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A cross-sectional study to evaluate the alteration of cytokine expression and activation of inflammatory pathway in response to NOD 1 and NOD 2 signal in leprosy

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Title - A cross-sectional study to evaluate the alteration of cytokine expression and activation of inflammatory pathway in response to NOD 1 and NOD 2 signal in leprosy

Introduction & Objectives: Leprae bacilli are identified as foreign by pattern recognition receptors (PRR) present in the microbes, but absent in host. The NOD-like receptor family (NLR) comprising the nucleotide- binding oligomerization domain (NOD1, NOD2) proteins are two well-known PRR. The objectives of this study were to study the expression of cytoplasmic NOD1 and NOD2 in the pathogenesis of leprosy, the serum level of expressed cytokines and to measure the mRNA expression.

Materials & Methods: A total of 457 clinically suspected Hansen’s patients were analyzed during a period of 4 years. Newly diagnosed leprosy patients were considered as leprosy disease control (LDC). The cases with active or new lesions and an increase in BI by at least 2+12 months after completion of MDT were considered leprosy disease relapse (LDR) cases. Age and sex-matched healthy individuals served as our control group (HC). ELISA was performed to measure the concentration of eight human cytokines including both pro-inflammatory (TNF-α, IFN-γ and IL-6), anti-inflammatory cytokines (IL-10), and one chemokine IL8. Quantitative expression of receptor genes (NOD1 and NOD2) and cytokine genes were evaluated by qRT-PCR. We studied NOD 1, NOD 2 expression in the tissues through Fluorescence Immune Histochemistry. Differential NLRs intracellular expression on peripheral blood monocytes (PBMC) and their response to stimulation with specific ligands (lipopolysaccharide, Muramyl dipeptide), were studied.

Results: A significant difference in the expression of NOD1 and NOD 2 genes was observed in unstimulated monocytes of the LDC and LDR cases when compared to HC. The LDC patients had a significantly higher level of pro-inflammatory cytokines than the HC.

Conclusion: In conclusion, this study has demonstrated the expression of both cytokines and chemokine in response to NLRs activation in skin of leprosy patients.

FIGURES
1A, 1B

NOD 1 expression in M. leprae infected patients skin
NOD 2 expression in M. leprae infected patients

Figure 3A, 3B: It represents the mRNA expression of NOD1, NOD 2 in the isolated cultured monocytes of HC, LDC patients and LDR cases with the respective effects of the ligands.

Figure 3C
Figure 3C: It represents the serum cytokine level for TNF-α in study subjects

Figure 3D: It represents serum level secretion of IL-6 in study subjects
Figure 3E: Shows serum level secretion of IL-8 in study subjects

Figure 3F: Shows serum level secretion of IFN-γ in study subjects

Figure 3G
Figure 3G: It represents mRNA expression of TNF – α from isolated cultured monocytes of HC, LDC, LDR patients

Figure 3H: Shows effect of ligands activation on mRNA expression of IL – 6 from the isolated cultured monocytes of HC, LDC patents and LDR cases
Figure 3I: Shows serum level secretion of IFN-γ in study subjects.

Figure 3J: Shows effect of ligands activation on the mRNA expression of IL-8 from isolated cultured...
monocytes of study subjects

Figure 3K

![Figure 3K](image1)

Figure 3K: Shows serum level secretion of IL-10 in study subjects

Figure 3L

![Figure 3L](image2)

Figure 3L: Shows serum level secretion of IL-10 in study subjects