

# DISERTASI

## HUBUNGAN CD -14, EKSPRESI TOLL-LIKE RECEPTOR-2, DAN TOLL-LIKE RECEPTOR-4 DENGAN TUMOR NECROSIS FACTOR- DAN INTERFERON- PADA TONSILITIS REKUREN



Oleh

**FATAH SATYA WIBAWA**

**NIM : 1131202118**

**Pembimbing :**

1. Prof.Dr.dr.Eryati Darwin, PA(K)
2. Dr.dr.Irza Wahid, Sp.PD, KHOM, FINASIM
3. Dr.dr.Netti Suharti, M.Kes

**PROGRAM STUDI S-3 BIOMEDIK**  
**FAKULTAS KEDOKTERAN UNIVERSITAS ANDALAS**  
**PADANG**  
**2018**

## ABSTRAK

### Hubungan CD-14, Ekspresi Toll Like Receptor-2, Toll Like Receptor-4 Dengan Tumor Necrosis Factor- Dan Interferon- Pada Tonsilitis Rekuren

Fatah Satya Wibawa

Tindakan tonsilektomi pada tonsilitis kronis atau rekuren, hingga saat ini masih menjadi kontroversi. Terjadinya tonsilitis rekuren ditentukan oleh faktor eksternal; banyak jenis bakteri yang bertanggung jawab terhadap terjadinya tonsilitis rekuren dan faktor internal, yaitu fungsi imunitas seseorang. Pada tonsilitis rekuren terjadi peningkatan ekspresi berbagai jenis *toll like receptors* (TLRs) di tonsil. TLRs bersama *co-receptor* CD-14 berperan dalam mengenali bakteri patogen dan memicu respon imun alamiah maupun adaptif. Penelitian ini bertujuan mengidentifikasi bakteri penyebab tonsilitis rekuren serta mengetahui hubungan CD-14, TLR-2, dan TLR-4 dengan *tumor necrosis factors-alpha* (TNF- $\alpha$ ), dan *interferon-gamma* (IFN- $\gamma$ ) pada tonsilitis rekuren.

Sebanyak 34 anak penderita tonsilitis rekuren, berumur 4 - 15 tahun, yang memenuhi kriteria inklusi ditetapkan sebagai subjek penelitian. Kultur apus tonsil diperiksa untuk mengidentifikasi bakteri patogen, sementara untuk mengetahui persentase ekspresi TLR-2 dan TLR-4 pada tonsil, dilakukan dengan metoda imunohistokimia. Darah vena digunakan untuk mengetahui persentase ekspresi CD-14 pada leukosit dengan metoda *flowcytometry*, serta menentukan kadar TNF- $\alpha$  dan IFN- $\gamma$  menggunakan metode ELISA.

Dari hasil kultur apus tonsil, 52,9 % tidak ditemukan bakteri patogen, 41,1 % ditemukan bakteri Gram positif (*S.aureus* dan *Streptococcus* non group A), dan 8,8 % bakteri Gram negatif (*K.pneumoniae*). CD-14 terekspresi paling banyak pada monosit (56,57 %), lalu pada limfosit (5,03 %), dan netrofil (0,55 %). Rata-rata ekspresi TLR-2 pada jaringan tonsil  $2,59 \pm 4,25$  %, sedangkan rata-rata ekspresi TLR-4 adalah  $28,78 \pm 10,49$  %. Rata-rata kadar TNF- $\alpha$  pada darah adalah  $5,20 \pm 4,21$  pg/ml, sedangkan rata-rata kadar IFN- $\gamma$  adalah  $9,32 \pm 1,27$  pg/ml.

Ekspresi TLR-4 jauh lebih besar daripada TLR-2, walaupun hanya ditemukan 8,8 % bakteri patogen Gram negatif. Tidak ditemukan hubungan korelatif yang signifikan antara CD-14, TLR-2 dan TLR-4 dengan TNF- $\alpha$  dan IFN- $\gamma$  pada penderita tonsilitis rekuren.

**Kata Kunci :** tonsilitis rekuren, tonsilektomi, bakteri patogen, CD-14, TLR, TNF- $\alpha$ , IFN- $\gamma$

## ABSTRACT

### **Relationship Between CD-14, Toll Like Receptor-2, Toll Like Receptor-4 Expression With Tumor Necrosis Factor- And Interferon- In Recurrent Tonsillitis**

**Fatah Satya Wibawa**

Tonsillectomy on chronic or recurrent tonsillitis still remain controversy. Cases of recurrent tonsillitis depends on external factor; many bacterias responsible for causing tonsillitis, and internal factor, meaning one's immunity. It's already known that various of toll like receptors (TLRs) showing increased expression in the mass of tonsil in case of recurrent tonsillitis. TLRs and CD-14, as co-receptor, play a role in recognizing cellular components of pathogenic bacteria and triggering both natural and adaptive immune responses. This study aims to identify the bacterias causing tonsillitis and the relationship between CD-14, TLR-2, and TLR-4 with tumor necrosis factors alpha (TNF- ), and interferon gamma (IFN- ) in patients with recurrent tonsillitis.

A total of 34 children with recurrent tonsillitis, aged 4 - 15 years, who fulfilled the inclusion criteria were subjected to the study. The tonsil tissue specimens from the subjects were taken for microbiological and immunohistochemical analysis. Microbiological analyzis using tonsil smear cultures were applied to identify pathogenic bacterias on the surface of the tonsil. Immunohistochemical technique applied to determine the expression of TLR-2 and TLR-4 in tonsillar mass. Venous blood used to determine CD-14 expression in leukocytes using flowcytometry technique and to determine levels of TNF- and IFN- in serum using ELISA method..

From the tonsillar swab cultures, 52,9 % were not overgrown with pathogenic bacteria, 41,1 % by Gram positive (*S. aureus* and *Streptococcus non group A*), and 8,8 % by Gram-negative (*K. pneumoniae*). CD-14 expressed most frequently in monocytes (56.57 %), then in lymphocytes (5.03 %), and in neutrophil (0.55 %). The expression of TLR-2 in tonsil tissue was  $2.59 \pm 4.25$  %, while the TLR-4 was  $28.78 \pm 10.49$  %. TNF- level was  $5.20 \pm 4.21$  pg/ml, whereas IFN- level was  $9.32 \pm 1.27$  pg/ml.

TLR-4 expression shows trully higher, eventhough only 8,8 % Gram negative bacteria existed. There was no significant correlationship found in this study between CD-14, TLR-2 and TLR-4 with TNF- and IFN- in children with recurrent tonsillitis.

**Keywords** : recurrent tonsillitis, tonsillectomy, pathogenic bacteria, CD-14, TLRs, TNF- , IFN-