# Impact of intermediate hyperglycaemia and diabetes on immune dysfunction in TB


The authors sought to identify mechanisms that can account for the increased susceptibility to tuberculosis (TB) disease among individuals with diabetes (DM). This was done by carrying out a blood-based transcriptomic study on individuals with diabetes as well as those with intermediate hyperglycemia (IH) since the latter are also said to be at risk for TB .TB patients with either IH or DM were found to have an altered immune phenotype. This altered gene expression reveals a potential mechanism of TB susceptibility in IH as well as in DM patients.

Venous blood was collected from study participants at TB diagnosis, before the initiation of TB treatment, and subject to RNA sequencing analysis. Using samples from South Africa, the authors investigated the effect of DM and IH on gene expression changes in TB patients' blood. Both DM and IH were shown to impact the peripheral host response to TB since DM-TB and IH-TB patients both had over 1000+ genes upregulated, in comparison to healthy controls. The authors went forward to validate these findings using their patient cohort from Romania. A similar pattern of gene expression in both DM-TB and IH-TB was observed relative to healthy controls.

To determine the reproducibility of results across geographical regions and different patient ethnicities, RNA-

seq data from DM-TB, IH-TB and TB-only patients from all four study sites; i.e. South Africa, Romania, Peru and Indonesia were combined. In the combined dataset, DM-TB and IH-TB patients showed similar altered gene expression patterns in blood compared to patients with TB only.

The authors went a step further to carry out modular analysis with a specific interest in the most significantly differentially expressed modules in both DM-TB and IH-TB. They were able to determine that the extent of hyperglycaemia does have an impact on gene expression because although DM-TB and IH-TB shared patterns in genes that were upregulated or downregulated, expression occurred at a greater magnitude in DM-TB patients, in comparison to those with IH-TB.

Interferon-related modules were all less up-regulated in the IH-TB and DM-TB groups compared to TB alone. This reduced IFN expression seen in IH-TB and DM-TB patients might indicate an insufficient immune response that permits continued growth of mycobacteria. There was greater upregulation, however, of genes involved in the inflammatory response in DM and TB comorbidity.

Overall, the transcriptomic profile for individuals with IH-TB was closer to those with DM-TB and not TB-only. The results demonstrate that patients with intermediate levels of hyperglycaemia also exhibit immune dysfunction, which could lead to an increased susceptibility to active TB disease.

**Journal Article:** Eckold et al., 2020. Impact of intermediate hyperglycaemia as well as diabetes on immune dysfunction in tuberculosis. Clinical Infectious Diseases.

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