

Neutrophil extracellular traps in obese asthma

E.J. Williams^{1,2}, L.G. Wood^{1,2}, L.R. Dowling^{1,2}, S. Stanton^{1,2} and K.J. Baines^{1,2}

¹School of Biomedical Sciences & Pharmacy, University of Newcastle, NSW, Australia and

²Immune Health Program, Hunter Medical Research Institute, Newcastle, NSW, Australia

In Australia asthma affects approximately 2.5 million people,⁽¹⁾ with this number expected to rise along with current obesity rates as obesity increases the risk of developing asthma by 2–3.8-fold. Obesity (BMI > 30 kg/m²) complicates asthma management as obese asthmatics have higher medication use, increased frequency of exacerbations and worse lung function compared to non-obese asthmatics. This is hypothesised to be driven by the increased airway neutrophilia observed in obese asthmatics, as neutrophilic airway inflammation in asthma is associated with more severe, steroid resistant asthma. Previous research has shown that neutrophil extracellular traps (NETs) are present in the airways of patients with asthma, particularly those with neutrophilic airway inflammation. Increased formation of airway NETs have been associated with poorer lung function in patients with chronic obstructive pulmonary disease and cystic fibrosis^(3,4); however, no studies have examined the role of NETs in the obese asthma phenotype. In this study, we investigated whether (NETs) are increased in the airways of obese asthmatics. Sputum samples collected from obese ($n = 69$) and non-obese ($n = 65$) asthmatic patients were analysed for their NET content by measuring the specific NET marker DNA-Elastase complex via Enzyme-Linked Immunosorbent Assay, and the non-specific NET marker extracellular DNA (eDNA) by Quant-iT™ PicoGreen™ dsDNA Assay. DNA-Elastase complexes were significantly increased in the obese asthma group (30.8 (11.8, 96.1) µg/mL v. 64.3 (17.6, 200.6) µg/mL; $p = 0.032$). Sputum eDNA however, was similar (7.3 (4.2, 17.2) pg/mL v. 8.18 (3.9, 21.1) pg/mL; $p = 0.890$) between the two groups. DNA-elastase was associated with % sputum neutrophils ($r = 0.218$; $p = 0.014$) and BMI ($r = 0.172$, $p = 0.047$), while increased eDNA was associated with poorer lung function as shown by negative associations with lung function markers FEV₁%predicted ($r = -0.324$, $p < 0.001$), FVC%predicted ($r = -0.277$, $p = 0.002$) and FEV₁/FVC ($r = -0.248$, $p = 0.005$). NETs are increased in the airways of obese asthmatics and are associated with poorer lung function. NETs may be a potential therapeutic target to improve outcomes in obese asthmatic patients.

References

1. Australian Institute of Health and Welfare (2018). *Asthma*. Canberra: AIHW. Cat. No.: ACM 33. Available from: <https://www.aihw.gov.au/getmedia/3739946f-90c4-4299-9144-3f50be030a46/Asthma.pdf.aspx?inline=true>
2. Young SY, Gunzenhauser JD, Malone KE, et al. (2001) *Arch Int Med* **161**, 1605–1611.
3. Dicker AJ, Crichton ML, Pumphrey EG, et al. (2018) *J Allergy Clin Immunol* **141**, 117–127.
4. Jones AP & Wallis CE (2003) *Cochrane Database Syst Rev* **3**, CD001127.