Title: Relationship of circulating hyaluronic acid levels to disease control in asthma and asthmatic pregnancy

Body: Asthma has a high burden of morbidity if not controlled and frequently complicates pregnancy posing a risk for complications. Serum hyaluronic acid (HA) is an acknowledged marker of tissue fibrosis which promotes eosinophil survival and plays a role in airway remodeling. Although circulating HA is easily measurable, and its role is supposed in asthmatic inflammation, tissue remodelling and maintenance of normal pregnancy as well, to date there are no data on its levels in asthmatic pregnancy. The possible relationship of circulating HA levels and clinical asthma control is also unknown. The aim of this study was to evaluate the serum levels of HA in asthmatic pregnant (AP; N=17) and asthmatic non-pregnant (ANP; N=42) patients. The possible relationship between HA levels and asthma control determinants (spirometry, symptoms) was also evaluated. Serum HA level was lower in AP than in ANP patients (27 [24.8-36.4] vs. 36.3 [27.35-52.60] ng/mL, p=0.026). A positive correlation was found between HA and airway resistance in ANP (r=0.3684, p=0.019) but not in AP patients. ROC analysis of HA values in asthmatic patients with Asthma Control Test total score above and below 20 yielded an AUC of 0.74 (95% CI: 0.58-0.90, p=0.015) and identified an optimal cut-off value of 25.8 ng/mL between controlled and not controlled asthmatic patients. Serum HA might be a marker of asthma control, since it correlates with airway resistance and has good sensitivity in the detection of impaired asthma control. Lower circulating HA level detected in pregnant than in non-pregnant asthmatics may be the consequence of pregnancy induced immune tolerance and attenuated systemic inflammatory responses.