

Research Article

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Role of Toll-Like Receptor 2 Immune Response in Mycobacterium Tuberculosis and Chronic Obstructive Pulmonary Diseased

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ABSTRACT

Background: Mycobacterium Tuberculosis and Chronic Obstructive Pulmonary disease (COPD) are of great public health concern due to high mobility and mortality rate recorded worldwide. Both diseases have similarities in their Immune pathogenesis such as the inflammation increased in the airway and lung parenchyma. Our study aimed at evaluating the implication of TLR2-mediated regulation in the pathogenesis of TB and COPD a pathway poorly elucidated.

Methods: We carried out a retrospective cross-sectional study amongst sixty enrolled participants from the Jamot Reference Hospital for Tuberculosis and other pulmonary respiratory diseases in Yaoundé Cameroon. An ethical clearance and consent were obtained from all our enrolled participants. They were confirmed positive cases for either TB using IDR of the tuberculin or COPD forcing expiratory volume in one second/forced vital capacity ratio of less than 70 percent of the predicted value. We collected 4 ml of whole blood into EDTA tubes. The genotyping of TLR-2, was using polymerase chain reaction-restriction fragment length polymorphism while respecting all the standards procedures.

Results: Of the total of 60 participants enrolled. In total (33%) were TB positive, (33%) COPD positive and 20 healthy controls. Both TB and COPD infection participants had their TLR-2 receptor higher than the control group 0.20ng/dl-0.80ng/dl whereas the level of the control was lower than 0.20g/dl it ranges from with a ($P < 0.001$).

Conclusions: From our study we could suggest that the Toll-like receptor 2 polymorphism response is imperatively important in studying the immunopathology of this disease and could open different horizons in research in this domain.

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Introduction

Tuberculosis remains a global emergency. The WHO Global TB Report 2023 reported 10.6 million new cases and 1.3 million deaths, with Africa accounting for 25% of cases. COPD is the third leading cause of death worldwide, responsible for 3.23 million deaths in 2019, and its prevalence is rising in sub-Saharan Africa due to tobacco smoking, biomass fuel exposure, and post-tuberculosis lung damage [1,2]. Both diseases converge on chronic airway inflammation, oxidative stress, mucociliary dysfunction, and parenchymal remodeling.

Previous TB is now recognized as an independent risk factor for COPD, increasing the risk of airflow obstruction by 2 to 4 times [3]. Innate immunity is the first line of defense. Toll-like receptors (TLRs) are pattern recognition receptors (PRRs). TLR2, which

forms heterodimers with TLR1 and TLR6, is highly expressed on alveolar macrophages, dendritic cells, and bronchial epithelial cells. It recognizes mycobacterial lipoproteins including LpqH (19-kDa antigen), LprG, and LprA. Upon ligation, TLR2 recruits MyD88, activates NF- κ B and MAPK pathways, and induces production of pro-inflammatory cytokines such as TNF- α , IL-1 β , IL-6, and IL-12 [4,5]. In TB, TLR2 activation is dual: it is essential for granuloma formation and intracellular killing, but chronic stimulation induces IL-10, inhibits MHC class II antigen presentation, and promotes tissue necrosis, favoring bacterial persistence. In COPD, chronic exposure to cigarette smoke, biomass particles, and Damage-Associated Molecular Patterns (DAMPs) leads to constitutive TLR2 activation, neutrophilic inflammation, and protease-antiprotease imbalance [6].

Polymorphisms in the TLR2 gene, particularly Arg753Gln (2258G>A) and Arg677Trp (2029C>T), alter the TIR domain

and impair signaling. These variants have been associated with increased susceptibility to TB in Tunisian, Turkish, and Chinese populations. However, data comparing TLR2 responses in TB and COPD in Central Africa are lacking [7,8]. The objective of this study was to evaluate the implication of TLR2-mediated regulation in the pathogenesis of TB and COPD in Yaoundé, Cameroon.

Materials and Methods

Study Design and Population: Retrospective cross-sectional study from January to June 2024 at Jamot Hospital, Yaoundé. we included 60 participants, aged ≥ 18 years divide into 3 groups, confirmed TB or Mycobacterium Tuberculosis and Chronic Obstructive Pulmonary disease (COPD), no immunosuppressive treatment.

Laboratory Procedures: Genomic DNA extraction, PCR amplification of TLR2 gene (Arg753Gln polymorphism), RFLP analysis, and ELISA quantification of soluble TLR2.

Statistical Analysis: Data analyzed with SPSS v25. ANOVA and Chi-square test. Significance at p < 0.05.

Results

The mean age was 48.5 ± 12.3 years with male predominance in the COPD group (70%). TLR2 levels were significantly higher in pathological groups vs controls.

Table 1: Distribution of TLR2 Levels by Group

Group	N	Mean TLR2 (ng/mL)	Ic 95C
TB	20	0.55 ± 0.18	0.20 - 0.80
COPD	20	0.52 ± 0.16	0.22 - 0.78
Controls	20	0.12 ± 0.05	0.05 - 0.19
p < 0.001 for TB vs Controls and COPD vs Controls; p = 0.68 for TB vs COPD.			

Discussion

Our findings demonstrate a significant upregulation of soluble TLR2 in both TB and COPD patients compared to healthy controls. This aligns with Thoma-Uszynski et al. who showed that mycobacterial lipoproteins are potent TLR2 agonists inducing direct antimicrobial activity. Similarly, studies on bronchial biopsies and induced sputum from COPD patients have shown increased TLR2 expression, particularly during exacerbations [4-9]. The common elevation suggests a shared innate inflammatory axis. In TB, M. tuberculosis exploits TLR2 signaling to induce anti-inflammatory IL-10 and evade immune clearance while maintaining chronic inflammation. In COPD, repetitive TLR2 triggering by colonizing bacteria such as Non-typeable Haemophilus influenzae and by oxidative stress leads to chronic NF-kB activation and release of IL-8, LTB4, and matrix metalloproteinases (MMP-8, MMP-9) [10].

Regarding genetics, Ogus et al. reported that the AA genotype of Arg753Gln confers a 6-fold increased risk of TB in Turkey, and Ben-Ali et al. found a similar association for Arg677Trp in Tunisia. Our study focused on phenotypic expression; future studies in Cameroon should include full genotyping of these SNPs given the high genetic diversity in the region [7,8]. Clinically, the TB-COPD overlap is underdiagnosed in Cameroon. Post-TB lung damage is a major driver of COPD in non-smokers, especially women exposed to biomass fuel. Identifying TLR2 as a common biomarker could help predict which TB patients will progress to COPD and could represent a target for host-directed therapies:

TLR2 antagonists to reduce parenchymal destruction in COPD, and regulated agonists to enhance mycobacterial clearance in TB. Limitations of our study include small sample size, single-center design, lack of downstream cytokine profiling (TNF-α, IL-10, IL-6), and lack of bronchoalveolar lavage analysis [11,12].

Conclusion

This study provides evidence that Toll-like receptor 2 is significantly upregulated in both tuberculosis and COPD in a Cameroonian cohort, highlighting a shared innate immune pathway. TLR2 could serve as a biomarker of chronic lung inflammation and as a potential therapeutic target. Multicentric longitudinal studies with larger cohorts, including functional genotyping and cytokine correlation, are needed to validate these findings and open new horizons in host-directed therapy for chronic lung diseases in Africa.

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Contributions of Authors

Chris André Mbongue-Mikangue: Conceptualization, data curation, laboratory experiments (PCR-RFLP, ELISA), writing – original draft.

George Ikomey Mondinde: Supervision, methodology validation, writing – review & editing, project administration at CSCCD.

Conflict of Interest: None declared.

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