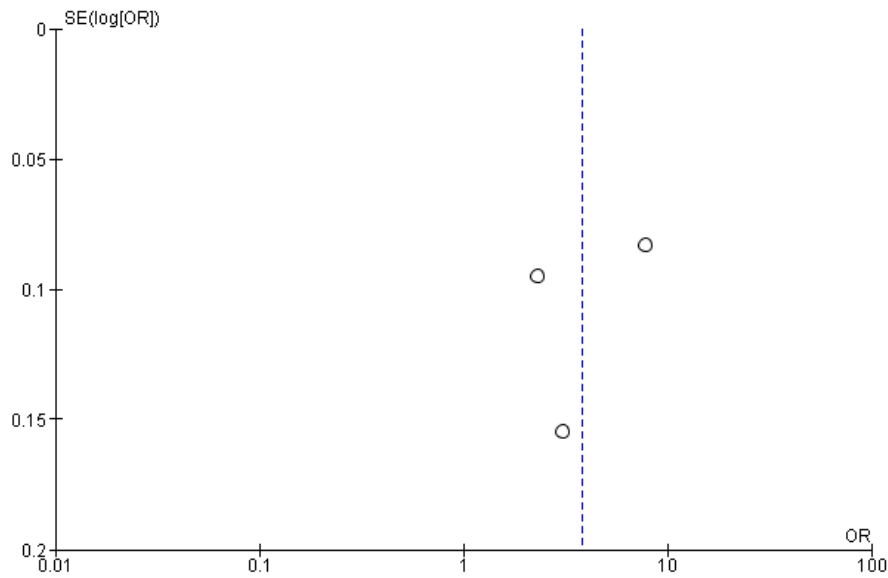

Figure 1. PRISMA Diagram

Table 1. Summary of characteristics in each article

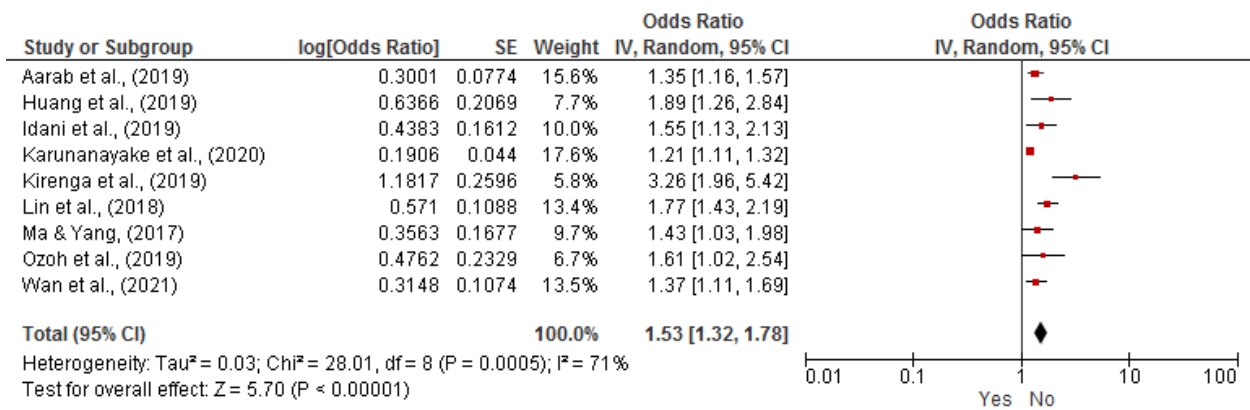| No	Author (year)	Title	Country	Study design	Sample size and age	aOR (95%CI)
1.	Aarab et al. (2019)	Prevalence of and factors associated with adult-onset asthma in different ethnic groups: The HELIUS study	Dutch, South-Asian Surinamese, African Surinamese, Moroccan, Turkish and Ghanaian.	Cross-sectional	23,256 respondents age 18 years or more	Smoke 1.35 (1.16 to 1.57)
2.	Eklund et al. (2018)	Prevalence, age at onset, and risk factors of self-reported asthma among Swedish adolescent elite cross-country skiers	Swedia	Cross-sectional	753 respondents age 16-20 years	Gender 2.0 (1.2 to 3.5)
3.	Huang et al. (2019)	Prevalence, risk factors, and management of asthma in China: a national cross-sectional study	China	Cross-sectional	57,779 respondents age 20 years or more	Allerghic Rhinitis 3.06 (2.26 to 4.15); smoke 1.89 (1.26 to 2.84)
4.	Idani et al. (2019)	Prevalence of asthma and other allergic conditions in adults in Khuzestan, southwest Iran, 2018	Iran	Cross-sectional	5708 respondents age 20-65 years	Smoke 1.55 (1.13 to 2.13); living in urban area 2.08 (1.21 to 3.56)
5.	Karunanayake et al. (2020)	Prevalence and determinants of asthma among aboriginal adolescents in Canada	Canada	Cross-sectional	respondents age 12-19 years	Smoke 1.21 (1.11 to 1.32); living in urban area 1.18 (1.09 to 1.29); gender 0.88 (0.82 to 0.94)
6.	Kirenga et al. (2019)	Prevalence and factors associated with asthma among adolescents and adults in Uganda: a general population based survey	Uganda	Cross-sectional	Respondents age 12 years or more	Gender 1.25 (0.89 to 1.74); living in urban area 2.01 (1.23 to 3.27); allerghic Rhinitis 3.26 (1.96 to 5.41)

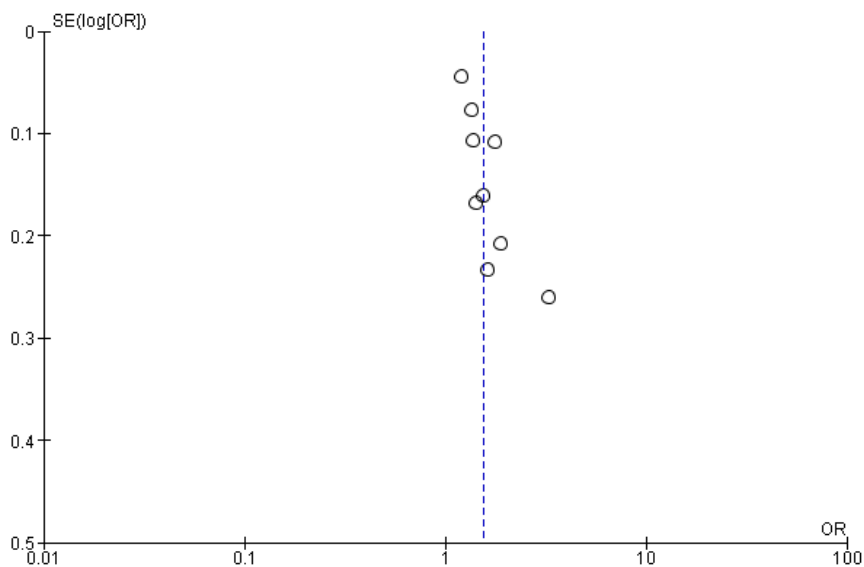| 7.	Lin et al. (2018)	Prevalence and risk factors of asthma in mainland China: The CARE study	China	Cross-sectional	164,215 respondents age 14 years or more	Allerghic Rhinitis 2.30 (1.91-2.81); smoke 1.77 (1.43 to 2.21); gender 1.21 (1.08 to 1.50)
8.	Ma and Yang, (2017)	Prevalence and influential factors for asthma among adults in Chinese	China	Cross-sectional	Respondents age 18 years or more	Smoke 1.43 (1.03 to 1.99); living in urban area 1.36 (1.03 to 1.79)
9.	Ozoh et al. (2019)	The prevalence of asthma and allergic rhinitis in Nigeria: A nationwide survey among children, adolescents and adults	Nigeria	Cross-sectional	respondents age 18 years or more	Allerghic Rhinitis 7.72 (6.56 to 9.09); smoke 1.61 (1.02 to 2.55)
10.	Wan et al. (2021)	Prevalence of and risk factors for asthma among people aged 45 and older in China: a cross-sectional study	China	Cross-sectional	19,816 respondents age 45 years or more	Smoke 1.37 (1.11 to 1.68)

Figure 2. Forest Plot Allergic Rhinitis

Picture 3. Funnel Plot Allergic Rhinitis

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
Aarab et al., (2019)	0.3001	0.0774	15.6%	1.35 [1.16, 1.57]	
Huang et al., (2019)	0.6366	0.2069	7.7%	1.89 [1.26, 2.84]	
Idani et al., (2019)	0.4383	0.1612	10.0%	1.55 [1.13, 2.13]	
Karunanayake et al., (2020)	0.1906	0.044	17.6%	1.21 [1.11, 1.32]	
Kirenga et al., (2019)	1.1817	0.2596	5.8%	3.26 [1.96, 5.42]	
Lin et al., (2018)	0.571	0.1088	13.4%	1.77 [1.43, 2.19]	
Ma & Yang, (2017)	0.3563	0.1677	9.7%	1.43 [1.03, 1.98]	
Ozoh et al., (2019)	0.4762	0.2329	6.7%	1.61 [1.02, 2.54]	
Wan et al., (2021)	0.3148	0.1074	13.5%	1.37 [1.11, 1.69]	
Total (95% CI)			100.0%	1.53 [1.32, 1.78]	

Heterogeneity: Tau² = 0.03; Chi² = 28.01, df = 8 (P = 0.0005); I² = 71%
Test for overall effect: Z = 5.70 (P < 0.00001)

Figure 4. Forest Plot Smokers

Figure 5. Funnel Plot Smoke

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
Idani et al., (2019)	0.7324	0.2764	14.7%	2.08 [1.21, 3.58]	
Karunanayake et al., (2020)	0.1655	0.0405	40.4%	1.18 [1.09, 1.28]	
Kirenga et al., (2019)	0.6981	0.2506	16.6%	2.01 [1.23, 3.28]	
Ma & Yang, (2017)	0.3038	0.1419	28.2%	1.35 [1.03, 1.79]	
Total (95% CI)			100.0%	**1.46 [1.13, 1.89]**	

Heterogeneity: Tau² = 0.04; Chi² = 8.92, df = 3 (P = 0.03); I² = 66%
Test for overall effect: Z = 2.86 (P = 0.004)

Urban   Rural

Figure 6. Forest Plot Living in Urban Areas
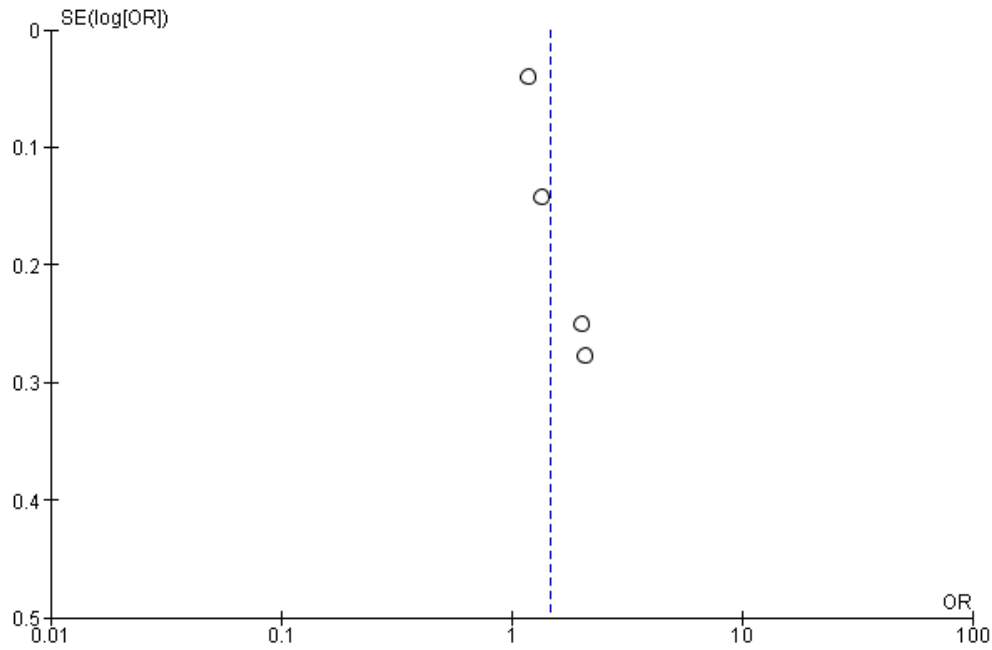
Figure 7. Living in Urban Area

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
Eklund et al., (2018)	0.6931	0.2606	15.0%	2.00 [1.20, 3.33]	
Karunanayake et al., (2020)	-0.1278	0.036	32.3%	0.88 [0.82, 0.94]	
Kirenga et al., (2019)	0.2231	0.1733	21.6%	1.25 [0.89, 1.76]	
Lin et al., (2018)	0.1906	0.058	31.1%	1.21 [1.08, 1.36]	
Total (95% CI)			100.0%	**1.19 [0.91, 1.55]**	

Heterogeneity: Tau² = 0.06; Chi² = 31.60, df = 3 (P < 0.00001); I² = 91%
Test for overall effect: Z = 1.24 (P = 0.21)

Female   Male

Figure 8. Forest Plot Gender
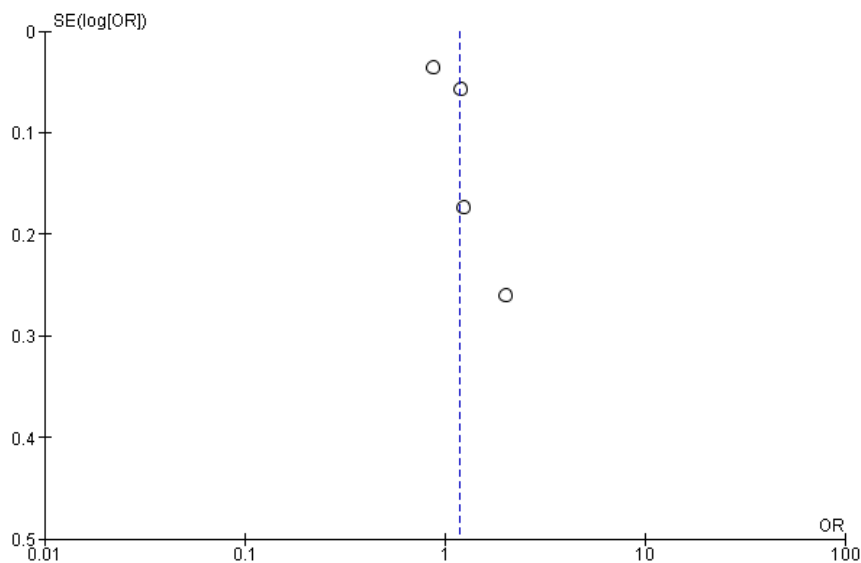
Figure 9. Funnel Plot Gender

DISCUSSION

The results of this meta-analysis suggest that people who have allergic rhinitis are more prone to developing asthma. This is in accordance with the statement by Shaaban et al. (2008) that allergic rhinitis with sensitization to mites is associated with an increased risk of asthma independently of other allergens. Anatomically, the nose and the lungs are related, so that both rhinitis and asthma are manifestations of an ongoing inflammatory process in the respiretory system. However, it is not known whether rhinitis is an early clinical manifestation of allergic disease in atopic subjects who later develop asthma or whether rhinitis itself is an actual risk factor for asthma (Bousquet et al., 2003, 2008; Bousquet et al., 2010; Nieuwenhof et al., 2010).

This study explains that people who smoke are more prone to developing asthma than those who do not. Kumar and Ram (2017) also explained the same thing that the likelihood of reporting asthma was higher for smokers. Nicotine has been shown to affect cellular and humoral immunity. Active smoking has been shown to alter the effects of T cell immunoregulation, namely reducing spontaneous secretion and stimulating IL2 and INFy mitogens as well as reducing IL1 receptor antagonist and IL6 production from cells in the human respiratory tract. In addition, nicotine has also been shown to decrease natural killer cell activity and immunoglobulin levels, decrease macrophage alveolar phagocytic activity and to increase bacterial attachment to epithelial cells (Avanzini et al., 2006; EIAhmer et al., 1999; Ferson et al., 1979; Hagiwara et al., 1999; Miller et al., 1982).

There is an influence between residence (urban and rural) with susceptibility to asthma. Lawson et al. (2017) stated that after adjusting for potential confounders, the association between residence location and asthma remained significant, with asthma prevalence being lower in rural areas. A recent study in Mongolia found that the risk of allergic conjunctivitis and allergic sensitization was lowest in rural subjects from birth, and moderate in subjects who had moved from rural to urban areas, compared with those living in cities since birth (Zheng et al., 2015).

Based on the results of this meta-analysis, women are more prone to asthma.

This is in line with the statement by Chen et al., (2002); Eagan et al., (2005); King et al., (2004) that women are more at risk for developing adult-onset asthma than men.

Butland et al. (2008) found that C-reactive protein (CRP), a biomarker for systemic inflammation, was associated with asthma (but only among non-atopics), and that the association was not significant when controlling for BMI, which suggests that CRP may be a causal pathway between obesity and obesity. and asthma. CRP levels were positively correlated with body mass index (BMI) and were found to be higher among women when compared to men, and higher among heavy smokers (> or = 20 cigarettes x day (-1)) when compared with nonsmokers (Butland et al., 2008).

The conclusion of this study is that asthma is more susceptible to people who have allergic rhinitis, smoke, live in urban areas, are female.

AUTHOR CONTRIBUTION

All authors have a role in selecting topics, tracking, collecting data, reviewing study documents, and analyzing data.

ACKNOWLEDGEMENT

FUNDINGS AND SPONSORSHIP

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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