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Early menarche and new onset of asthma: Results from the SAPALDIA cohort study

Sofie Hansen[a,b,*], Nicole Probst-Hensch[a,b], Robert Bettschart[c], Marco Pons[d], Bénédicte Leynaert[e], Francisco Gómez Real[f,g], Thierry Rochat[h,i], Julia Dratva[a,b], Cornelia Schneider[a,b], Dirk Keidel[a,b], Christian Schindler[a,b], Elisabeth Zemp[a,b]

[a] Swiss Tropical and Public Health Institute, Socinstrasse 57, 4051 Basel, Switzerland
[b] University of Basel, Klingelbergstrasse 50, 4056 Basel, Switzerland
[c] Lungenpraxis, Medizinische Klinik Hirslanden, Schanzweg 7, 5000 Aarau, Switzerland
[d] Sede Civico, Ospedale Regionale di Lugano, Via Tesserete 46, 6900 Lugano, Switzerland
[e] INSERM, Faculty de Medicine X, Faculté de Médecine site Bichat, 16 Rue Henri Huchard, 75890 Paris cedex 18, France
[f] Department of Gynecology and Obstetrics, Haukeland University Hospital, Jonas Lies vei 71, N-5058 Bergen, Norway
[g] Department of Clinical Science, University of Bergen, Jonas Lies veg 87, 5021 Bergen, Norway
[h] Division of Pulmonary Medicine, University Hospitals of Geneva, Rue Gabrielle-Perret-Gentil 4, 1205 Genève, Switzerland
[i] Hôpital du Valais (RSV) – Centre Hospitalier du Valais Romand, Av. du Grand Champsec 86, case postale 696, 1951 Sion, Wallis, Switzerland

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ABSTRACT

Rationale: The association between early menarche and new onset of asthma warrants further investigation in those aged > 30 years.
Objectives: Using data from the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA), we investigated whether early menarche was associated with new onset of asthma in women aged 18–60 years at baseline.
Methods: Our analysis included 2492 women with information on age at menarche and doctor-diagnosed asthma, who had been asthma free at the time of menarche and had complete covariate information. New onset of asthma was defined as newly reported doctor-diagnosed asthma which occurred at least one year after menarche. Asthma incidence and its association with early menarche was analysed using logistic regression, adjusting for age, atopy, smoking, BMI, parental asthma, urbanity, education and study area, and additionally stratifying by atopy and BMI.
Results: After adjustment of relevant confounders, women with early menarche did not have a significantly higher risk of onset of asthma than women without early menarche (OR 1.23, 95% CI 0.85–1.80). Young atopic women with early menarche appeared to have an increased risk of asthma compared with non-atopic women (OR 2.21, 95% CI 0.90–5.43); however, our results did not reach statistical significance.
Conclusion: We could not substantiate an association of early menarche with new onset of asthma in this Swiss population-based cohort aged 18–60 years at baseline. Future studies may need to prospectively assess age of menarche to investigate the association with new onset of asthma in those aged > 30 years.

1. Introduction

The gender-related life-course pattern of asthma is characterised by higher incident rates in boys than girls, followed by a female preponderance in early and middle-adulthood [1,2]. Because this switch takes place around puberty, hormonal factors have been suggested as one possible explanatory pathway. Observations of increasing asthma incidence and decreasing age at menarche, have led investigators to hypothesize potential associations of age at menarche with incident asthma.

Studies have consistently found an association between early menarche and new-onset of asthma [3], at least in young adulthood. The cause for the observed association between early menarche and asthma is poorly understood. Some suggest that it could reflect genetic and early life environment as the timing of both events are affected by early life factors, or that menarche itself might induce immunological and hormonal changes as well as changes in airway function [4]. Higher levels of leptin and increased insulin resistance in women with

* Corresponding author at: Swiss Tropical and Public Health Institute, Socinstrasse 57, 4051 Basel, Switzerland.
E-mail address: sofie.hansen@unibas.ch (S. Hansen).

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early menarche may influence inflammation and innate immunity, potentially contributing to higher risk of asthma [5,6]. Animal studies have provided evidence that estrogen and progesterone have effects on humoral and cellular immunity and smooth muscle function [7]. Therefore, hormonal factors might be expected to be associated with the clinical occurrence of asthma in humans.

What remains unclear is whether the observed association between early menarche and asthma, also holds for older adulthood. With the exception of five studies [4,6,8–10], the association between early menarche and asthma incidence has not been investigated in adults > 30 years. Lieberoth et al. (2015) [4] found a significant association in women aged 12–41 years, Macsali et al. (2011) [8] in women aged 27–57 years, and Fida et al. (2012) [9] in women aged 18–35 years. However, in the study by Gnatiuc et al. (2013) [10] they did not find a significant association between early menarche and asthma at age 33 and neither did Jartti et al. (2009) [6] in women at ages 24–39 years. The association between early menarche and new-onset of asthma warrants further investigation in those aged > 30 years.

Making use of the on-going Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA), [11,12], we investigated whether early menarche was associated with new-onset of asthma in women aged 18–60 at baseline.

2. Methods

2.1. Study design & population

The "Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults" (SAPALDIA) (see Appendix A) was initiated in 1991 (SAPALDIA 1 [S1]) in eight geographically diverse areas in Switzerland, recruiting 9651 participants (51% female) aged 18–60 at baseline through random population sampling. Re-assessments took place in 2002/2003 (SAPALDIA2 [S2], n = 8047) and in 2010/2011 (SAPALDIA3 [S3], n = 6088). The protocol and participation rates have been described elsewhere [11,12]. Starting in SAPALDIA 2, the Women's Health Questionnaire of the European Community Respiratory Health Study was introduced [13] which included detailed questions on women's reproductive histories. This analysis includes 2,492 women who provided retrospective information on age at menarche in either S2 or S3, provided information on doctor-diagnosed asthma in at least S1, S2 or S3, reported asthma-onset after menarche, and had complete covariate information (Fig. 1). Ethical approval was obtained from the Swiss Academy of Medical Sciences, the regional committees, and written informed consent was obtained from all participants.

2.2. Definition of asthma and asthma incidence

New-onset of adult asthma was defined as newly reported doctor-diagnosed asthma at baseline or follow-up which occurred at least one year after reported age at menarche. Doctor diagnosed asthma was defined as a positive answer to both questions 'have you ever had asthma?' and 'was this confirmed by a doctor?' For the purpose of sensitivity analyses, two additional definitions of asthma were created: (a) self-report only and (b) doctor-diagnosed asthma with current medication.

2.3. Definition early menarche

The primary definition of early menarche used for our analysis, as also defined in other studies [4,10,14], was menarche < 12 years. If age of menarche was reported < 12 years in S2 or S3, then the individual was considered as having early menarche. For the purpose of sensitivity analyses, three further definitions were created based on other literature findings (Table 1): age at menarche 1 standard deviation (SD) less than the mean [7,9,15], age at menarche 2 SD less than the mean [16,17], and finally age at menarche 1 SD less than the language region specific mean (German, French and Italian), based on findings by Dratva et al. (2007) that age at menarche differs in these three Swiss language regions [18]. Additionally, we grouped early menarche into a categorical variable of whole years and compared the risk of new-onset of asthma in women with menarche at 10 years to women with menarche at the mean age of menarche, as done by Macsali et al. (2011) [8].

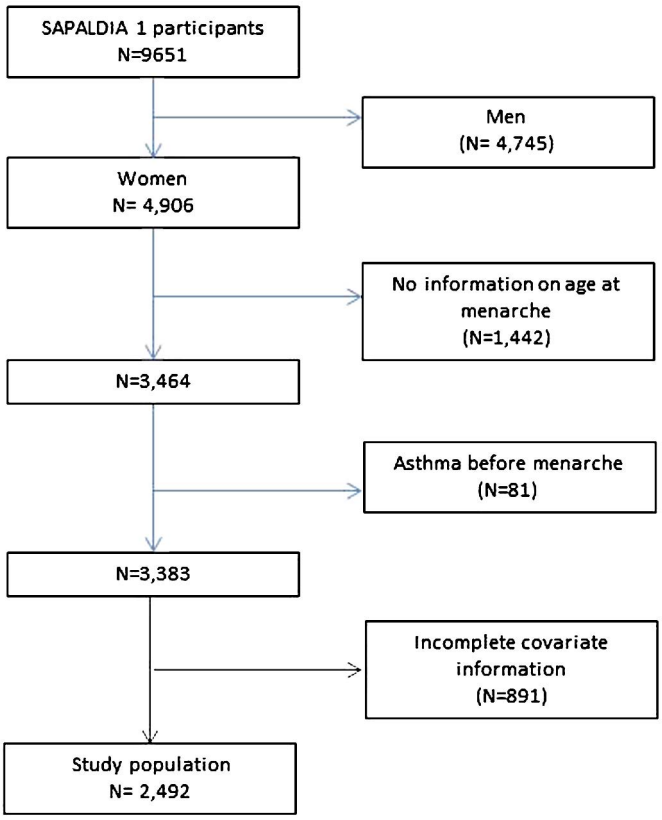

Fig. 1. Study population.

2.4. Atopy & BMI

Atopy was defined as a positive response to the skin prick test or Phadiatop test (Phadia, Uppsala, Sweden) at baseline. Allergically sensitised subjects with doctor-diagnosed asthma were considered as having allergic asthma. Body mass index (BMI) at baseline was calculated as weight in kilograms, divided by the square of height in meters. For the descriptive tables and stratification by BMI, 3 categories were created according to the WHO cut off points (47) for underweight (BMI < 18.50), normal weight (BMI 18.50–24.99), and overweight/obese (BMI ≥ 25.00).

2.5. Further covariates

Smoking status at baseline, S2 and S3 were categorized as never-smoker, former-smoker and current-smoker. Smoking status at S3 was defined in a cumulative way, never-smokers being consistent never smokers across all three surveys, current smokers being smokers at S3, and ex-smokers being people who were smokers at S1 and/or S2, but not at S3. Education was categorized into primary education (low), secondary or middle school education (intermediate), and having a technical or university degree (high). For the descriptive tables and models, cumulative education, (the highest educational level reported at S1/S2), was used. Parental asthma was defined as a positive answer to the question 'did one or both of your parents ever have asthma?' Urbanity was defined as residing in the following study areas: Basel,