DIFFERENTIAL EXPRESSION OF INTERFERON INDUCIBLE PROTEIN: GUANYLATE BINDING PROTEIN (GBP1 & GBP2) IN SEVERE DENGUE

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Expressed in response to interferon, GBP1 and GBP2 exhibit marked upregulation in influenza, dengue, and other viral infections. As cytokines play a pivotal role in the pathogenesis of these diseases, the study aimed to examine the association between GBP1 and GBP2 proteins and disease severity in dengue infection. The research focused on patients beyond the first week of fever, who were classified as critical or non-critical based on their clinical condition.

**ABSTRACT**

Dengue virus is known to activate endothelial cells (ECs), but the precise cause for severe dengue (SD) is not well understood. Guanylate binding proteins (GBP1 & GBP2) are IFN-inducible proteins secreted by ECs and are involved in the anti-oxidant and anti-viral response. The involvement of GBP1 & GBP2 in the pathogenesis of dengue remains to be explored. We have quantified the mRNA and protein levels of GBP1 & GBP2 in severe dengue patients during different phases of infection and have consistently observed positive correlations in plasma samples of different groups. The efficacy of the proteins in indicating disease severity was evaluated using Support Vector Machine (SVM).

**AIM & OBJECTIVES**

To see the role of GBP proteins on dengue disease progression by:

a) quantifying the mRNA and protein levels of GBP1 & GBP2 in severe and non-severe forms of DENV infected patients during the course of infection
b) Assessing GBP proteins as effective prognostic markers using machine-based mathematical models
c) Finding the association between GBP oxidative stress markers and severity markers during the course of DENV infection

**METHODOLOGY**

- 3 mL of venous blood was collected under aseptic conditions at the Day of admission (1st day, DOA), Day of defervescence (4th day, DOD), and Day of convalescence (11th day, DOC) from patients.
- The PBMCs were isolated from whole blood samples, DNA extraction using the isolot method, and mRNA was converted into complementary DNA (cDNA) and the cDNA was used as a template for qPCR analysis.
- Protein & DNA (lipid peroxidation) was estimated by the Kei Satoh method.
- Data analysis and statistical analysis of the result were performed with 5% level of significance (P value ≤0.05).

**RESULTS**

- mRNA levels GBP1 and GBP2

  - GBP1 and GBP2 expression was measured by qRT-PCR and normalized by β-actin. DOA of all the groups is taken as a baseline P-value ≤0.05 is considered significant.

- ELISA (Plasma Level) GBP1 and GBP2

  - Plasma levels of GBP1 and GBP2 in all the study groups. Wilcoxon signed-rank test was used to compare within the groups. P-value ≤0.05 is considered significant.

- **LEVEL OF MDA (lipid peroxidation)**

  - Plasma levels of MDA in all the study groups. Wilcoxon signed-rank test was used to compare within the groups. P-value ≤0.05 is considered significant.

- **LEVEL OF DNA OXIDATION**

  - Plasma levels of DNA damage in all the study groups. Wilcoxon signed-rank test was used to compare within the groups. P-value ≤0.05 is considered significant.

- **LEVEL OF PROTEIN OXIDATION**

  - Plasma levels of AOPP in all the study groups. Wilcoxon signed-rank test was used to compare within the groups. P-value ≤0.05 is considered significant.

**DISCUSSION**

- GBP1 and GBP2 were found to be negatively correlated with plasma leakage and elevated levels of oxidative stress with the decreased expression of GBP1 & GBP2 during the course of DENV infection.
- Increased oxidative stress may downregulate both GBP1 and 2 thereby enhancing disease manifestation by creating a suitable micro-environment for virus propagation accompanied by endothelial dysfunction.
- Thus, the study found that the expression pattern of GBP1 and 2 were found to be negatively correlated with plasma leakage, and elevated levels of oxidative stress are associated with the decreased expression of GBP1 & GBP2 during DENV infection.

**SUMMARY AND CONCLUSION**

- Expression pattern of GBP1 and 2 were found to be negatively correlated with plasma leakage and elevated levels of oxidative stress are associated with the decreased expression of GBP1 & GBP2 during the course of DENV infection. Thus, antioxidant supplement as adjuvant therapy would modulate the expression of GBP1 & GBP2 and disease virulence. Nevertheless, machine models found that the plasma levels of GBP1 & 2 along with routine clinical symptoms could predict the dengue disease severity with higher accuracy. A large prospective cohort study may be required to ascertain the role of GBP1 & GBP2 as effective prognostic markers of dengue severity.
- The findings have been published in Free Radical Biology and Medicine, 194: 131-46, 2023.

**REFERENCES**