

## Chronic Respiratory Diseases and Age at Menarche: A Short Communication

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### DESCRIPTION

As underline in our recent report entitled “Delayed age at menarche in chronic respiratory diseases”, during the routinely checkup clinicians should obtain accurate information and screen all the predictor factors for delayed puberty in adolescents with cystic fibrosis and asthma.

Several studies have suggested that inflammation influences the reproductive function in chronic respiratory disease. Age at Menarche (AAM) is an important indicator of physiological development in women and delayed AAM has been associated with chronic illnesses.

The aim of this commentary was reviewed the literature, reporting relevant and recent data about factors that influence AAM in adolescents with chronic respiratory diseases.

Age At Menarche (AAM) is a major Darwinian parameter influencing the reproductive fitness of our species [1]. It has a strong genetic determinants [2-4] and it is influenced by body size and composition as well as by lifestyle and environmental conditions [2,5,6].

During the 20th century has been reported a decline of AAM: the mean AAM declined by approximately 2-3 months per decade from 16.5 years in 1840 to 13 years in 1960 in Europe [7]. Recently the downward trend in AAM may be slowing in some countries [8,9].

The timing of puberty influences women’s health: delayed AAM is associated with increased risks of developing vascular heart disease, hypertension [10], osteoporosis, early menopause [11], infertility and endometrial and ovarian cancer [12].

Delayed onset of puberty and reduced pubertal growth spurt has been reported in adolescents affected by chronic disease [13].

Cystic Fibrosis (CF) is associated with a puberty delay despite good nutrition and clinical status [14] and AAM in adolescents with CF is delayed when compared with that of their respective mothers [15]. Our recent study conducted in Italy on 47 girls

affected by CF, confirmed that AAM was significantly higher compared to AAM in healthy adolescents [9].

The correlation between onset of menarche and both type of CFTR mutation and respiratory parameters is debated: on one hand the type of CFTR mutation seems to be significantly related to the onset of menarche and statistically differentiated respiratory parameters [16] although our recent study showed no correlation between CFTR mutation, respiratory parameters and AAM [9].

There are few and controversial studies regarding the assessment of sexual maturation in patients with bronchial asthma. AAM in girls with asthma has been described to be delayed in patients don’t treated with long-term corticosteroid [17] and to be dependent on disease severity and control [18]. According to another research, the first menstruation occurred much earlier in asthmatic patients compared to healthy ones and a clear environmental differentiation was also observed [19].

Our study conducted in Italy on 98 asthmatic girls reported a delayed AAM in asthmatic patients when compared to healthy adolescents. No significantly difference were found evaluating patients with different control of the disease [9]. We supposed that chronicity plays a central role in determining delayed AAM in patients affected by chronic respiratory illness [9].

Systemic chronic inflammation, mediated by TNF- $\alpha$ , is involved in both CF and asthma [20,21]. TNF- $\alpha$  can influence the neuroendocrine system, including both the Hypothalamic-Pituitary-Adrenal (HPA) and Hypothalamic Pituitary Gonadal (HPG) axes [22]. Moreover, in CF patient’s inflammatory dysregulation influences the bioactivity of IGFs [23]. It seems that the IGF1 system plays a key role in the onset of menarche by stimulating ovarian folliculogenesis [24]. In patients affected by asthma has been reported an important rule of mediated systemic IL-6 inflammation [25] also involved in influencing HPA and HPG axes [22].

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## TAKE HOME MESSAGE

Biomarkers of inflammation may influence the reproductive function in chronic respiratory disease. Adolescents with cystic fibrosis and asthma should be screened for delayed puberty.

## CONCLUSION

Evaluation of the development of puberty development in patients with chronic respiratory diseases is often left in the background by clinicians. Importantly, we need emphasize that all patients with CF and asthma should be screened for delayed puberty and AAM due to the impact on growth, bone health and psychosocial well-being. Finally, the observed discrepancies among studies, particularly between the results of epidemiological and experimental studies, strongly suggest that further studies are required to reveal the mechanisms by which chronic respiratory diseases contribute to puberty, AAM and sex hormones in children, especially during adolescence.

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