

PSYCHOLOGICAL DISORDERS

Asthma and Major Depressive Episode in Adolescents in France

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Rationale. The association between asthma and anxiety disorders in teenagers is well documented, but data about the association with mood disorders are scarce. **Methods.** We analyzed data from a cross-sectional study conducted among ninth grade schoolchildren in France in 2003–2004. The teenagers were selected by two-stage sampling and interviewed by school doctors/nurses using a standardized questionnaire including questions about asthma and asthma-like symptoms. They also completed a self-administered questionnaire in which the occurrence of major depressive episodes (MDEs) during the past 12 months was assessed by the Composite International Diagnostic Interview—Short Form. **Results.** A total of 7000 teenagers (mean age 15.1 years) were included. The prevalence of wheezing in the past 12 months was 10.0% and that of current asthma (wheezing in the past 12 months in children who had already had asthma attacks, or treatment for wheezing or asthma in the past 12 months) was 8.5%. The prevalence of MDE during the past year was 14.2% in teenagers with current asthma versus 9.2% among the others. The association between current asthma and past-year MDE remained significant after adjustment for age, gender, family structure, and the father's employment status. Asthma was uncontrolled (at least four attacks of wheezing, one awakening per week due to wheezing, one severe wheezing, four unplanned medical visits, or one hospitalization for a wheezing attack in the past year) in more than half (58.3%) of asthmatic teenagers with an MDE in the past year versus 35.3% of those without an MDE. **Conclusion.** Asthma is associated with a higher prevalence of MDE. Among adolescents with asthma, MDE is associated with poorer asthma control. These findings highlight the need for a comprehensive care management of asthma in France that takes the psychological dimension into account.

Keywords adolescent, asthma, depressive disorder, epidemiology

INTRODUCTION

Asthma is the most common chronic childhood disease. In France, the cumulative prevalence of asthma in children is over 10% (1). Major depression in adolescents is now recognized as a serious psychiatric disorder with a pattern of symptoms and prevalence rates similar to those reported for adults (2). Moreover, adolescent-onset depression is associated with an increased risk of suicide attempts and the recurrence of major depressive disorder in adulthood (3).

Higher rates of mental disorders including anxiety, depression, and suicidal ideation have been reported in adults with asthma than in healthy people (4–8). Among children and adolescents, while cross-sectional studies have repeatedly found an increased prevalence of anxiety disorders in those with asthma (7, 9–11), results concerning mood disorders are less consistent (9, 10, 12–14). Depression has been found to be associated with sociodemographic characteristics (15–17). While depression is relatively rare during the juvenile period, a marked increase in prevalence is observed in older adolescents during their transition to adulthood (15). During adolescence, prevalence rates of depression have been consistently found to be higher among girls than boys.

Sociodemographic variables that represent indirect indicators of environmental adversity, such as low social class and growing up in a single-parent household, have all been found to be related to a wide range of child and adolescent mental disorders including depression (16, 17). Sociodemographic conditions also represent indirect indicators of differential environmental exposures that influence the development and the expression of asthma. Hence, they could explain, at least partly, the relationship that has been evidenced between asthma and depression.

Poor mental health has heavy consequences on asthma care: both anxiety and depression have been linked to lower functional status in patients with asthma and poorer asthma control and it has been shown that adherence to asthma treatment is lower in patients who are depressed (18–22).

The triennial cycle of surveys in French schools is a comprehensive epidemiological health survey including the assessment of respiratory health. Estimates of the prevalence of asthma according to sociodemographic conditions have already been published (1). The survey conducted among ninth grade students during the 2003–2004 academic year included a standardized diagnosis instrument assessing depression disorders. In the present analysis, we hypothesized that there is a link between asthma and depression, first that the prevalence of depression is higher among adolescents with asthma than in those without asthma, and second that depression is associated with a poorer asthma control.

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METHODS

Study Population

The triennial cycle of surveys in school has been carried out in France (including the overseas territories) since the 1999–2000 academic year. It is performed consecutively among pupils in the last year of nursery school, in the ninth grade, and in the fifth grade. In 2003–2004, the survey was conducted among pupils in the general and technical sections of the ninth grade. Pupils were selected by a two-stage sampling procedure including a random sampling of 1000 secondary public and private schools and then, within each school selected, a random sampling of 10 children. A letter was sent to the parents informing about the survey and specifying that participation was on a voluntary basis, hence their child or themselves were free to refuse. If they gave consent for their child's participation, the latter was asked to bring his/her personal immunization record on the day of the medical visit. According to the French regulation, the examination of the study protocol by the National Ethics Committee was not required as the triennial cycle of surveys in school was implemented by the Ministries of Health and Education as part of a national health program.

Data Collection

Students were interviewed by the school doctor or nurse using a standardized questionnaire about the socioeconomic background of the family, the family structure (living with both parents or with a lone parent), and the parents' employment status and occupation. Questions on asthma and asthma-like symptoms were those of the French version of the standardized International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire (23), completed by items about treatment and medical care for asthma or wheezing attacks in the previous 12 months. A medical examination including anthropometric measures was performed.

A self-administered questionnaire assessing the occurrence of major depressive episodes (MDEs) during the previous 12 months by the Composite International Diagnostic Interview—Short Form (CIDI-SF) (24) was completed by the respondents. The CIDI is a structured diagnostic questionnaire capable of generating diagnoses according to the definitions and criteria of the *Diagnosis and Statistical Manual of Mental Disorders* (DSM) and *International Classification of Diseases* (ICD). The short form has been devised to provide a quick screen for the most common disorders. The CIDI-SF for MDEs began with two stem questions about whether the interviewee had experienced at least 2 weeks of continuous dysphoric mood or anhedonia during the past 12 months. If neither of the questions elicited a positive response, the rest of the questionnaire was skipped, and the interviewee was automatically classified as not having MDE. On the other hand, endorsement of at least one of the stem questions led on to seven additional questions about associated symptoms: feeling tired, change in weight, trouble with sleep, trouble concentrating, feeling down,

losing interest, and thoughts about death. A question was also asked about impairment in daily activities, coded on a four-level scale (none, little, moderate, high).

Data Analysis

Following the DSM-IV classification, MDE in the past 12 months was defined as four or more symptoms including at least a dysphoric mood or an anhedonia, associated with impairment in daily activities. MDE was classified as being mild (four or five symptoms and little impairment), moderate (four or five symptoms and moderate or high level of impairment, or more than five symptoms and little or moderate impairment), or severe (more than five symptoms and high level of impairment).

Current asthma was defined as the occurrence of wheezing in the past 12 months in pupils who had already had asthma attacks or as the administration of treatment for wheezing or asthma in the past 12 months. In children with current asthma, asthma was considered to be uncontrolled if the child experienced at least four attacks of wheezing, one awakening due to wheezing per week on average, one severe wheezing (with difficulty in talking), four unplanned medical visits, or one hospital admission for a wheezing attack in the past year. Children who had experienced asthma attacks during their lifetime but did not suffer from current asthma were considered to have past asthma.

The associations between current asthma and past-year MDE and, among pupils with current asthma, between past-year MDE and asthma control were studied. Covariates included in these analyses consisted of potential confounding factors (i.e., sociodemographic factors found in previous studies to be associated with both asthma and MDE): age, gender, corpulence, socioeconomic factors assessed by the family structure, the parents' employment status and occupation, the type of education (general or technical), the status of the school (public school located in a priority educational zone, public school outside a priority educational zone, private school), and the geographical location of the school (15–17, 25, 26). Four groups of corpulence (thinness/normal corpulence/overweight/obesity) were defined using the body mass index (BMI) thresholds defined by the International Obesity Task Force for children aged less than 18 years and the thresholds of 18.5, 25, and 30 kg/m² for the older students (27, 28).

The analysis was performed using Stata software version 9.2 (Stata Corp., College Station, TX, USA) taking into account the complex sampling design. In order to adjust for the unequal probability of inclusion and non-response, and to provide valid estimates for the French schoolchild population, a weight was assigned to each child. Weighted proportions and means are reported but the numbers of children are those of the sample. Weighted proportions were compared using the design-adjusted Rao–Scott χ^2 -test. Multivariate analyses were conducted using multiple logistic regression models: all variables that were significantly associated with MDE (or with uncontrolled asthma) in the univariate analysis

were introduced into the model. The level of significance was 0.05, and prevalence rates and adjusted odds ratios (aOR) are presented with their 95% confidence intervals (CI).

RESULTS

Description of the Study Population

Of the 10,000 expected questionnaires, 7760 were actually collected. After excluding children with uncompleted questionnaires (corresponding to the schoolchildren who did not bring their immunization record to the medical visit and whose data on birth date, gender, weight, and height were all missing), the sample comprised 7538 pupils from the ninth grade (75.4% of the expected sample).

Any schoolchildren who did not answer the questions on wheezing in the previous year or the two stem questions about MDE were excluded from the present analysis. Our study population thus consisted of 7000 pupils. They had an average age of 15.1 years at the time of the study. Most of them were aged 14 years (45.6%) or 15 years (39.7%); 11.7% were aged 16 years or more and only 3.0% were aged 13 years or less. About half of the pupils (49.7%) were boys. The majority (89.2%) were in the general education section (85.3% boys, 93.1% girls).

Association between MDE and Asthma

The prevalences of asthma and asthma-like symptoms are presented in Table 1. The prevalence of current asthma was 8.5% (95% CI: 7.6–9.4%). A total of 637 pupils had experienced at least one MDE in the past 12 months leading to a weighted MDE prevalence rate of 9.6% (8.6–10.7%) divided into 1.5% (1.1–1.9%) mild, 6.4% (5.6–7.3%) moderate, and 1.7% (1.3–2.2%) severe MDE.

The prevalence of MDE in the previous year was 14.2% among the 571 adolescents with current asthma, and 9.2% among the 6429 remaining respondents ($p < .01$) (Table 2). Of the 6429 adolescents without current asthma, 412 reported having had an asthma attack in the past. No difference in the past-year prevalence of

MDE was observed between children with past asthma and those who had never experienced any asthma attack (9.2% for both groups).

Sociodemographic factors significantly associated with past-year MDE are presented in Table 2. Although the difference did not reach significance ($p = .14$), a higher prevalence of MDE was observed in obese children (14.2% vs. 7.8% in thin adolescents, 9.4% in those with normal corpulence and 9.1% in overweight adolescents). No significant association was found with the mother's employment status ($p = .14$), the father's and mother's occupations ($p = .10$ and $p = .41$, respectively), the geographical location of the school ($p = .58$), the type of education ($p = .28$), or the status of the school ($p = .40$) (data not shown).

The association between current asthma and past-year MDE persisted after taking into account the children's gender and age, the family structure, and the father's employment status (Table 2). The increase in the risk of past-year MDE related to the presence of current asthma was similar among boys and girls [aOR: 1.8 (1.0–3.2) in boys and 1.6 (1.0–2.5) in girls]. The results remained unchanged when obese children ($n = 342$) and children with unmeasured BMI ($n = 177$) were excluded from the analysis, and the aOR associated with current asthma was 1.7 (1.2–2.4). After adjustment for gender, age, family structure, and the father's employment status, the risk of MDE was significantly higher in children with current asthma than in those who had never had asthma [aOR: 1.7 (1.2–2.4)], but the increase in risk among children with past asthma was not statistically significant [aOR: 1.2 (0.7–2.0)].

When we defined asthma as the occurrence of wheezing in the past 12 months, the results were similar to those for current asthma: after adjustment for gender, age, family structure, and the father's employment status, the aOR measuring the association between past-year MDE and past-year wheezing was 2.0 (1.5–2.7).

Association between MDE and Asthma Control

Asthma was uncontrolled in more than one-third (38.6%) of the pupils with current asthma. The proportion of uncontrolled asthma was higher in girls than in boys ($p < .01$) and in pupils who experienced an MDE in the previous year ($p < .01$), but did not differ significantly with age ($p = .48$) (Table 3). The association between MDE and uncontrolled asthma remained statistically significant after adjustment for gender.

DISCUSSION

The triennial cycle of surveys in French schools is a precious tool for monitoring children's health. Based on large, nationally representative samples of schoolchildren, it provides regular estimates of asthma prevalence and control in children. In the present study, in ninth grade schoolchildren, the prevalence of current asthma (wheezing in a child who had already had an asthma

TABLE 1.—Prevalence of asthma and asthma-like symptoms, 7000 ninth grade pupils.

	<i>n</i>	%	95% CI ^a
Symptoms in the past 12 months			
Wheeze	659	10.0	9.1–10.9
Exercise wheeze	676	10.1	9.1–11.1
Night cough	761	10.5	9.5–11.6
Asthma			
Ever asthma	917	13.4	12.2–14.6
Treatment for wheezing or asthma in the past 12 months	505	7.5	6.7–8.4
Current asthma ^b	571	8.5	7.6–9.4

Notes: ^aConfidence interval.

^bWheezing in the past 12 months in a child having already had asthma attacks or treatment for wheezing or asthma in the past 12 months.

TABLE 2.—Factors associated with major depressive episode (MDE) in the previous year, 7000 ninth grade pupils.

	N	MDE				
		n	%	p ^a	aOR ^b	95% CI ^b
Current asthma ^c						
No	6429		9.2	<.01	1	
Yes	571		14.2		1.7	1.2–2.3
Gender						
Male	3422	174	5.3	<.001	1	
Female	3578	463	13.8		3.0	2.4–3.8
Age						
≤13 years	180	10	6.5	.04	1	
14 years	3033	265	8.8		1.4	0.6–3.0
15 years	2817	262	9.8		1.6	0.7–3.7
≥16 years	970	100	13.0		2.2	1.0–5.1
Family structure						
Both parents	4809	382	8.3	<.001	1	
Mother only	1161	147	14.8		1.8	1.3–2.4
Mother and stepfather	484	56	12.1		1.4	1.0–2.1
Other	377	40	9.7		1.1	0.7–1.8
No response	169	12	8.5		1.1	0.6–2.4
Father's employment status						
Employed	5301	473	9.0	<.01	1	
Unemployed	428	30	9.6		1.0	0.6–1.9
Homemaker/retired	358	34	13.6		1.5	0.9–2.5
Not applicable ^d	244	33	19.4		1.7	1.0–3.1
No response	669	67	10.8		0.8	0.5–1.2

Notes: ^aDesign-adjusted Rao-Scott χ^2 -test^bMultiple logistic regression odds ratio (and 95% confidence interval) adjusted for current asthma, gender, age, family structure, and the father's employment status.^cWheezing in the past 12 months in a child having already had asthma attacks, or treatment for wheezing or asthma in the past 12 months.^dThe child declared having no father.

TABLE 3.—Major depressive episode (MDE) and asthma control in the previous year, 471 ninth grade pupils with current asthma.

	N	Uncontrolled asthma			
		n	%	aOR ^a	95% CI ^a
Gender					
Male	269	86	30.3	1	
Female	302	146	47.0	1.9	1.2–4.2
Age					
≤14 years	261	101	37.8		
15 years	227	91	37.0		
≥16 years	83	40	48.1		
MDE					
No	492	191	35.3	1	
Yes	79	41	58.3	2.2	1.1–3.1

Note: ^aMultiple logistic regression odds ratio (and 95% confidence interval) adjusted for gender and MDE.

attack or the administration of treatment for asthma in the previous year) was estimated at 8.5%. More complete results have already been published (1).

We found that 1 in 10 of these ninth grade students had experienced an MDE during the past 12 months. Direct comparison with other studies is difficult due to methodological issues, mainly differences in the instruments and time frames used to assess depression. Among US children and adolescents, point prevalence estimates of major depression based on diagnostic interview range from 1% to 6%, and lifetime prevalence

ranges from 4% to 25% (29). To the best of our knowledge, little data about depression among children and adolescents are available in France, and this study is the only one in which a standardized diagnostic interview questionnaire has been administered to a large, national, community-based sample of adolescents. The CIDI is a structured diagnostic questionnaire developed by the WHO. It has been shown to have good concordance with blinded clinical diagnoses, in both adults and adolescents (30, 31). The CIDI-SF used in our study has been derived from the CIDI to provide a quick screen for the most common disorders with a sensitivity of 89.6% and a specificity of 93.9% for MDE compared to the CIDI (32).

The past-year prevalence of MDE was higher in children with current asthma (14.2%) than in other children (9.2%). The strength of this association between MDE and current asthma was similar among boys and girls. As far as we are aware, little data are available about the prevalence of MDE in asthmatic young people in France. The only study was carried out in a sample of 82 outpatient children aged 8–15 years with moderate to severe persistent asthma, 29 (35%) were identified as suffering from an anxious disorder, and 4 (5%) from an affective disorder; none had major depressive disorder (9). Mood disorders in children have been inconsistently found to be associated with asthma. However, many studies of mental health in children have used behavioral scales that do not assess specific internalizing disorders

and only a few studies have been based on structured interview schedules (33). When the Diagnostic Interview Schedule for Children (DISC) was used in a multicentric study conducted among youths (9–17 years) in the United States (10), having a history of asthma was not found to be associated with having an affective disorder. In another US study among 11–17-year-old teenagers, the increase in the past-year prevalence of MDE in asthmatic adolescents was no longer statistically significant after adjustment for ethnicity, parental education and marital status, and comorbidity (14). In contrast, in Puerto Rican children (4–17 years) parental reports of child asthma attacks were found to be associated with major depression (13).

Obesity is a known confounding factor that has been found to be associated with both asthma and MDE (25, 26). A recent meta-analysis of longitudinal studies confirmed the reciprocal link between depression and obesity: obesity increases the risk of depression and depression is predictive of developing obesity (26). When we excluded obese children, we found that the relationship between current asthma and past-year MDE remained unchanged. Due to the small number of obese children, we could not study specifically the relationship between MDE and asthma in this population.

The sociodemographic factors that we found to be associated with past-year MDE have also been identified in previous studies (15–17). Concerning the positive association between age and MDE, however, due to the cross-sectional design of the study, which focused on school grade rather than age, we cannot ignore the fact that the age trend could also reflect the higher probability for a depressive student to be behind his/her age group at school or the higher prevalence of MDE in pupils who have repeated one or more school grades. The lack of a statistically significant association with the parents' occupation could be due to an inaccurate reporting by the adolescents of their parents' occupation.

We also found that asthma had more often been uncontrolled in the previous year among asthmatic adolescents who had experienced MDE than among those who had not. However, the definition we used for uncontrolled asthma was very broad. The triennial cycle of surveys in French schools is a comprehensive health survey in which it is not possible to collect detailed information on asthma which could have allowed an assessment of asthma control according to the GINA or NAEPP guidelines. Nevertheless, numerous studies have investigated the association between depression and non-adherence to treatment in patients with various chronic conditions, including asthma (18, 22, 34). It has been shown that in patients with asthma, depression displays significant negative correlations with factors—for example, acceptance of illness-related limitations, knowledge about the illness, and ability to identify worsening signs—that may affect adherence to treatment (35). Asthmatic patients with depressive symptoms have been reported as having a five times greater risk of using less than half the medications prescribed when

they were discharged from hospital than those without depression (22).

One important limitation of our study is that asthma was assessed only through an interview of the adolescents, and neither data on physician-diagnosed asthma nor objective measurements (e.g., airway hyperresponsiveness) were available. Defining asthma in population studies is difficult (36). In our study, data were collected using the ISAAC questionnaire, which is a standardized questionnaire largely used in epidemiological studies. Because all children with asthma are not referred to medical care and do not receive the diagnosis, the ISAAC protocol uses wheezing to detect asthma in children without previous diagnosis. However, defining asthma by wheezing does not take into account people with diagnosed asthma in whom asthma is well controlled by adequate treatment and, by contrast, includes people with wheezing not due to asthma (e.g., non-specific virus-induced wheeze). We chose to define current asthma by combining different questions (wheezing in the past 12 months in children who had had asthma attacks in their life or treatment for wheezing or asthma in the past 12 months). In addition, it has to be noted that defining asthma by the sole occurrence of wheezing in the past 12 months did not change the results.

Unfortunately, we did not collect any data about tobacco use in our study. Internalizing disorders have been found to be associated with a higher risk of smoking in both adolescents with asthma and healthy adolescents (37, 38). In addition, in young people with asthma, smoking has been shown to be associated with a greater symptom burden and less use of controller medication (37).

The link between asthma and depression is not yet clearly understood (39). One of the simplest possibilities is that asthma, through inadequately controlled illness, could lead to distress, which can sometimes induce psychological disorders. On the other hand, depression could exacerbate asthma symptoms through poor illness self-management, including non-adherence to asthma treatment. Another hypothesis involves the potential role of depression in physiological changes, such as inflammation. Family and twin studies provide some support for the hypothesis of a shared genetic vulnerability linking asthma, atopy, and mood disorder. However, none of these potential explanations fully accounts for the current body of evidence, and it is likely that the causal model actually encompasses several of them. Further research is needed to better understand the underlying relationship so that an appropriate prevention strategy of depression can be developed for patients suffering from asthma. Nevertheless, evidence of a link between mood and asthma is sufficient for clinical practice. Asthma patients presenting with a mood disorder should be referred for psychological intervention, without which improvement in mood and asthma control are unlikely. That implies a better knowledge by the physician of the risk of depression in asthmatic adolescents and a better assessment of the psychological dimension within asthma care in order to detect any alteration in the mood.

CONCLUSION

This study conducted in a large sample of French teenagers provides additional evidence of the need to identify and treat depression as part of a strategy intended to improve asthma management and outcomes in adolescents. Increased awareness of, and attention to, the assessment and management of psychiatric symptoms in young people with asthma may help to reduce the burden of the disease. This implies that adolescents with asthma who experience psychological problems may benefit from joint case management involving a psychologist or psychiatrist.

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DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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