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Spirometry testing in a population of Italian children: Age and gender differences

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Summary
Aim: To estimate how many asthmatic children underwent spirometry testing in one year in a large Italian region, and evaluate sociodemographic determinants.
Methods: Data were retrieved from the administrative databases that store all pharmacological and diagnostic prescriptions issued to individuals living in the Lombardy Region. The analysis involved prescriptions dispensed to all 6–17 year olds (1,047,241 subjects) during 2008. Youths were identified as asthmatics by a previously validated strategy. Number of subjects having ≥1 spirometry claims was calculated, and factors associated with the probability of undergoing spirometry were evaluated by multivariate analysis.
Results: A total of 40,528 (3.9%) asthmatic subjects were identified. Only 30% of them underwent ≥1 spirometry during 2008, with differences between local health units (range 22–45%) and degree of anti-asthmatic use (26–35%). Moreover, in a multivariate analysis, the chance of undergoing spirometry was greater in boys than in girls (OR = 2.3).
Conclusions: A low percentage of asthmatic children, especially girls (who are more at risk of developing severe disease in adulthood), underwent spirometry during 1-year period. This highlights a low compliance with guidelines in the monitoring of childhood asthma. Educational intervention is needed in order to encourage use of spirometry in primary care settings.

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Introduction

The burden of childhood asthma worldwide varies, but it is substantial everywhere.[1] The prevalence of lifetime asthma for Italian 6–7 years of age children did not change significantly between 1995 and 2002 (from 9.1 to 9.5%), while it increased significantly for adolescents 13–14 years of age (from 9.1 to 10.4).[2] Patients' perceptions of airflow obstruction are highly variable, and under-reporting of symptoms is frequent among children. In order to obtain objective measures of lung function and optimize asthma control, periodic monitoring of airway function is necessary in asthma management. Guidelines for the diagnosis and treatment of asthma in childhood[3–5] recommend the use of spirometry every 1–2 years or more frequently, and always at the following times: at the initial assessment; after treatment is initiated and symptoms have stabilized; and during periods of progressive or prolonged loss of asthma control. It has been reported that a decreased FEV_1/FVC ratio not only suggests current obstruction, but also represents a measure of exacerbation risk and likely persistence of disease in adulthood.[6] Although a reliable spirometry can be performed in many children as young as 4 years of age,[7,8] only in older children the risk of misdiagnosis of asthma is reduced and less confused with transitory wheezing, which in the majority of the cases disappears by school age. However, even though many transient early wheezers no longer wheeze at age 6, they still maintain an impaired lung function at 9–11[9] and at 16 years,[10] and are more likely to eventually develop chronic obstructive pulmonary disease. Although spirometry is a key clinical test for asthma diagnosis and management, in a cohort of 2688 American children only 23% had $\geq$1 spirometry testing during a three year observation period[11] and only 43% of a population of Canadian children received spirometry to establish asthma diagnosis.[12] The objective of this study was therefore to assess the extent of use of spirometry testing in a population of children and adolescents previously identified as asthmatic by a validated strategy based on anti-asthmatic prescriptions.[13]

Methods

The data sources were health administrative databases of the Lombardy Region, and in particular: database collecting prescriptions dispensed by the retail pharmacies of the 15 local health units (LHUs) in the Lombardy Region and reimbursed by the Italian national health service; hospital discharge form database; database collecting prescriptions for diagnostic tests and specialist visits performed in hospital outpatient ambulatories. The study period was from January 1 to December 31, 2008. The study population was composed of 1,047,241 children and adolescents 6–17 years old, male/female ratio 1.06, living in the Lombardy Region. The population sample represented 15% of the overall Italian 6–17 year old paediatric population for the year 2008. Data were managed and analysed using an anonymous patient code. Anti-asthmatics were classified as drugs belonging to the R03 main therapeutic group of the Anatomical Therapeutic Chemical classification system (ATC). As previously described,[14] subjects 6–17 years old receiving at least one package of anti-asthmatic drugs in age-appropriate formulations were defined as Potential Asthmatics (PA). This strategy for the identification of PA patients has been validated as a good proxy of disease prevalence (sensitivity 90%, specificity 98%).[13] PA were divided into three groups based on number of packages received during 2008: (A) "occasional users", subjects receiving only one package; (B) "low users", subjects receiving 2–4 packages; (C) "high users", subjects receiving 5 or more packages. Percentage of spirometry testing claims during 2008 was calculated in the three different subgroups and in each of the 15 LHUs. Prevalence data by age and gender were calculated as number of children treated with anti-asthmatic drugs per 100 inhabitants. The prevalence of asthma at LHU level was estimated by dividing the number of PA by the residents of each LHU. A chi-square test was performed to compare the proportion of youths with spirometry testing by gender, age group, and degree of anti-asthmatic drug utilization. Finally, a logistic regression analysis was performed in order to identify the determinants of spirometry testing. The dependent variable was at least one claim for spirometry testing during 2008. Independent variables were degree of anti-asthmatic drug use (no use, occasional, low, high use) and LHU of residence. The LHU of Mantova was taken as reference because, as previously reported,[15] after adjustment for age, gender and degree of drug use, it has been identified as the LHU with the highest prevalence of PA. After adjustment for age (continuous variable), the odds ratio (OR) and relative 95% confidence interval (CI) between the groups were calculated. Statistical analysis was performed using SAS software, version 9.1 (SAS Inc., Cary, NC, USA). A p value <0.05 was considered to be statistically significant.

Results

Characteristics and drug prescription profile of the PA 6–17 year old population

During 2008, 40,528 children and adolescents 6–17 years old received at least one age-appropriate anti-asthmatic drug prescription and were therefore identified as PA. This represents 3.9% of the 6–17 year old population studied (4.9 and 2.9% of the 6–17 year old boys and girls, respectively). Mean age of PA was 11 and percentage of boys was 64% (Table 1), with a boy/girl ratio of 1.8. Among PA, occasional users were 10,091 (prevalence 0.96%), low users were 18,066 (prevalence 1.73%), and high users were 12,371 (prevalence 1.18%).

The population prescription profile showed that 79% received inhaled corticosteroids (ICS) and 38% received ICS without any other controller drug. Seventy percent of PA received short-acting beta2 agonists (18% exclusively). No differences in these percentages were found between boys and girls.

Specialist visits

In all, 4900 PA subjects (12%) underwent allergologist or pneumologist visits and, among these, 2897 subjects had

Table 1 Characteristics of children undergoing spirometry.

	Spirometry			*p*
	Yes ($N = 12{,}018$)	No (28,510)	Total ($N = 40{,}528$)	
Age (mean ± SD)	12.4 ± 2.9	10.8 ± 3.4	11.3 ± 3.4	< 0.0001
No. anti-asthma drug prescriptions (mean ± SD)	3.7 ± 3.4	3.2 ± 3.0	3.4 ± 3.1	<0.0001
Male (%)	71.3	61.2	64.3	<0.0001
Hospitalized for asthma (%)	1.3	1.0	1.1	0.005

only one visit (59%), 1243 had two visits (25%), and 15% had three or more visits during the year considered. The proportion of PA children with a specialist visit increased with the degree of anti-asthmatic drug use, from 10% in occasional users to 20% in high users ($\chi^2_t = 382$, $p < 0.0001$), and no differences were found between genders (Fig. 1A). Of the overall PA subjects who underwent a specialist visit, 50% did not undergo spirometry testing during the same observation period (Fig. 1A).

Spirometry rate of the PA 6–17 year old population

A total of 158,137 children and adolescents underwent at least one spirometry test during 2008, 12,018 of whom were identified as potential asthmatics (29.7% of the total PA). (Table 1)

As shown in Fig. 1B, the proportion of PA with at least one spirometry test was greater in males than females (32.9 vs. 23.9%; $\chi^2 = 361$, $p < 0.0001$). Moreover, this percentage increased with degree of anti-asthma medication use, from 26.3% in occasional users to 35% in high users ($\chi^2_t = 209$, $p < 0.0001$). Ninety-three percent of the overall PA subjects had only one spirometry testing during the period considered and 7% had two, with no difference between girls and boys. The prevalence of spirometry testing among the non-potential asthmatic youths was 14.6%, again with a difference between genders. Seventy-five percent of the overall PA youths undergoing spirometry did not receive any specialist visit claims during the same observation period (Fig. 1B).

In Fig. 2 the age and gender differences of PA subjects receiving a spirometry are reported. From age 6–11, spirometry claims increased in both genders, after which boys received more spirometry claims than girls. A decrease for both genders followed after age 13.

Differences among LHUs

The proportion of children with at least one claim for spirometry differed among LHUs. The proportion ranged between 20.6% in Sondrio and 39.7% in Lodi.

No statistically significant correlation was found between the rank distribution at LHU level of percentage of

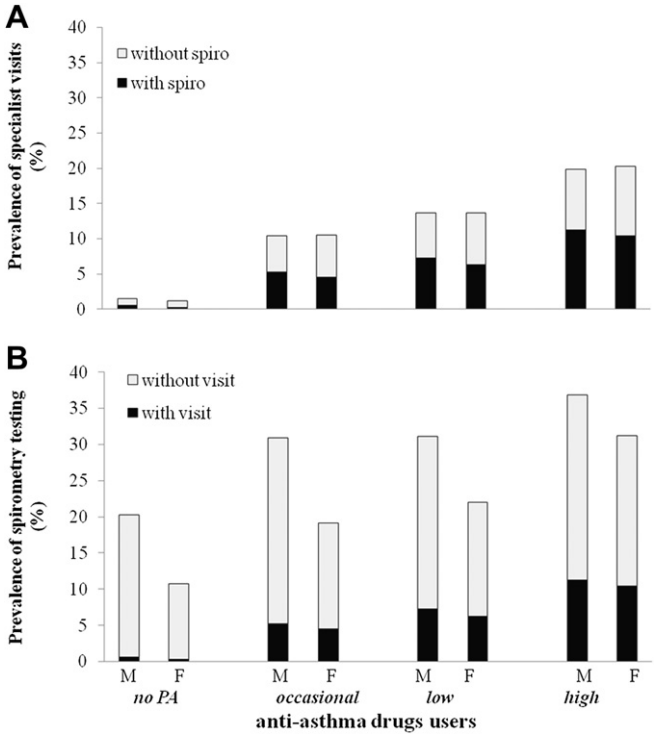

Figure 1 Prevalence of youths performing specialist visit (A) and undergoing spirometry test (B). M = males ; F = females.

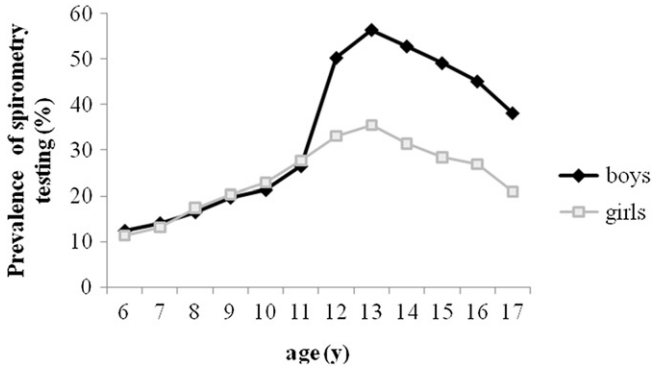

Figure 2 Prevalence of youths, by gender and age, performing at least one spirometry test during 2008.

PA children with spirometry testing and prevalence of potential asthmatic patients, hospitalization rate for asthma or proportion of children with allergologist and/or pneumologist visits.

Rate of hospitalization among the PA 6—17 year old population

A total of 449 (1.1%) PA children and adolescents were hospitalized (Table 1), with statistically significant differences in rates of occasional, low and high users (0.3, 0.7 and 2.5 respectively). No significant differences were found in hospitalization rate by gender, but after adjusting for degree of anti-asthmatic drugs use, high user girls were more hospitalized than boys (2.5 vs. 2.1).

Multivariate analyses

Table 2 reports the results of logistic regression analysis. After adjusting for age (in continuous variable), the probability of undergoing spirometry testing was greater in males and in high anti-asthmatic users. Moreover, the LHU of residence was one of the determinants of spirometry, with OR ranging from 1.07 to 2.01 vs. Mantova, which was the LHU used as reference.

Discussion

Although periodic assessment of lung function by spirometry is recommended by guidelines,[3—5] and it has been reported that spirometry can be performed in a reproducibly good quality in children and adolescents,[16] our analyses highlighted that only 30% of asthmatic youths underwent spirometry testing in an outpatient ambulatory during 2008. This percentage was slightly higher (35%) in children who were high users of anti-asthma therapy. Even considering a longer observation period of 24 months, less than half of youths (37%) receiving asthma therapy, also received spirometry testing every one to two years.

Comparing our study results with the very few studies regarding rates of spirometry among asthmatic children, the percentage observed in the Lombardy Region (ranging among LHUs from 22 to 45%) is slightly higher than that found in a cohort of 2688 asthmatic American children (23%), enrolled in a managed care organization and followed for three years ,[11] and slightly lower than that found in a Canadian population of the same age range receiving spirometry for asthma diagnosis (38%).[12]

In the Lombardy Region the likelihood of receiving spirometry was associated with several factors: age, gender, setting (LHU) and, as expected, degree of anti-asthmatic drug use (proxy for severity of asthma). It is important to note that after adjusting for degree of anti-asthmatic drug use and age (as a continuous variable), the chance to undergo spirometry was two-fold greater in boys than in girls. The gender gap in spirometry testing was found also in the non PA group (Fig. 1B) and decreased with increasing severity of asthma but nevertheless remained in high users (37% in boys vs. 31% in girls). The possibility of

Table 2 Results of multivariate analysis.

	No.	OR	95% CI	
Gender				
Female	507,152	Reference		
Male	540,089	2.25	2.22	2.23
LHU				
Mantova	41,718	Reference		
Sondrio	20,708	1.07	1.02	1.13
Pavia	51,764	1.18	1.13	1.23
Milano	119,188	1.22	1.18	1.27
Brescia	130,074	1.43	1.38	1.48
Varese	93,599	1.45	1.40	1.51
Como	64,079	1.53	1.47	1.59
Vallecamonica	10,420	1.56	1.46	1.56
Milano 3	11,5682	1.64	1.58	1.70
Lodi	25,048	1.67	1.60	1.75
Milano 2	64,947	1.68	1.62	1.75
Bergamo	126,210	1.79	1.73	1.85
Milano 1	108,759	1.83	1.76	1.89
Cremona	37,009	1.86	1.79	1.94
Lecco	38,036	2.01	1.93	2.09
Anti-asthma drug use				
No	1,006,713	Reference		
Yes				
Occasional	10,091	1.70	1.62	1.78
Low	18,066	2.18	2.10	2.25
High	12,371	3.64	3.64	3.95

under-diagnosis in the female gender is suggested by the Yentl's syndrome.[17] Mainly described for adult women and in cardiology,[18,19] the Yentl syndrome has been reported also for childhood asthma[20] in a Swiss study, in which for any particular asthma-related symptom, significantly more boys than girls received treatment. Another, or concomitant, explanation could be that boys have worse asthma control and need more frequent lung function monitoring. Girls seem to be monitored less frequently than boys, and to receive occasional anti-asthma therapy more often than boys, who are, instead, more chronically treated. Guidelines distinguish between degree of asthma severity and asthma control.[3] Although it has been reported that in a population younger than 18, the characteristics of severe asthma were more present in boys than in girls,[21] in adult populations several studies suggested that females might have a worse control of asthma symptoms, despite better pulmonary function.[22–25]

According to our data, no difference in hospitalization rates for asthma was found between male and female PA youths and this did not support the hypothesis of a worse asthma control in boys than in girls. On the contrary, a slightly higher risk of hospitalization was found in high user girls compared with boys (2.5% vs. 2.1%), suggesting that an inadequate management might be responsible of hospitalization.

Limitations of the study

This study has some limitations. The observation period was short, and it is possible that the proportion of asthmatic children with one spirometry testing in a longer period may be greater. However, an additional analysis of one-third of the PA subjects here considered, evaluated also during 2007, confirmed the reported finding. The rate of potential asthmatics with at least one spirometry test in 2007 or 2008 was slightly higher than the rate of spirometry testing in 2008 only (36.6 vs. 29.6%, respectively), and differences between boys and girls were maintained using the 2007–2008 observation period (39.8 vs. 31.1%, respectively), and the rate of spirometry among the high users in the 24-month period was 42.1% (34.4% in 2008 only). Finally, it might be possible that, at the time of specialist visit, a spirometry testing was performed but the sum of subjects with spirometry claim and subjects with visit claim is still only 42% of PA children/adolescents.

Conclusion

In conclusion, educational interventions are needed in order to encourage use of spirometry in primary care setting and initiative to address deficiencies in test performing and interpretation.[26,27] The main finding of this study is the low spirometry testing rate in girls. Since females have more severe asthma in adulthood, an accurate, early monitoring of impaired lung function in girls is an important piece of paediatric asthma management. To the best of our knowledge, this is the first study that finds gender differences in the rate of spirometry testing in a population of asthmatic children.

Conflict of interest

All authors have no conflicts of interest associated with this publication.

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