Genetic Susceptibility to Air Pollution-Induced Inflammation, and Haemo-adaptation in a Birth Cohort in South Africa

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Problem Statement - Aim

- Cytokine genetic variability may contribute to differences in susceptibility to air pollution-induced inflammatory pathology.
- Immune response-type alterations may affect neonatal developmental outcomes, exacerbated by air pollution.
- The study aims to define the maternal cytokine single nucleotide polymorphism (SNP) prevalence, and susceptibility to chronic air pollution exposure in a birth cohort in Durban, KwaZulu Natal South Africa.
- The study aims to evaluate the haemoglobin (Hb) response to Oxides of Nitrogen (NOx) exposure.

Methodology

- The MACE (Mother and Child in the Environment) birth cohort was recruited from public sector antenatal clinics, at first trimester in Durban, South Africa.
- Land-use regression modelling was used to characterise exposure.
- Polymerase Chain Reaction-Restriction fragment length polymorphism (PCR/RFLP) was used to determine the maternal genotypic (n = 333) frequency for SNPs in :
  - ➢ pro-inflammatory IL-1β [1464 G/C & 511-C/T] & IL-6 [174-G/C] &
  - ➢ anti-inflammatory IL-10 [592-C/T & 819 C/T].
- Maternal clinical outcome data was collected from mothers at clinic or hospital visits.
- Associations with clinical data and SNPs were determined using the Spearman's correlation.
- Genotypic associations within the cohort were determined using the chi-squared or Fisher's exact test.

Results

- There is a high prevalence of high-producing pro-inflammatory cytokine-SNPs i.e. IL-6 174-GG, IL-1ß 511-CT and low-producing anti-inflammatory IL-10 592-CA indicating susceptibility to chronic disease and pollutant induced pathology (Figure 1).
- NOx levels significantly inversely correlated with Hb in the Low NOx Exposure group (LN) (r = -0.19, p = 0.04) (Figure 2A) and there is a trend for a positive association with Hb in the High Nox Exposure group (HN) indicating an adaptive physiological response to elevated NOx (r = 0.16, p = 0.07) Figure 2B).
- In LN, for IL-1β-511 CC and CT and Il-10 592 CA, there is an inverse association with Hb (r = -0.29 p = 0.01; r = -0.26; p=0.03) (Figure 2C & D).
- In IL-1β-511 CT there is significantly greater Hb in HN compared to LN (11.77 g/dl, S.E. – 0.37; 10.92 g/dl, S.E. -0.27; p = 0.033) (Figure 2E).

Figure 1. Cohort Cytokine SNP Prevalence

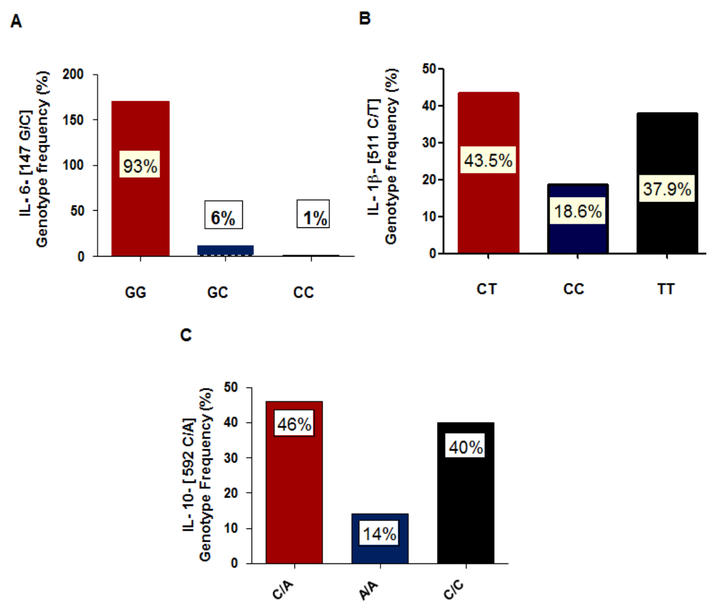
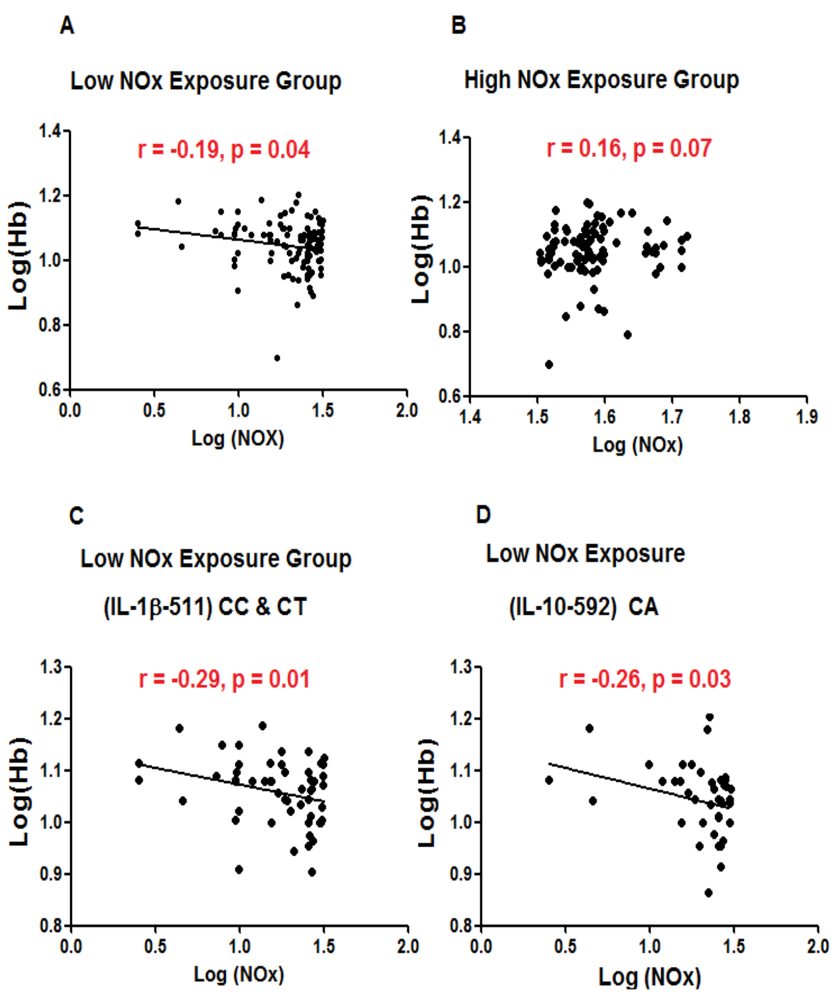


Figure 2. NOx Exposure and Haemoglobin Levels



Conclusions

- The high prevalence of high pro-inflammatory cytokine-producing SNPs i.e. IL-6 174-GG, IL-511 CT and low-IL-10- producing anti-inflammatory IL-10 592-CA suggest that the cohort is susceptible to pollutant-induced pathological inflammatory processes and chronic morbidity in the mother, also increasing the risk for adverse developmental outcomes in the foetus that may manifest later in life.
- In chronic nitrogen dioxide or NOx exposure, binding of oxygen to haemoglobin is prevented, causing oxygen depletion.
- In the LN group, there is a natural response of an inverse correlation between haemoglobin and increasing NOx levels.
- However in individuals with pathological pro-inflammatory genotypes, where further protective/compensatory mechanisms are required, there is an adaptive compensatory increase in haemoglobin levels in response to elevated chronic NOx levels.

Proposal

- ➢ Revision of vehicle emission standards.
- ➢ Revision of atmospheric emission licences which govern the amount of pollution industries can emit; and compliance reports for refineries.
- ➢ Call for adopting regulations that require many facilities to reduce NOx emissions.
- ➢ Emissions may be reduced by:
  - making process changes (viz. modifications to the combustion process)
  - or by installing air pollution control equipment (such as selective non-catalytic reduction (SNCR) or selective catalytic reduction (SCR)).

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