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PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Pakistan Journal of Biological Sciences 14 (19): 887-893, 2011
ISSN 1028-8880 / DOI: 10.3923/pjbs.2011.887.893

Prevalence of Asthma in Elementary School Age Children in Iran- A Systematic Review and Meta Analysis Study

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Abstract: Asthma is a common chronic disease of childhood which causes considerable morbidity. Asthma affects 1 in 13 school-age children and is a leading cause of office and emergency department visits, hospitalizations, and school absenteeism. Estimating the prevalence of asthma in the community is important in assessing the impact of asthma at the level of population. Since the pooled prevalence of asthma in Iranian elementary school age children (6-12 years old) was not identified, we decide to conduct a meta-analysis study to estimate the prevalence of asthma in elementary school age children in Iran. In order to gather the data, we searched a number of international electronic sources such as Pub Med, Embase, science direct, and ISI for English articles, and Iranian National Knowledge Infrastructure (scientific information) sources such as Iranmedx, Iran-doc, and SID for Persian articles from February 1995 to January 2010 to access the data. We used the words childhood, asthma, prevalence, and Iranian for searching relevant papers and used a data extraction form for the extracted data. The outcome in this Meta analysis study was response to the question, "Ever had asthma", based on the ISSAC program questionnaire. Eleven relevant articles were included for the Meta analysis. The pooled prevalence for girls, boys, and the two genders was obtained as 3.2% (CI; 2.5 to 3.9%), 4.3% (CI; 3.5 to 5.1%) and 3.9% (CI; 3.2 to 4.7%), respectively. The pooled prevalence of asthma in Iranian elementary school age children is low in comparison to the other reports.

Key words: Asthma, Meta analysis, prevalence, Iran, ISSAC

INTRODUCTION

Asthma is a common chronic inflammatory disease of the airways which carry a significant burden of disease during the childhood (Kurukulaaratchy *et al*., 2002; Marks *et al*., 2008). The disease presents as episodes of wheezing, breathlessness and chest tightness due to a widespread narrowing of the airways. The symptoms of asthma are usually reversible, either spontaneously or with treatment. Asthma affects people of all ages and is associated with a substantial impact on the community. While there is currently no cure for asthma, there are effective management strategies available to control the disease and prevent the worsening of asthma symptoms. It is important to have continuous planning to monitor the prevalence of asthma, its distribution within the community, markers of asthma exacerbations and the uptake of effective clinical management practices (Marks *et al*., 2008). Andrew *et al*. (2007) have expressed asthma as a common chronic disease of childhood which causes considerable morbidity. Based on the report of the National Center for Health Statistics of the Centers for Disease Control and Prevention in 2002, 8.9 million children (12.2%) had been diagnosed with asthma in their lifetime and 4.2 million children (5.8%) had an asthma attack in the preceding 12 months which is the indicator of their current disease. According to this information, the prevalence of asthma in boys is higher than girls (14 vs. 10%) (Andrew *et al*., 2007).

It seems that in spite of the considerable improvements in management and treatment of the disease, the prevalence of childhood asthma is rising around the world. Numerous studies conducted in different countries have reported an increase in the prevalence of asthma (Asher *et al*., 1995; Banner, 1995; Singh, 2005; Cho *et al*., 2006; Andrew *et al*., 2007;

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Galassi *et al*., 2006). Akinbami *et al*. (2011) reported that, there were 1.75 million asthma-related emergency visits as well as 456,000 asthma inpatient need in 2007. In 2008, people suffering from asthma missed 10.5 million school days and 14.2 million work days due to their disease. Asthma is a leading cause of office and emergency department visits, hospitalizations and school absenteeism (Akinbami *et al*., 2011). Some studies showed that the emergency visits of asthma and hospitalization rates are higher among females than males, among children than adults and among black than white people (Akinbami *et al*., 2011).

Although asthma-related deaths are relatively uncommon in children (0.3 deaths per 100,000 people per year), many of these asthma-related deaths could probably have been avoided. The major international study on the prevalence of childhood asthma (by report) in 56 countries (International Study of Asthma and Allergies in Childhood) found about a 20-fold variation in the prevalence of asthma (range: 1.6-36.8%) (Andrew *et al*., 2007).

Estimating the prevalence of asthma in the community is fundamentally important in assessing the impact of asthma at the level of population. Evaluation levels and trends in the prevalence of asthma allows planners and health policy managers to estimate the need for and priorities both now and in the future (Marks *et al*., 2008).

Childhood asthma seems particularly common in modern metropolitan areas and is associated with other allergic conditions. In contrast, children living in rural areas of developing countries (e.g., rural Africa, China and India) and farming communities (e.g., in Germany, Austria, Switzerland, Finland and Quebec) are less likely to have asthma and allergy (Andrew *et al*., 2007). Several risk factors such as viral infections, exercise, air pollutants, tobacco smoke and many specific allergens such as house dust mites, pollens and animal's dander can trigger the airway narrowing as well as the symptoms (Marks *et al*., 2008). This striking variation in the prevalence of childhood asthma has led to investigations of potential environmental and lifestyle factors that may explain these differences as well as the recent rise in asthma (Andrew *et al*., 2007; Kuehni *et al*., 2007; Kwon *et al*., 2011). Approximately 80% of asthmatics have reported their disease to have begun before the age of 6. However, of all young children who experience recurrent wheezing, only a minority will go on to have persistent asthma in later childhood. Several risk factors for persistent asthma have been identified. Allergy in these young wheezier has emerged as a major risk factor for persistent childhood asthma and may be evident in early childhood just like clinical conditions (atopic dermatitis, allergic rhinitis, food allergies) (Andrew *et al*., 2007).

While Iran is a country with a variety of climates, geographical states and ethnics groups and due to the fact that these factors may affect the pooled prevalence of childhood asthma especially in elementary school age children and taking what was mentioned before into account, we decided to evaluate the pooled prevalence by a Meta analysis study.

MATERIALS AND METHODS

Search strategy for identification of papers: In order to gather the data, a number of international electronic sources such as Pub Med, Embase, science direct and ISI for English articles and Iranian National Knowledge Infrastructure (scientific information) sources such as Iranmedx, Iran-doc and SID for Persian articles were searched.

In the first step for finding the articles needed for this Meta analysis study, we used these words childhood, pediatric, asthma, prevalence and Iranian. Moreover, the investigators checked the bibliographies of review articles for additional studies which were not identified by the electronic search. All study reports were full-length articles and abstracts published in English or Persian sources in refereed journals. There were no language restrictions and abstracts of the papers which were identified by the initial search were evaluated for appropriateness to the study question. Then, all potentially relevant papers were obtained and evaluated in detail. The bibliographies of all identified eligible studies were used to perform a recursive review of the literature. Foreign language articles were translated where required. The reviews were obtained following the Cochrane Collaboration steps and the Meta-analysis of Observational Studies in the Epidemiology (MOOSE) Group (Stroup *et al*., 2000).

The reference lists from relevant review articles as well as all eligible studies were manually searched. Other relevant articles and reports released by WHO and the Iran Ministry of Health and Education were also utilized. Using a data extraction form, data were extracted based on the terms child age, methods, questioner (ISSAC), sample size and type of design.

The Inclusion criteria for meta-analysis: Studies which were published in English and Persian were eligible if they fulfilled the following criteria:

- **Study design:** Only cross-sectional studies were used in the present meta-analysis and studies with other designs were excluded

- **Sample size:** It had to be equal to or more than 1000 subjects
- **Sample origin:** The population under study-including both sexes-had to be in childhood (6-12 years old)
- **Sampling method:** It had to be random
- **The questionnaire:** It had to be ISSAC (The International Study of Asthma and Allergies in Childhood), which is a unique worldwide epidemiological research program established in 1991 to investigate asthma, rhinitis and eczema in children due to the considerable concern that these conditions were increasing in western as well as developing countries (ISSAC, 2011). Definition of asthma used in this study was equivalent to the term "ever had asthma" in the ISSAC Questionnaire

Our keywords for searching were ISSAC, asthma prevalence, children, Iranian and elementary school.

The exclusion criteria were:

- Studies with non-specification of sample origins
- Studies which combined other age groups with elementary school age children
- Duplicated published articles

Data extraction: The titles were obtained and the abstracts of citations through the search strategy were screened. Then, the full texts of potentially eligible studies were obtained. In the primary stage of this step, two investigators assessed each article independently for eligibility and abstracted data with standardized data-abstraction forms. The investigators settled their disagreement about the consensus.

We extracted the following data for each study: the year the study was conducted, province or city of sample origin, (geographical region), type of study (cohort, case-control, or cross-sectional), method of sampling [random or non-random sampling], procedure of data collection (standard instrument), type of questionnaire (ISSAC or non-ISSAC), prevalence of asthma for boys, girls, as well as both genders and sample size.

No studies with duplicated publishing were found among the articles. Performing the study, the researchers obtained 33 papers. We select the primary articles according to the major criteria of the article such as the year the study was conducted, city or province, study design and the ISSAC questionnaire. At this stage, 20 articles were rejected: Two papers dealt exclusively with inappropriate designs (Alyasin *et al*., 2004; Amra *et al*., 2005), one paper with non-ISSAC questionnaire (Elahi and Ghaem, 2006), seven papers with other age groups (Rahimian, 1999; Boskabadi and Karimian, 2000; Golshan *et al*., 2002c; Hatami *et al*., 2003; Karimi *et al*., 2007; Bazzazi *et al*., 2007), one paper with an under-1000-people sample size (Amra and Golshan, 2000), two papers with no relevant data (Amra and Golshan, 2000; Golshan *et al*., 2002a) and seven articles for ambiguous reports or a number of causes which were discussed above.

One investigator reviewed all the selected papers separately. After the second critical review, we finally selected 11 articles for the meta-analysis that have been summarized in Table 1 (Golshan *et al*., 2001, 2002b, d; Khorasani *et al*., 2002; Masjedi *et al*., 2004; Zohal and Hasheminasab, 2006; Fadaizadeh *et al*., 2008; Mohammadzadeh *et al*., 2008; Najafizadeh *et al*., 2008; Rad and Hamzezadeh, 2008; Shakurnia *et al*., 2010).

Data were entered in the "STATA" software (version 8). The homogeneity between studies (subject unit) was assessed by Cochran statistical test (The significance level was equal to .05). Then, we evaluated the publication bias by the informal graphical procedure (funnel graph) and formal Begg's and egger statistical tests.

RESULTS

From 33 papers which were selected in the primary search, 11 articles were relevant. The minimum sample size was equal to 1309 children in Zarinshahr (Golshan *et al*., 2002b) and the maximum sample size included 3915 children in Esfahan (Golshan *et al*., 2001). Four articles were published in English while the rest were published in Persian. Except for one study which included a range of age groups (6-13 years old) (Golshan *et al*., 2002b), the range of age groups in the rest of the studies was from 6-12 years old. One article w as written in 1999, one in 2007 and 9 articles (82%) were written between 2000 and 2004. Table 1 shows the details of the included studies in this meta-analysis.

Publication bias was evaluated by the use of Informal funnel plot (Fig. 1-3) and Begg's and Egger's formal statistical tests. Results of the formal tests for girls, boys and both genders for the publication bias appear in Table 2. Statistical values and their corresponding significant levels were separately measured for the two groups and are shown in Table 3.

Figure 1 shows the overall pooled prevalence of asthma in the girls' group. Base on this plot, the overall pooled estimate in girls is equal to 3.2% with the range of 1.7 to 7% for the studies in the meta-analysis.

Table 1: Characteristics of studies included in the meta-analysis

Row	Author's name	Study region	Year of study	Population target	Sample size	Girl prevalence	Boy prevalence	Total prevalence
1	Khorasani	KERMAN	2000	6-11	2217	0.023	0.032	0.027
2	Golshan	borojerd	2001	6-12	1331	0.021	0.076	0.057
3	Zohal	Gazvin	2004	6-12	2518	0.015	0.023	0.020
4	Mohammadzadeh	Babol	2003	6-7	3044	0.021	0.040	0.030
5	Shakorinia	Ahvaz	2007	6-7	1410	0.070	0.066	0.068
6	Najafzadeh	Rasht	2003	6-7	3065	0.056	0.091	0.071
7	Masjedi	tehran	2001	6-7	3015	0.0263	0.017	0.022
8	Rahimirad	uromieh	2004	6-7	3000	0.011	0.021	0.016
9	Golshan	zarinshar	2000	6-13	1309	0.017	0.015	0.016
10	Golshan	esphahan	1999	6-12	3915	0.069	0.076	0.084
11	Fadaeezadeh	tehran	2003	6-7	3015	0.027	0.017	0.022

Table 2: Pooled prevalence of child asthma and 95% CI

	Pooled prevalence	Lower limit	Upper limit
Girls	0.032	0.025	0.039
Boys	0.043	0.035	0.051
Total	0.039	0.032	0.047

Table 3: Results of statistical tests for the publication bias

	Begs	Z	p-value	Egger	T	p-value
Girl	39	2.96	0.003	49.095	7.76	0.000
Boy	42	3.19	0.001	50.344	8.07	0.000
Total	33	2.49	0.013	56.072	4.01	0.003

Table 4: Results of the statistical test for the heterogeneity among the studies

	Q	df	p-value
Girl	1680.401	10	0.000
Boy	7695.036	10	0.000
Total	6476.005	10	0.000

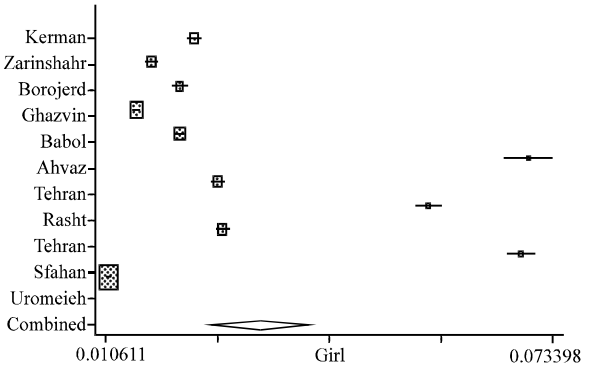

Fig. 1: Pooled prevalence of asthma among Iranian girls in elementary school

Pooled estimate of asthma in the boys' group is equal to 4.3% with the range of 1.5 to 9.1% for the studies in the meta-analysis (Fig. 2). The pooled prevalence in the boys' group is greater than the girls' group and the 95% CI is a little wider for girls.

Figure 3 shows the pooled prevalence of asthma for the two genders which is measured as 3.9% with the range of 1.6 to 8.4% for the studies in the meta-analysis.

Heterogeneity among the sample subjects under study was evaluated by Cochran's test (Q-statistic). Results of this test in the three groups shows heterogeneity between the studies (Table 4).

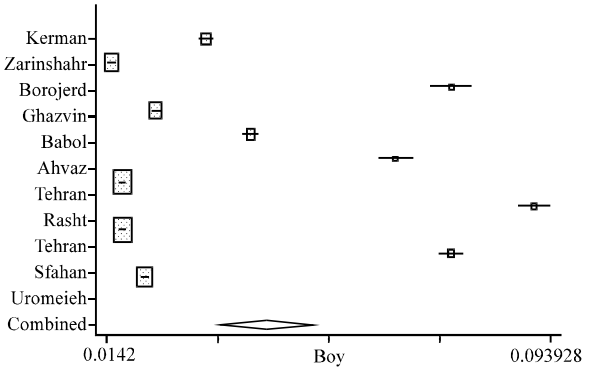

Fig. 2: Pooled prevalence of asthma among Iranian boys in elementary school

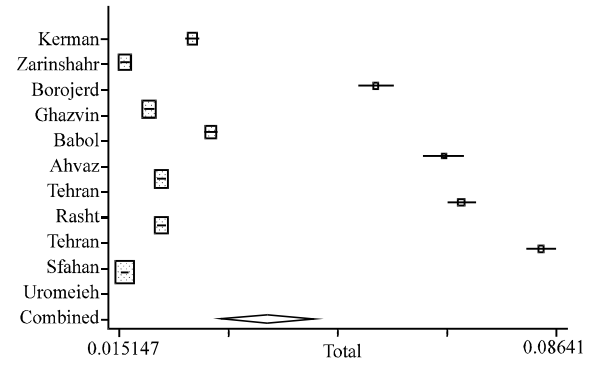

Fig. 3: Pooled prevalence of asthma among Iranian children in elementary school

In this meta-analysis, the pooled prevalence for girls, boys and both genders is equal to 3.2% (95% CI, 2.5 to 3.9%), 4.3% (95% CI 3.5 to 5.1%), 3.9% (95% CI, 3.2 to 4.7%), respectively (Table 2).

DISCUSSION

Based on this meta-analysis, the pooled prevalence of asthma in Iranian elementary school age children is equal to 3.9%. Of course it has revealed to be slightly higher among boys (4.3 among boys vs. 3.2 among girls).

The minimum prevalence in our sample subject is equal to 1.6 which was reported in Zarinshahr by a sample size of 1309 subjects (Golshan *et al*., 2002b). Also, the maximum estimated prevalence was reported as 8.4 in Esfahan by a sample size of 3915 subjects (Golshan *et al*., 2001).

Evaluating this article, we noticed that his meta-analysis consisted of studies which did not have the ISSAC protocol, paid less attention to the sample size (Elahi and Ghaem, 2006) and used a wide range of age groups.

In this meta-analysis, we included a number of checkpoints in order to minimize the biased selection, as explained in the methods. Many factors related to the design as well as the performance of the primary studies may have had an effect in estimating the prevalence. There was a marked variation in the prevalence from as low as 1.6 up to 7.1%. This may be due to a variety of conditions and factors such as different socioeconomic, ecologic and ethnic factors which might have affected the prevalence of asthma in Iran.

Various methods may be used by different authors in order to define asthma; However, we decided to restrict the definition of the terms to "ever had asthma". Besides, in case this term was not clearly reported in a study, we contacted the authors via e-mail and received the precision value for our study (Golshan *et al*., 2002b; Masjedi *et al*., 2004).

Anderson (2005) expressed that trends in the cultural perception and naming of symptoms might explain the increasing trends observed in prevalence studies (Anderson, 2005). Also other studies mentioned a rising trend in prevalence in different places of the world (ISAAC, 1998; Moala and Pearce, 2001; Ones *et al*., 2006; Brim *et al*., 2008; Hwang *et al*., 2010; Varela *et al*., 2010; Kwon *et al*., 2011).

The study in any total group and subgroup shows a publication bias; this may be due to the fact that only studies with large sample sizes were selected while those with lower sample sizes were excluded.

Forasmuch as informal and formal assessment methods of 11 studies, the current study has demonstrated a marked heterogeneity for the prevalence estimates; therefore, we decided to evaluate the heterogeneity and the publication bias on sex subgroups. In this sub group, also, marked heterogeneity and publication bias was observed. This is a natural finding in our study because, based on the ISSAC questionnaire, we included only over-1000-subjects sample sizes in our study and this might have distorted the result as well as the sources of heterogeneity.

Sutton mentioned that heterogeneity in meta analysis occur due to many factors such as chance, spurious, scale used to measure the outcome and unexplainable causes (Sutton *et al*., 2000). Heterogeneity may either arise from systematic differences between studies or random differences between effect sizes, or both. Much for more than clinical trials, performing meta-analyses of observational studies have the challenge of incorporating various designs and levels of quality. If the heterogeneity is due to random differences, it can be modeled (Monroe, 2007). Other authors mentioned that in observational meta-analysis study bias can occur in the original studies that a large number of variables will be collected in questionnaires as potential confounders. Sometimes many regional studies may not be published in international journals. They suggest that inclusion criteria, data collection methods and statistical analysis cannot be changed if published data are used for the meta-analysis (Blettner *et al*., 1999). Although characteristics of quality evaluation can contribute to understanding some of the variations in the observational studies themselves, methods should be used to aid in the detection of the publication bias as well as the funnel plots (Hedges and Olkin, 1985).

Based on the results, the random effect model was used in order to estimate the pooled prevalence in our study.

In comparison to the study conducted by Morales-Suarez-Varela, the prevalence of ever asthma in primary schools age children in Iran is lower than the pooled prevalence estimated for Asian groups. Of course, it must be considered that the study was conducted on migrant Asian children (Varela *et al*., 2010).

Pal *et al*. (2009) conducted a systematic review as well as a meta-analysis on Indian children in 15 relevant articles which were selected among 300 published articles and scientific meetings from 1966 to 2008. They reported the pooled prevalence of asthma as 2.74%. They estimated the mean prevalence and the overall weighted mean prevalence as 7.24 and 2.74%, respectively. Moreover, the prevalence of childhood asthma among Indian children of 13- 14 years old was less than those of 6-7 years old (Pal *et al*., 2009).

According to ISSAC Steering committee study, the overall asthma prevalence in Iran-based on two studies conducted in Rasht and Tehran-was equal to 3%. This estimation is less than our estimation (3.5%). The authors mentioned that the prevalence of asthma among Iranian children is less than other countries in the eastern Mediterranean region (6.5%) (Pearce *et al*., 2000).

CONCLUSION

Results of the present study showed that the prevalence of asthma in Iranian children is 3.9 and ranged form 3.2 to 4.7%. This value and the 95%CI for the

prevalence are not more than the overall prevalence reported in a large number of studies but forasmuch as other studies that shows variety in increasing trend of asthma in other region of world, more attention must be paid to the trend of asthma in Iran.

ACKNOWLEDGMENT

The authors would like to thank all authors who conducted these studies as well as the systematic reviews. They are also grateful for the schoolchildren, their parents and other staff who participated in these studies. Emam Reza clinic's Research Center, Shiraz, Iran and Ms. A. Keivanshekouh are also appreciated for their cooperation in improving the use of English in the manuscript.

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