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Patterns and determinants of exhaled nitric oxide trajectories in schoolchildren over a 7-year period

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ABSTRACT Fractional exhaled nitric oxide ($F_{ENO_{50}}$), a marker of allergic airway inflammation, is used in respiratory research and asthma clinical care; however, its trajectory with increasing age during childhood has not been well characterised. We examined $F_{ENO_{50}}$ longitudinally during a period of important somatic growth to describe trajectories across childhood and adolescence in healthy participants and evaluate clinical factors as potential determinants of trajectories.

$F_{ENO_{50}}$ was collected at six visits over 8 years in a population-based cohort of 1791 schoolchildren without asthma (median age at entry 8.4 years). Smooth sex-specific $F_{ENO_{50}}$ trajectories were estimated using generalised additive mixed models, with participant-level random effects. We evaluated whether sex-specific trajectories were influenced by race/ethnicity, body mass index (BMI) percentile, allergic rhinitis or puberty.

Different $F_{ENO_{50}}$ patterns were observed by sex in later childhood and several factors were associated with either $F_{ENO_{50}}$ level or change in $F_{ENO_{50}}$ as participants aged. $F_{ENO_{50}}$–age trajectories were similar by sex until age ∼11.5 years, after which males had greater $F_{ENO_{50}}$ change than females. This divergence in $F_{ENO_{50}}$–age trajectories coincides with puberty. Males with higher starting BMI percentile had attenuated $F_{ENO_{50}}$–age slopes. Among males, $F_{ENO_{50}}$ levels were lower in non-Hispanic white subjects. Among both sexes, participants with rhinitis had higher $F_{ENO_{50}}$. $F_{ENO_{50}}$ levels within individuals tracked over time; however, there was considerable variation in $F_{ENO_{50}}$ patterns across participants.

$F_{ENO_{50}}$ trajectories from longitudinal data provide evidence of sex differences coinciding with puberty, suggesting potential hormone link. Improved understanding of determinants of $F_{ENO_{50}}$ trajectories is needed to realise the potential for using individualised predicted $F_{ENO_{50}}$ trajectories.