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ORIGINAL ARTICLE

The role of Human Development Index in the epidemiology of asthma in adolescents in Kosovo: A cross-sectional multicentre Global Asthma Network (GAN) study

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Abstract
Background: Very limited information is available on the prevalence and risk factors of asthma in adolescents in Kosovo, and no study has previously addressed the role of Human Development Index (HDI) on asthma in the region. The present study addresses these two issues.
Methods: Following the Global Asthma Network (GAN) methodology, a cross-sectional survey, through standardised self-completed questionnaires, was conducted in the following six centres of Kosovo: Ferizaj, Gjakova, Gjilan, Peja, Prishtina and Prizren. Current asthma symptoms (CAS) and severe current asthma symptoms (sCAS) were defined according to the GAN standards. Environmental questionnaire inquired about gender, exercise, screening time, siblings, truck traffic, use of paracetamol, pet ownership, and smoking habits. Height and weight were also measured. Multivariate logistic regression analyses were performed in each centre along with meta-analyses to summarise the overall effects of each factor in the centres as a whole. Meta-regression of the prevalence rates was calculated using HDI as a moderator.

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Results: Participation rate was high (80.0–99.9%). Prevalence of CAS ranged from 4.6% to 11.3%, and sCAS from 1.7% to 4.5%. Factors associated with CAS were exercise, computer time, paracetamol use and dog ownership. sCAS was associated with paracetamol use and physical exercise. HDI explained 46% and 80% of prevalence variability of CAS and sCAS between centres, respectively.
Conclusions: Prevalence of CAS and sCAS in Kosovo varies highly between centres. This variability is explained partly by HDI. Individual risk factors are common, with some determined in other studies conducted in other regions.

SYNOPSIS

Study question: Kosovo is a small country with the lowest gross national income (GNI) in Europe. Asthma epidemiology is unknown. We intended to know the prevalence of asthma in adolescents and the factors, both individual and ecological, associated with it.

What's already known: Prevalence of asthma varies enormously between and within the countries, and a trend of lower prevalence was observed in the areas with lower GNI. Additionally, the degree of westernization and the environment, which includes factors such as unhealthy diet, sedentariness, stress, etc., have been pointed out as main causes of differences in asthma prevalence.

What this study adds: Differences in the prevalence of asthma within Kosovo are high. Individual factors associated with asthma do not seem to be different from other countries. However, disparities in the Human Development Index seem to explain an important part of these differences.

INTRODUCTION

Asthma is the most prevalent condition among children and adolescents, causing high morbidity and unacceptable mortality, especially in low-income countries.[1] Kosovo, a young country with virtually no epidemiological data on asthma, was enrolled in the Global Asthma Network (GAN) Phase I study, a continuation of the International Study of Asthma and Allergies in Childhood (ISAAC), which has recently offered data on global asthma prevalence trends.[2]

To the best of our knowledge, only one study on asthma epidemiology in Kosovo, also as a part of GAN, was published. In the city of Gjilan, prevalence of asthma among adolescents aged 13–14 years, was quite low (6.4%) with no difference found between genders.[3]

Some epidemiological studies have been conducted on asthma in the nearby geographical areas, some of them previously part of the former Yugoslavia, such as Kosovo. For instance, the cities of Belgrade, Novi Sad, Sombor, Nis (Serbia) and Podgorica (Montenegro) reported, within the ISAAC phase III study (2002–2005), that the prevalence of current asthma symptoms (CAS) in 6–7-year-old children ranged from 8.7% (Podgorica and Novi Sad) to 16.5% (Nis, situated only 90 km from Prishtina, the capital city of Kosovo). In adolescents aged 13–14 years, the range of asthma prevalence was 5.8% (Novi Sad) to 12.4% (Nis). According to the authors, these differences could be related to different health institutions in both rural and urban areas that treated asthma patients.[4] In Croatia, also within the ISAAC phase III study, the prevalence of CAS in children and adolescents was 9.7% and 8.4%, respectively.[5] In Tirana (Albania), which participated in the three phases of ISAAC study, the overall prevalence of CAS was quite low: 2.6% among adolescents within the ISAAC phase I study (1994–1997); 4.8% among schoolchildren aged 9–11 years in phase II study (2002–2004); and 3.4% among adolescents in phase III study.[6,7] Skopje (Macedonia), included in the ISAAC phase III study, showed that the prevalence of CAS among adolescents was 8.8%.

The aim of the present study was to offer epidemiological information on asthma among adolescents in six of the seven districts of Kosovo as part of the GAN study. The information gathered was at both individual and ecological levels, in particular on the prevalence variability attributed to Human Development Index (HDI),[8] which, to the best of our knowledge, has not been explored in Europe.[9–11]

MATERIAL AND METHODS

Administration of questionnaire and sample size

The present survey was included in the GAN phase I study and followed GAN's exact methodology.[12,13] Questionnaires were translated from English into Albanese, and back-translated into English, following the ISAAC procedures.[14,15] The fieldwork was carried out between 2017 and 2018 in Ferizaj, Gjakova, Gjilan, Peja, Prishtina and Prizren districts. A detailed description of administration of questionnaires and rate of participation have been published elsewhere.[12,13] Briefly, school adolescents, aged 13–14 years, from each class in each centre were included in the survey. All students were called for to fill in the questionnaire. Except for Prishtina (which included a random sample of schools to reach the proposed number of students), all schools in each city were included, as the number of students hardly reached the minimum required number of 1000. Participation rate in each city is as follows: Ferizaj 99.9%, Gjakova 90.1%, Gjilan 80.0%, Peja 92.5%, Prishtina 99.9% and Prizren 89.0%.

Definitions

Asthma symptoms were defined as follows: "Current asthma symptoms (CAS)" was defined by a positive answer to the question: "Have you had wheezing or whistling in the chest in the past 12 months?" "Severe CAS (sCAS)" was defined as current wheeze with ≥4 attacks, or causing sleep disturbance for >1 night per week, or affecting speech in the past 12 months, according to the following questions: "How many attacks of wheezing have you had in the past 12 months?" (None; 1–3; 4–12; more than 12); "In the past 12 months, how often, on average, has your sleep been disturbed due to wheezing?" (Never; less than 1 night per week; ≥1 night per week); and "In the past 12 months, has wheezing ever been severe enough to limit your speech to only one or two words at a time between breaths?" (Yes; No).

Adolescents responded themselves to the symptom and environmental questionnaires. This included questions on smoking, pet ownership, use of paracetamol, truck traffic in the street adolescents lived, siblings, time spent using screens or watching television, and exercise. Additionally, height and weight were measured at school by fieldworkers in a standardised manner.

Statistics

Individual study

Bivariate analyses between environmental factors and CAS and sCAS were performed by means of the Chi-square statistic and expressed as raw odds ratio (OR) and their 95% confidence interval (95% CI). Then, logistic regression analyses were performed with two outcomes as dependent variables and all environmental factors as independent variables, and were expressed as adjusted OR (aOR) and their corresponding 95% CI. Those analyses were performed for each centre. To summarise the overall results in Kosovo, both prevalence[16,17] and associations (aOR) of each environmental factor with each outcome in each centre were meta-analysed (random effects, restricted maximum likelihood) and expressed as summary of the adjusted odds ratios (SaOR). All calculations were carried out by means of Stata, version 17.[18]

Ecological study

After encountering a very high variability in the prevalence of CAS and sCAS between centres in the meta-analyses, and considering that the study method should not be an important source of variation, a meta-regression was carried out, including, alternatively, the following moderators: population, population density, urban versus Rural, longitude, latitude, and HDI. This index is calculated according to the United Nations Development Programme Human Development Reports,[8] and specific values for each city of Kosovo were obtained from the Nijmegen Center for Economics (NiCE).[19] Meta-regressions for the prevalence of CAS and sCAS with the aforementioned moderators were carried out by means of a comprehensive meta-analysis package.[20]

Ethics

Prior to the start of the study, permission was taken from the education authorities of each municipality. Passive informed consent was used. The study was approved by the Ethics Committees of both Ministry of Health and Ministry of Education of Kosovo according to the Helsinki Declaration (approval No. 21/550).

RESULTS

Individual analyses

The number of adolescents per centre was quite close or over the planned number of 1000 (Table 1). Participation rate was high, ranging from 80.0% (Gjilan) to 99.9% (Prishtina).[13] Prevalence rates of CAS and sCAS are shown in Table 1. The prevalence of CAS ranged from 4.6% in Ferizaj to 11.3% in Prizren, and that of sCAS was lowest in Ferizaj (1.7%) and highest in Prizren (4.5%).

Table 2 shows associations of the environmental factors with CAS. Although not all centres showed the same associations, some general trends were observed. For instance, the use of computers, tablets, or smart phones for longer periods per day was independently associated with the outcome in all centres except for Ferizaj. Figure 1A shows the summary of the effects of all centres in the meta-analysis and indicates that this factor was significantly associated with CAS (SaOR 1.36; 95% CI: 1.21–1.52). Physical exercise was another factor significantly associated with CAS. In the summary of effects (Figure 1), it does not seem that exercise has a dose-effect association: rather, doing some exercise is associated with the outcome (SaOR for exercise 1–2 times per week: 2.33; 95% CI: 1.87–2.91 vs. 3+ times per week: 2.20; 95% CI: 1.58–3.05). What seems to have a dose-effect association is the intake of paracetamol: having this medicine at least once a year was associated with asthma symptoms (SaOR 1.69; 95% CI: 1.15–2.48), but having it at least once a month increased the association considerably (SaOR 2.81; 95% CI: 2.00–3.94). Having a pet at home did not seem to be associated with asthma symptoms in either of the centres, as most centres showed a positive trend of such an association (Table 2). However, when meta-analysing values of all the centres, it became clear that an association existed between having a pet and suffering from asthma (Figure 1A). A similar picture was observed for smoking water pipe currently (after adjusting for cigarette smoking either in the past or currently). Although the point SaOR for smoking cigarette in the past or currently was higher, the 95% CI was higher, considering this factor as statistically non-significant. As observed in Table 1, the proportion of adolescents smoking cigarettes either in the past or currently was much lower than those smoking water pipe.

Factors associated with sCAS (Table 3) did not follow the same pattern, although three of them maintained a statistically significant association in meta-analysis (Figure 1B). These were (1) physical exercise (SaOR for exercise for

Table 1 Demographic and environmental characteristics of the six Kosovar centres included in the study (% and 95% CI).

	Ferizaj N = 890	Gjakova N = 676	Gjilan N = 1200	Peja N = 1433	Prishtina N = 1056	Prizren N = 1427
Males	45.3 (42.1-48.6)	39.5 (35.9-43.2)	51.5 (48.7-54.3)	54.1 (51.5-56.7)	46.7 (43.7-49.7)	50.8 (48.2-53.4)
Wheezing	4.6 (3.2-6.0)	6.5 (4.6-8.4)	6.4 (5.0-7.8)	9.0 (7.5-10.5)	7.7 (6.1-9.3)	11.3 (9.6-12.9)
Severe asthma	1.7 (0.8-2.6)	2.4 (1.2-3.6)	2.8 (1.8-3.7)	4.1 (3.1-5.2)	2.8 (1.7-3.8)	4.5 (3.4-5.6)
Exercise						
Never or occasionally	77.0 (74.0-79.8)	75.6 (72.2-78.7)	72.5 (69.9-74.9)	70.0 (67.6-72.3)	62.2 (59.1-65.2)	67.1 (64.6-69.6)
Once or twice per week	17.5 (15.0-20.2)	20.2 (17.4-23.5)	18.9 (16.8-21.3)	20.0 (18.0-22.1)	27.2 (24.5-30.1)	25.0 (22.8-27.4)
Three or more times per week	5.5 (4.1-7.3)	4.2 (2.9-6.0)	8.6 (7.1-10.3)	10.0 (8.6-11.7)	10.6 (8.8-12.7)	7.8 (6.5-9.4)
Television-watching per day						
<1 h	24.9 (22.1-27.9)	16.7 (14.1-19.7)	24.7 (22.3-27.2)	30.0 (27.7-32.4)	14.9 (12.9-17.3)	20.6 (18.6-22.8)
≥1 h but <3 h	44.6 (41.3-48.0)	63.3 (59.6-66.9)	47.8 (45.0-50.7)	47.4 (44.8-50.0)	51.6 (48.5-54.6)	50.5 (47.9-53.2)
>3 h but <5 h	19.3 (16.8-22.1)	14.9 (12.4-17.8)	17.3 (15.3-19.6)	14.6 (12.9-16.5)	23.4 (20.9-26.1)	19.6 (17.6-21.8)
5+ h	11.2 (9.3-13.5)	5.0 (3.6-7.0)	10.2 (8.6-12.0)	8.0 (6.7-9.5)	10.1 (8.4-12.1)	9.2 (7.8-10.9)
Computer/tablet/smart phone use per day						
<1 h	25.1 (22.3-28.2)	20.6 (17.7-23.8)	26.5 (24.1-29.1)	31.3 (28.9-33.7)	15.5 (13.4-17.9)	24.0 (21.8-26.3)
≥1 h but <3 h	39.8 (36.6-43.2)	47.2 (43.4-51.0)	38.4 (35.6-41.2)	39.1 (36.6-41.7)	39.6 (36.7-42.7)	40.0 (37.5-42.7)
>3 but <5 h	18.0 (15.6-20.8)	21.9 (18.9-25.2)	21.8 (19.5-24.2)	17.7 (15.8-19.8)	25.3 (22.7-28.1)	20.1 (18.1-22.3)
5+ h	17.1 (14.7-19.8)	10.4 (8.3-12.9)	13.3 (11.5-15.4)	11.9 (10.3-13.7)	19.5 (17.2-22.1)	15.9 (14.0-17.9)
Older siblings						
0	28.9 (26.0-31.9)	23.5 (20.5-26.9)	35.9 (33.3-38.7)	36.1 (33.6-38.6)	34.3 (31.5-37.3)	30.1 (27.8-32.6)
1	31.2 (28.3-34.4)	34.2 (30.7-37.8)	29.6 (27.1-32.3)	28.9 (26.6-31.4)	32.7 (30.0-35.6)	27.8 (25.5-30.1)
2	19.7 (17.2-22.4)	31.8 28.4-35.4)	21.2 (19.0-23.6)	20.3 (18.3-22.5)	18.0 (15.8-20.4)	21.9 (19.9-24.2)
3+	20.2 (17.7-23.0)	10.5 (8.4-13.1)	13.3 (11.5-15.3)	14.6 (12.9-16.6)	14.9 (12.9-17.2)	20.2 18.2-22.3)
Younger siblings						
0	24.9 (22.2-27.9)	38.3 (34.7-42.0)	39.7 (37.0-42.5)	35.4 (33.0-37.9)	34.7 (31.9-37.6)	31.6 (29.2-34.1)
1	41.0 (37.8-44.3)	39.8 (36.2-43.5)	35.6 (33.0-38.4)	32.4 (30.0-34.9)	37.8 (34.9-40.8)	36.3 (33.8-38.8)
2	19.6 (17.1-22.3)	17.0 (14.4-20.0)	17.7 (15.6-20.0)	23.2 (21.1-25.5)	17.9 (15.7-20.3)	21.1 (19.0-23.3)
3+	14.5 (12.3-17.0)	4.9 (3.5-6.8)	6.9 (5.6-8.5)	9.0 (7.6-10.6)	9.6 (8.0-11.5)	11.0 (9.5-12.8)
Truck traffic (street where adolescent lives)						
Never	10.4 (8.5-12.6)	8.7 (6.8-11.1)	12.1 (10.4-14.1)	12.1 (10.5-13.9)	9.9 (8.2-11.9)	12.8 (11.2-14.7)
Seldom (not often)	48.1 (44.8-51.5)	39.8 (36.2-43.5)	56.4 (53.6-59.2)	54.9 (52.3-57.5)	51.0 (48.0-54.1)	56.0 (53.4-58.6)
Frequently through the day	28.0 (25.1-31.1)	40.2 (36.6-44.0)	23.4 (21.1-25.9)	23.2 (21.1-25.5)	28.7 (26.2-31.6)	24.9 (22.7-27.2)

(Continued)

Table 1 (Continued)

	Ferizaj N = 890	Gjakova N = 676	Gjilan N = 1200	Peja N = 1433	Prishtina N = 1056	Prizren N = 1427
Almost the whole day	13.5 (11.3-15.9)	11.2 (9.1-13.9)	8.1 (6.7-9.8)	9.8 (8.4-11.4)	10.4 (8.7-12.4)	6.3 (5.1-7.7)
Paracetamol intake, last year						
Never	19.9 (17.2-22.9)	17.3 (14.6-20.4)	23.3 (20.9-25.9)	31.7 (29.3-34.2)	22.0 (19.5-24.7)	19.9 (17.8-22.1)
At least once a year	41.0 (37.6-44.6)	63.5 (59.8-67.0)	43.8 (40.9-46.8)	37.9 35.4-40.5)	46.8 (43.7-50.0)	39.6 (37.0-42.3)
At least once per month	39.0 (35.6-42.6)	19.2 (16.4-22.4)	32.9 (30.1-35.7)	30.4 28.0-32.8)	31.2 (28.3-34.2)	40.5 (37.9-43.2)
Current cat ownership	7.2 (5.7-9.2)	10.5 (8.4-13.1)	12.4 (10.7-14.4)	14.9 (13.2-16.9)	9.1 (7.5-11.1)	14.3 (12.5-16.3)
Current dog ownership	25.3 (22.5-28.4)	15.4 (12.9-18.3)	24.6 (22.2-27.1)	27.8 (25.5-30.1)	15.9 (13.7-18.2)	25.8 (23.5-28.1)
Past cigarette smoker	3.5 (2.4-5.0)	0.9 (0.4-2.0)	1.5 (0.9-2.4)	2.2 (1.6-3.2)	1.9 (1.2-2.9)	2.4 (1.7-3.4)
Current cigarette smoker	2.2 (1.4-3.4)	0.7 (0.3-1.8)	0.8 (0.4-1.5)	2.0 (1.4-2.9)	1.1 (0.6-2.0)	1.5 (1.0-2.3)
Current wáter pipe smoker	6.3 (4.8-8.2)	3.1 (2.0-4.7)	13.3 (11.5-15.3)	8.0 (6.7-9.6)	8.4 (6.9-10.3)	12.1 (10.5-14.0)
Weight						
Overweight	6.2 (4.8-8.0)	6.7 (5.0-8.8)	8.8 (7.4-10.6)	9.8 (8.4-11.5)	10.2 (8.5-12.2)	10.2 (8.7-11.8)
Obese	3.6 (2.6-5.0)	0.9 (0.4-2.0)	2.4 (1.7-3.5)	1.6 (1.1-2.4)	6.6 (5.3-8.3)	2.7 (2.0-3.7)

95% CI: 95% confidence intervals (in parenthesis).

1-2 times per week: 2.62; 95% CI: 1.38-4.95 vs. 3+ times per week: 3.37; 95% CI: 2.06-5.53); (2) paracetamol intake, with some indications of a dose-effect association (SaOR for at least once a year: 2.02; 95% CI: 1.05-3.90 vs. at least once a month: SaOR 3.21; 95% CI: 1.70-6.05); and (3) time spent with computers, tablets or smart phones was also independently associated with sCAS (SaOR 1.32; 95% CI: 1.00-1.75).

Ecological analyses

The only moderator of the factors tested which significantly explained a high proportion of prevalence variation between centres was HDI. As seen in Figures 2B and 3B, an inverse relationship was observed between the logit of prevalence for CAS and sCAS and HDI. According to the meta-regression analyses, the beta coefficient of HDI for CAS was: -14.92 (95% CI: -29.13, -0.72, P = 0.039); and that for sCAS was -17.62 (95% CI: -30.11, -5.12, P = 0.006). For CAS, the null model expressed the following statistics: $\tau^2 = 0.096$, $I^2 = 88.0\%$ and Q = 41.80, P < 001, while the model, including HDI, resulted in: $\tau^2 = 0.051$, $I^2 = 75.9\%$ and Q = 16.6, P = 0023. Thus, the proportion of total variability explained by HDI (an analogue to R^2) was 0.46 or 46%. The corresponding figures for sCAS were as follows: $\tau^2 = 0.102$, $I^2 = 75.8\%$ and Q = 20.70, P = 0009; and $\tau^2 = 0.020$, $I^2 = 42.7\%$ and Q = 6.98, P = 0.137, with the proportion of total variability explained by HDI being 0.80 (80%).

DISCUSSION

The present study demonstrated low prevalence of CAS and sCAS in Kosovo. Compared with other countries in the GAN study,[21] Ferizaj had the lowest prevalence of CAS (4.6%) among the European centres. Only Athens (Greece) had a value of 6.2%, low enough to be compared with centres in Kosovo, such as Gjilan (6.4%) or Gjakova (6.5%). All Spanish centres had higher prevalence values than Prizren (11.3%), except for Cartagena (10.2%). Overall, centres in Kosovo, compared with other centres, had a low range of prevalence in other continents, such as Karthum in Sudan (5.7%), Quito in Ecuador (6.3%), Jaipur in India (6.8%) and Tyumen in Russia (8.5%).

With respect to sCAS, centres in Kosovo had a low prevalence, which, within the European centres in GAN, could be compared with Athens in Greece (1.8%) in the lower range, or Cartagena in Spain (4.1%) in the higher range. This low prevalence was again comparable with centres in India, such as Kottayam (1.5%) and Misuru (1.9%), in the lowest range of Kosovo, or with Santiago in Chile (3.9%) and Gadarif in Sudan (4.8%) in the highest range.

Environmental factors associated with CAS and sCAS were quite similar. Both paracetamol intake and exercise were the factors with the highest effect size and were comparable for CAS and sCAS. Whether paracetamol contributed to increased asthma prevalence or the association was just a consequence of reverse causation is still debatable, although its avoidance during the first year of life has

Table 2 Factors associated with current asthma symptoms in the six Kosovar centres included in the study.[†]

	Ferizaj N = 890		Gjakova N = 676		Gjilan N = 1200		Peja N = 1433		Prishtina N = 1056		Prizren N = 1427	
	OR	aOR	OR	aOR	OR	aOR	OR	aOR	OR	aOR	OR	aOR
Males	0.61 (0.32-1.18)	0.40 (0.15-1.03)	1.92 (1.04-3.55)	1.98 (1.01-3.88)	1.28 (0.80-2.03)	1.12 (0.64-1.96)	0.82 (0.57-1.18)	0.76 (0.50-1.13)	0.55 (0.34-0.88)	0.61 (0.34-1.10)	1.37 (0.98-1.91)	1.24 (0.83-1.86)
Exercise												
Never or occasionally	1	1	1	1	1	1	1	1	1	1	1	1
Once or twice per week	5.18 (2.55-10.5)	4.33 (1.81-10.4)	2.61 (1.32-5.16)	2.25 (1.09-4.65)	1.70 (0.96-3.01)	1.26 (0.67-2.38)	2.83 (1.88-4.26)	2.60 (1.70-3.99)	3.02 (1.81-5.06)	2.36 (1.32-4.23)	2.48 (1.73-3.54)	2.39 (1.60-3.55)
Three or more times per week	4.80 (1.67-13.8)	5.4 (1.44-20.2)	5.75 (2.13-15.6)	3.0 (0.96-9.34)	3.36 (1.79-6.31)	2.14 (1.03-4.49)	2.60 (1.53-4.41)	2.50 (1.42-4.39)	2.86 (1.43-5.71)	2.44 (1.06-5.58)	1.36 (0.71-2.59)	1.19 (0.60-2.37)
Television-watching[‡]	1.50 (1.08-2.10)	1.18 (0.73-1.93)	1.39 (0.93-2.07)	0.91 (0.56-1.49)	1.40 (1.10-1.79)	0.99 (0.72-1.37)	1.13 (0.92-1.38)	0.90 (0.71-1.16)	1.60 (1.23-2.08)	1.23 (0.88-1.73)	1.20 (1.00-1.45)	0.96 (0.76-1.23)
Computer/tablet/ smart phone use[‡]	1.35 (0.99-1.84)	1.07 (0.66-1.72)	1.80 (1.29-2.51)	1.68 (1.13-2.49)	1.83 (1.45-2.32)	1.68 (1.23-2.28)	1.29 (1.08-1.54)	1.29 (1.04-1.61)	1.67 (1.31-2.13)	1.37 (1.00-1.86)	1.43 (1.22-1.69)	1.26 (1.02-1.56)
Older siblings[‡]	1.16 (0.88-1.54)	1.13 (0.78-1.64)	0.65 (0.46-0.92)	0.52 (0.34-0.80)	1.00 (0.80-1.25)	0.93 (0.71-1.22)	1.02 (0.86-1.21)	1.05 (0.87-1.27)	0.94 (0.76-1.17)	0.90 (0.68-1.20)	0.98 (0.84-1.14)	0.97 (0.81-1.17)
Younger siblings[‡]	1.27 (0.93-1.73)	1.15 (0.76-1.75)	0.87 (0.60-1.27)	0.64 (0.41-1.00)	0.89 (0.69-1.16)	0.97 (0.71-1.33)	1.06 (0.88-1.28)	1.08 (0.88-1.32)	1.19 (0.94-1.49)	1.34 (0.98-1.83)	0.92 (0.78-1.10)	1.07 (0.87-1.32)
Truck traffic (street adolescent lives)												
Never	1	1	1	1	1	1	1	1	1	1	1	1
Seldom (not often)	1.31 (0.29-5.94)	0.84 (0.16 -4.51)	2.17 (0.49-9.56)	2.41 (0.52-11.2)	0.80 (0.37-1.70)	0.68 (0.28-1.63)	1.46 (0.76-2.83)	1.33 (0.66-2.71)	0.97 (0.42-2.24)	0.81 (0.29-2.29)	0.95 (0.57-1.60)	0.92 (0.50-1.69)
Frequently through the day	3.32 (0.75-14.7)	1.64 (0.30-8.90)	2.14 (0.48-9.45)	3.27 (0.68-15.7)	1.48 (0.67-3.25)	1.41 (0.57-3.52)	1.63 (0.80-3.30)	1.21 (0.56-2.60)	1.47 (0.63-3.48)	1.57 (0.55-4.50)	1.03 (0.58-1.82)	0.88 (0.45-1.69)
Almost the whole day	3.25 (0.67-15.7)	1.35 (0.23-7.92)	1.58 (0.28-8.95)	1.82 (0.30-11.1)	1.55 (0.59-4.04)	1.02 (0.34-3.02)	1.64 (0.72-3.73)	1.29 (0.54-3.10)	1.25 (0.45-3.48)	0.73 (0.20-2.59)	1.51 (0.72-3.16)	0.80 (0.33-1.96)
Paracetamol intake, last year												
Never	1	N.A.	1	1	1	1	1	1	1	1	1	1
At least once a year	7.60 (0.99-58.1)	N.A.	0.85 (0.35-2.04)	0.79 (0.31-2.03)	3.17 (1.08-9.26)	2.58 (0.86-7.77)	2.15 (1.26-3.68)	2.10 (1.21-3.65)	3.70 (1.29-10.6)	2.91 (0.96-8.83)	1.28 (0.72-2.26)	1.32 (0.70-2.48)
At least once per month	11.5 (1.53-86.1)	N.A.	2.05 (0.81-5.22)	1.57 (0.56-4.43)	8.76 (3.10-24.7)	6.02 (2.05-17.7)	3.41 (2.01-5.76)	2.58 (1.49-4.48)	7.97 (2.81-22.6)	5.40 (1.77-16.5)	2.67 (1.57-4.54)	2.47 (1.36-4.47)
Current cat ownership	1.91 (0.72-5.07)	1.40 (0.43-4.60)	1.38 (0.56-3.38)	1.51 (0.56-4.08)	2.31 (1.32-4.04)	2.59 (1.34-5.00)	2.04 (1.33-3.13)	1.98 (1.24-3.19)	1.13 (0.53-2.43)	0.64 (0.22-1.93)	0.69 (0.40-1.19)	0.47 (0.24-0.92)
Current dog ownership	1.45 (0.73-2.86)	1.60 (0.69-3.70)	1.93 (0.94-3.96)	1.34 (0.57-3.15)	1.52 (0.92-2.49)	0.86 (0.46-1.59)	1.56 (1.07-2.27)	1.29 (0.85-1.96)	1.44 (0.81-2.56)	1.22 (0.58-2.56)	1.34 (0.94-1.92)	1.59 (1.03-2.45)

Past cigarette smoker	2.38 (0.69-8.21)	0.80 (0.06-9.92)	N.A.	N.A.	4.34 (1.39-13.5)	1.78 (0.25-12.7)	1.90 (0.72-5.02)	2.99 (0.90-9.86)	5.78 (2.13-15.6)	1.73 (0.15-20.1)	3.44 (1.61-7.34)	0.94 (0.28-3.17)
Current cigarette smoker	4.17 (1.16-15.0)	2.78 (0.22-35.5)	N.A.	N.A.	3.71 (0.77-17.8)	3.19 (0.28-36.3)	0.74 (0.17-3.16)	0.42 (0.08-2.25)	15.2 (4.53-51.0)	8.46 (0.61-117.6)	5.06 (2.06-12.4)	6.17 (1.35-28.2)
Current water pipe smoker	3.74 (1.56-8.97)	2.32 (0.71-7.54)	1.54 (0.35-6.82)	1.75 (0.32-9.39)	2.12 (1.22-3.70)	1.21 (0.61-2.39)	1.45 (0.80-2.62)	1.16 (0.59-2.31)	3.22 (1.76-5.89)	2.17 (1.04-4.55)	2.17 (1.42-3.32)	1.36 (0.80-2.31)
Weight												
Overweight	N.A.	N.A.	0.31 (0.04-2.29)	0.29 (0.04-2.21)	1.04 (0.46-2.32)	1.18 (0.48-2.93)	1.22 (0.69-2.15)	1.15 (0.62-2.11)	0.80 (0.36-1.79)	0.64 (0.25-1.68)	1.67 (1.04-2.68)	1.68 (1.00-2.80)
Obese	1.31 (0.30-15.66)	3.61 (0.66-19.8)	N.A.	N.A.	1.09 (0.25-4.66)	0.63 (0.08-5.24)	0.47 (0.06-3.48)	0.22 (0.03-1.98)	0.70 (0.25-1.98)	0.64 (0.18-2.26)	1.24 (0.48-3.22)	1.21 (0.37-3.94)

†OR: odds ratio; aOR: adjusted odds ratio (for all factors in the table); 95% CI: 95% confidence intervals (in parenthesis).
‡For the purpose of this analysis, these four variables were treated as continuous, thus OR or aOR indicates the odds of current asthma symptoms for every increase of category (i.e., increasing the time or the number of siblings). See Table 1 for categories in each of these variables.
N.A.: Not enough numbers in the cell to obtain a sound result.

been recently suggested by the Global Initiative for Asthma strategy.[22] However, the role of this medicine as a genuine risk factor for asthma or only as a marker of asthma exacerbations in asthmatics is difficult to distinguish in adolescence.

Exercise has been very consistently found to be associated with CAS and sCAS. Although two different incremental categories were discovered, this association did not show a dose–response pattern. Reports have shown that exercise is associated with both decreased and increased risk of asthma.[23,24] However, this could depend on the age (for instance, being a risk in adolescents but not in children[23]) or on the intensity and duration of the exercise. In this regard, a recent study has shown that physical exercise for less than 4 h per week could be protective, while above 8 h per week could be a risk of asthma.[25] With the question used in the GAN questionnaire, it was rather difficult to know the exact amount of time spent exercising per week. On the other hand, this association (positive or negative) could be different when the environment is different in terms of air pollution, obesity, type of exercise, etc.

Similar to exercise, pet ownership, especially cat or dog, has been a controversial factor in relation to asthma.[26] In the present study, both pets have quite similar point estimates in the corresponding SaOR; however, only dog ownership is associated with CAS (and marginally to sCAS). This difference in association of pets with asthma could be due to differences in occurrences of cat and dog ownership in Kosovo, ranging from 7.2% to 14.9% for cats versus 15.4 to 27.8% for dogs. This difference probably accounted for smaller confidence intervals (and thus statistical significance) in the case of dog ownership.

Sedentariness has been quite consistently associated with the increased risk of asthma independent of body mass index (BMI), and could be due to unfit bronchial muscles.[27] Bivariate analyses conducted in the present study demonstrated that more the time spent watching television or managing computers, tablets or smart phones, higher was the proportion of individuals suffering from asthma. When both factors were introduced in the logistic regression, only time spent with computer/tablet/smart phone was significantly associated with higher prevalence of asthma. This also accounted for overweight or obesity.

Tobacco smoking, which has been consistently shown as a risk factor for CAS[28] in other studies, is a somewhat erratic factor with quite high and quite low aORs depending on the centre. This is probably explained by the very low smoker proportion of adolescents (range: 0.7–2.2% for the current study and 0.9–3.5% constantly). Curiously, water pipe smoking was much more frequent, ranging from 3.1% to 13.3%. This smoking habit, identified as a risk factor for bronchial inflammation,[29] was consistently associated with more asthma symptoms in all centres and resulted in a statistically significant factor in the meta-analysis of CAS, but not for sCAS, probably due to severity precluding any smoking method.

It is of considerable interest that HDI explained a high proportion of prevalence variability of both CAS and sCAS. The association of higher asthma prevalence rate with lower HDI had been previously shown in Latin America.[9]

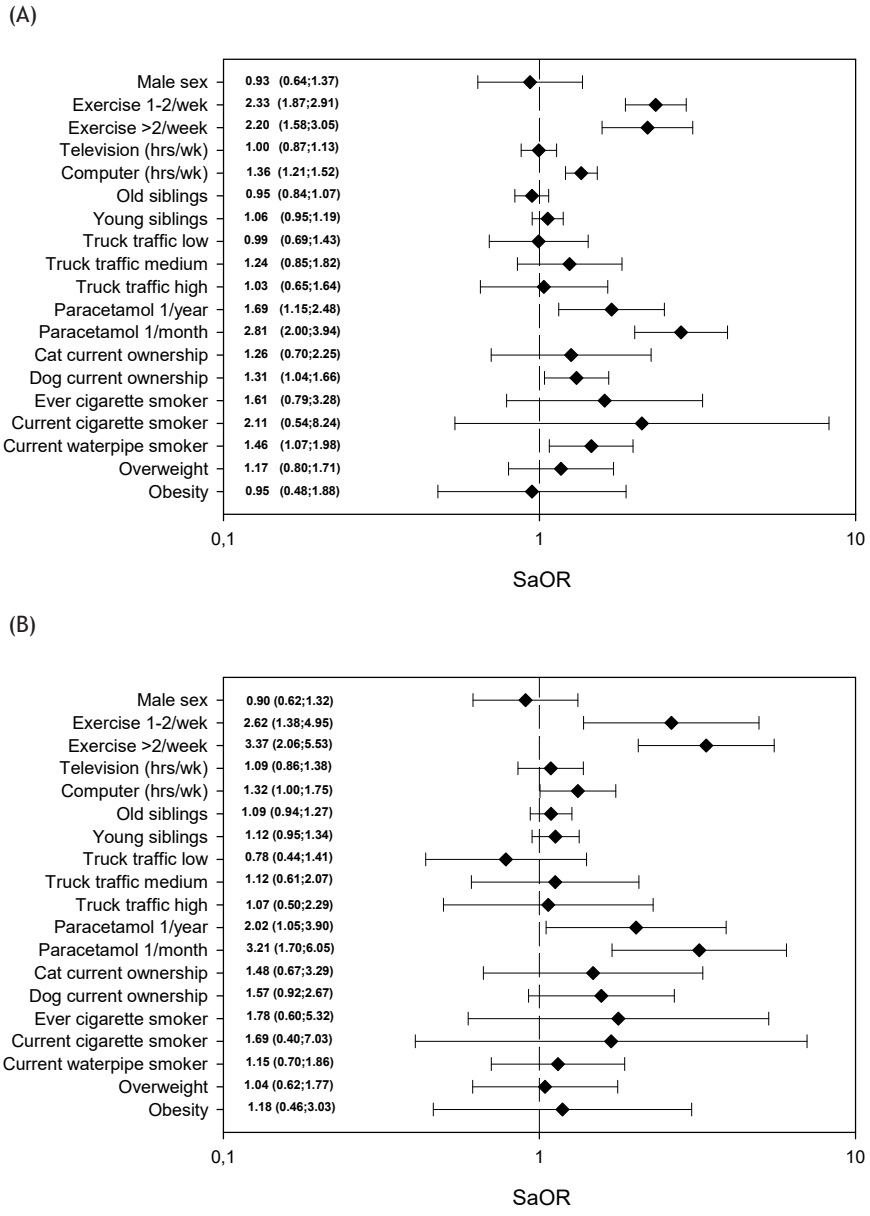

Figure 1 Meta-analyses of the summary of adjusted odds ratios (SaOR) for different factors in each centre for (A) current asthma symptoms (CAS); and (B) severe current asthma symptoms (sCAS). Note that for clarity of presentation, the x-axis has been converted to log scale.

Inadequate diagnostic facilities in less developed countries which could lead to underestimation of prevalence has been claimed to be an explanation for this finding.[10] However, this is probably not the case of a small country, such as Kosovo, with a quite uniform health system and relatively uniform HDI between centres (0.724–0.766). However, the "HDI pack" seems to have a quite influential function, which could be better explored globally.[11]

The present study has two main limitations: firstly, in individual analyses, its cross-sectional quality must be considered, thus causal relationships could not be established. Secondly, in the ecological analyses, only six centres were considered, making the robustness of meta-analyses and meta-regressions not as high as desired.

Conclusion

The present study established the first epidemiological data on asthma in adolescents in most district centres of Kosovo. It observed that HDI was the factor that could better explain the differences of prevalence between six of the seven districts of the country

Author contributions

The following individual contributions were made by authors: Conceptualisation: Global Asthma Network Steering Committee, including Luis García-Marcos; data curation: Global Asthma Network Global (Auckland) and data

Table 3 Factors associated with current severe asthma symptoms in the six Kosovar centres included in the study.[†]

	Ferizaj N = 890		Gjakova N = 676		Gjilan N = 1200		Peja N = 1433		Prishtina N = 1056		Prizren N = 1427	
	OR	aOR	OR	aOR	OR	aOR	OR	aOR	OR	aOR	OR	aOR
Males	0.80 (0.28-2.27)	0.69 (0.16-2.94)	0.92 (0.33-2.55)	0.82 (0.26-2.65)	1.29 (0.80-2.03)	1.06 (0.45-2.49)	0.66 (0.39-1.11)	0.65 (0.36-1.16)	0.43 (0.19-0.97)	0.68 (0.24-1.95)	1.65 (0.98-2.77)	1.52 (0.80-2.89)
Exercise												
Never or occasionally	N.A.	N.A.	1	1	1	1	1	1	1	1	1	1
Once or twice per week	N.A.	N.A.	2.30 (0.82-6.44)	2.12 (0.69-6.54)	0.67 (0.19-2.31)	0.55 (0.15-1.99)	4.27 (2.37-7.69)	3.80 (2.06-7.00)	4.41 (1.74-11.2)	3.32 (1.12-9.79)	2.31 (1.33-4.03)	2.03 (1.09-3.80)
Three or more times per week	N.A.	N.A.	N.A.	N.A.	6.00 (2.73-13.2)	4.63 (1.85-11.6)	4.06 (1.97-8.40)	4.14 (1.91-8.99)	7.18 (2.54-20.2)	4.16 (1.07-16.1)	2.14 (0.92-5.02)	1.65 (0.65-4.20)
Television-watching[‡]	1.50 (0.89-2.51)	1.88 (0.82-4.33)	1.22 (0.63-2.37)	0.55 (0.23-1.29)	1.03 (0.70-1.51)	0.71 (0.44-1.16)	1.34 (1.02-1.77)	1.20 (0.85-1.69)	1.48 (0.97-2.26)	1.38 (0.76-2.50)	1.47 (1.11-1.95)	1.18 (0.83-1.69)
Computer/tablet/smart phone use[‡]	1.28 (0.79-2.08)	0.58 (0.25-1.34)	2.04 (1.19-3.48)	2.41 1.21-4.80)	1.88 (1.32-2.69)	1.94 (1.21-3.12)	1.23 (0.96-1.59)	1.11 (0.81-1.54)	1.68 (1.14-2.48)	1.11 (0.65-1.88)	1.74 (1.36-2.24)	1.35 (0.98-1.88)
Older siblings[‡]	1.14 (0.72-1.80)	1.19 (0.65-2.18)	0.88 (0.52-1.51)	0.63 (0.32-1.24)	1.12 (0.81-1.55)	0.92 (0.61-1.39)	1.11 (0.88-1.42)	1.16 (0.89-1.50)	1.10 (0.78-1.55)	1.25 (0.79-1.99)	1.09 (0.87-1.36)	1.12 (0.85-1.48)
Younger siblings[‡]	1.18 (0.71-1.96)	1.44 (0.75-2.76)	0.82 (0.44-1.52)	0.63 (0.30-1.31)	0.74 (0.49-1.13)	0.82 (0.49-1.36)	1.09 (0.84-1.42)	1.13 (0.84-1.50)	1.31 (0.91-1.88)	1.49 (0.88-2.53)	0.96 (0.74-1.24)	1.20 (0.88-1.65)
Truck traffic (street adolescent lives)												
Never	N.A.	N.A.	N.A.	N.A.	1	1	1	1	1	1	1	1
Seldom (not often)	N.A.	N.A.	N.A.	N.A.	1.00 (0.28-3.52)	0.96 (0.20-4.70)	1.29 (0.49-3.38)	0.93 (0.34-2.54)	0.62 (0.20-1.94)	0.47 (0.11-1.99)	0.76 (0.34-1.71)	0.78 (0.29-2.07)
Frequently through the day	N.A.	N.A.	N.A.	N.A.	1.93 (0.53-7.02)	2.18 (0.43-11.1)	1.81 (0.66-5.00)	1.05 (0.37-3.04)	0.77 (0.23-2.55)	0.68 (0.15-3.14)	1.30 (0.56-3.02)	1.14 (0.42-3.13)
Almost the whole day	N.A.	N.A.	N.A.	N.A.	2.57 (0.60-11.0)	2.43 (0.41-14.5)	2.04 (0.65-6.37)	1.21 (0.36-4.01)	0.71 (0.15-3.24)	0.06 (0.002-1.44)	2.15 (0.78-5.93)	0.96 (0.27-3.48)
Paracetamol intake, last year												
Never	N.A.	N.A.	1	1	N.A.	N.A.	1	1	N.A.	N.A.	1	1
At least once a year	N.A.	N.A.	3.34 (0.43-25.9)	3.67 (0.42-31.9)	N.A.	N.A.	2.13 (0.93-4.89)	1.87 (0.80-4.37)	N.A.	N.A.	1.35 (0.52-3.49)	1.97 (0.61-6.38)
At least once per month	N.A.	N.A.	2.74 (0.28-26.7)	2.35 (0.22-25.3)	N.A.	N.A.	4.28 (1.94-9.42)	2.73 (1.20-6.23)	N.A.	N.A.	3.27 (1.36-7.83)	4.55 (1.52-13.6)
Current cat ownership	3.32 (0.91-12.1)	3.09 (0.54-17.8)	1.22 (0.27-5.50)	0.70 (0.13-3.83)	1.94 (0.83-4.56)	3.65 (1.32-10.1)	2.42 (1.35-4.34)	2.29 (1.20-4.38)	1.69 (0.57-4.98)	1.55 (0.38-6.45)	0.67 (0.28-1.58)	0.30 (0.09-0.96)
Current dog ownership	2.63 (0.94-7.35)	2.80 (0.69-11.4)	2.58 (0.88-7.57)	3.03 (0.78-11.7)	0.82 (0.35-1.91)	0.38 (0.12-1.15)	1.70 (1.00-2.91)	1.47 (0.81-2.65)	1.90 (0.79-4.56)	1.52 (0.46-4.97)	1.83 (1.08-3.08)	2.28 (1.22-4.25)
Past cigarette smoker	2.00 (0.25-15.8)	N.A.	N.A.	N.A.	7.67 (2.11-27.9)	6.78 (0.61-75.4)	1.57 (0.37-6.72)	2.08 (0.35-12.4)	N.A.	N.A.	3.90 (1.46-10.5)	0.80 (0.15-4.35)

(Continued)

Table 3 (Continued)

	Ferizaj N = 890		Gjakova N = 676		Gjilan N = 1200		Peja N = 1433		Prishtina N = 1056		Prizren N = 1427	
	OR	aOR	OR	aOR	OR	aOR	OR	aOR	OR	aOR	OR	aOR
Current cigarette smoker	3.34 (0.41-26.8)	N.A.	N.A.	N.A.	4.02 (0.49-32.7)	1.09 (0.04-27.2)	0.83 (0.11-6.18)	0.63 (0.06-6.23)	N.A.	N.A.	7.01 (2.48-19.8)	4.60 (0.58-36.4)
Current wáter pipe smoker	1.25 (0.16-9.78)	0.26 (0.02-7.39)	4.82 (1.02-22.7)	5.79 (0.79-42.5)	2.15 (0.95-4.86)	0.92 (0.31-2.74))	0.83 (0.29-2.33)	0.64 (0.20-1.99)	3.85 (1.59-9.35)	0.96 (0.22-4.16)	3.12 (1.76-5.54)	1.51 (0.72-3.19)
Weight												
Overweight	N.A.	N.A.	0.92 (0.12-7.16)	1.25 (0.15-10.6)	1.45 (0.50-4.22)	1.56 (0.43-5.61)	0.84 (0.33-2.15)	0.90 (0.34-2.36)	1.50 (0.51-4.43)	0.91 (0.20-4.22)	0.91 (0.39-2.16)	0.99 (0.40-2.42)
Obese	N.A.	N.A.	N.A.	N.A.	1.32 (0.17-10.1)	1.20 (0.12-12.5)	1.04 (0.14-7.88)	0.66 (0.07-6.15)	1.74 (0.51-5.97)	1.50 (0.29-7.69)	1.15 (0.27-4.87)	1.26 (0.24-6.53)

†OR: odds ratios; aOR: adjusted odds ratios (for all factors in the table); CI 95%: 95% confidence intervals (in parenthesis).
‡For the purpose of this analysis, these four variables were treated as continuous, thus OR or aOR indicates the odds of current asthma symptoms for every increase of category (i.e., increasing the time or the number of siblings). See Table 1 for categories in each of these variables.
N.A.: Not enough numbers in the cell to obtain a sound result.

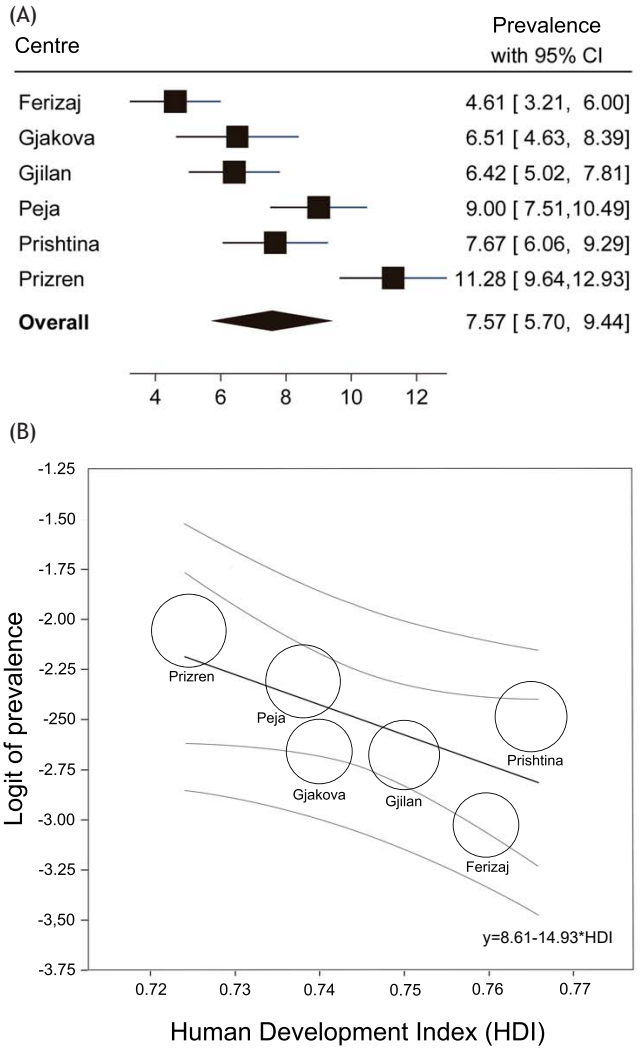

Figure 2 (A) Forest plot with per centre prevalence and overall prevalence of current asthma symptoms: z = -18.6, P < 0.001. (B) Meta-regression plot and equation: null model: $\tau^2 = 0.096$, $I^2 = 88.0\%$ and Q = 41.80, P < 001; model, including HDI: $\tau^2 = 0.051$, $I^2 = 75.9\%$ and Q = 16.6, P = 0023. Proportion of total variability explained by HDI: 46%.

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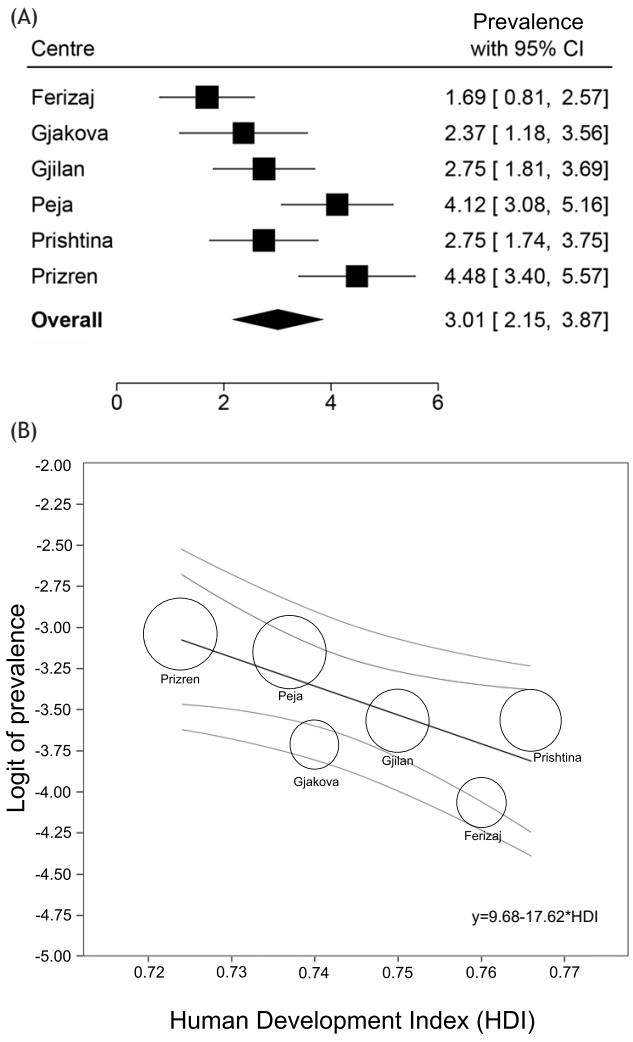

Figure 3 (A) Forest plot with per centre prevalence and overall prevalence of current severe asthma symptoms: z = -23.4, P < 0.001. (B) Meta-regression plot and equation. Null model: τ^2 = 0.102, I^2 = 75.8% and Q = 20.70, P = 0009; model, including HDI: τ^2 = 0.020, I^2 = 42.7% and Q = 6.98, P = 0.137. Proportion of total variability explained by HDI: 80%.

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Conflict of interest

The authors declared no conflict of interest.

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Impact statement

This study provided the first epidemiological data on asthma in Kovoso. Prevalence of asthma in Kovoso is quite low, compared to the other countries of the European continent. A great proportion of difference in prevalence between locations, especially severe asthma symptoms, could be explained by HDI, which moves in a relatively low range within the country. Hence, the use of HDI must be expanded to explain differences in the prevalence of asthma globally.

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