## ABSTRACT


### MECHANISM of CORNEAL EPITHELIAL CELLS DEATH by INFECTION of *PSEUDOMONAS AERUGINOSA* through ANALYSIS EXPRESSION of CASPASE-1, TNFα, RIPK1, RIPK3, CASPASE-3 in RATS MODEL

***Background***: *Pseudomonas aeruginosa* is one of the leading causes of severe keratitis that may cause in progressive inflammation with rapid onset, resulting in permanent tissue destruction, then eventually, blindness and damage to corneal integrity. It is important to know the virulence factor of *Pseudomonas aeruginosa* mechanism and modes of regulation in corneal epithelial cells to prevent progressivity, increasing chance of recovery, and decreasing perforation corneal complication.

***Objective***: The aim of this study to investigate mechanism of corneal epithelial cell death by *Pseudomonas aeruginosa* infection through the analysis of expressions of caspase-1, TNFα, RIPK1, RIPK3, and caspase-3.

***Methods*:** The study design was randomized post-test only with control group. Fifty-three Wistar rats are divided into 2 groups, each of them with 6 treatments. One control group and one experimental group. In the experimental group, three epithelial abrasions were produced on the left cornea with a 26-gauge needle and inoculated with $2x10^6$ CFU/ml in 5µl of bacterial suspension, while in the control group only three epithelial abrasions. In both groups use waiting time 1 hour, 6 hours, 12 hours, 24 hours, 48 hours, 72 hours after that the eyeball was enucleated and rat was terminated thus examine for histology and immunohistochemical staining examination.

***Result***: *Pseudomonas aeruginosa* was shown to cause increasing expression of caspase-1 ($p = 0.006$), TNFα ($p = 0.000$), caspase-3 ($p = 0.061$), and decreasing expression of RIPK3 ($p = 0.047$). TNFα showed to cause increasing expression of RIPK1 ($p = 0.000$), RIPK1 showed to cause increasing expression of RIPK3 ($p = 0.000$), but TNFα showed not to cause change of expression of caspase-3 ($p = 0.141$).

***Conclusion***: This study demonstrated infection of *Pseudomonas aeruginosa* in corneal rats model showed to cause increasing expression of caspase-1, TNFα, caspase-3, increasing RIPK1 through TNFα, and decreasing expression of RIPK3 in 1 hour until 72 hours after inoculation as prime biomarkers in mechanism of corneal epithelial cell death.


**Keyword**: *Pseudomonas aeruginosa*, corneal epithel, cell death, caspase-1, TNFα, RIPK1,RIPK3, caspase-3.