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Title: Methacholine airway hyperresponsiveness is associated with fraction of nitric oxide irrespective of asthma

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Body: Background: Augmented levels of fractional exhaled nitric oxide (FeNO) reflect airway inflammation and associated airway hyperresponsiveness (AHR) in asthma patient. There are many children who had no asthma but increased level of FeNO. We sought to evaluate the correlation between FeNO and AHR in children. Methods: Two hundred fourteen children, who had controlled asthma without controller, aged 8 to 16 years were included. Forty seven children without asthma were recruited from community school. Children were evaluated using FeNO measurements, skin prick test, spirometry, and methacholine challenge tests. Results: AHR was diagnosed in 153 (71.5%) children with asthma and 27 (57.4%) children without asthma. Geometric mean (GM) of FeNO was significantly higher in children with AHR compared children without AHR in both group (all, $p < 0.001$). FeNO and PC_{20} were negatively correlated for both children with asthma and children without asthma ($r=-0.364$, $p<0.001$; $r=-0.603$, $p<0.001$). The sensitivity, specificity, and positive (PPV) and negative predictive values (NPV) of FeNO measurements in children with asthma for the diagnosis of AHR at the best cut-off value of 22 ppb were 58.2%, 86.9%, 91.8%, and 45.3%, respectively. In the children without asthma, the cutoff value of FeNO 10 parts per billion (ppb) was associated with the highest combination of sensitivity (96.3%) and specificity (74.3%). At a cut-off value of 27 ppb, specificity and PPV of diagnosis of AHR were above 90% (95.0% and 92.9%). Conclusions: Airway hyperresponsiveness is associated with level of FeNO irrespective asthma. These findings shows that inflammation of airway is associated with asymptomatic AHR.