Stimulator of interferon genes/Interferon regulatory factor 3 (STING-IRF3) and inflammasome-activation mediated pyroptosis biomarkers: a network of integrated pathways in diabetic nephropathy

Omnia Safwat El-Deeb [1], Yasser Mostafa Hafez [2], Amira Kamel Eltokhy [1], Marwa Mahmoud Awad [3], Rehab Ahmed Ahmed El-shaer [3], Muhammad Tarek Abdel Ghafar [4], Marwa Mohamed Atef [1].

1 Medical Biochemistry Department, Faculty of Medicine, Tanta University, Tanta, Egypt

2 Internal Medicine Department, Faculty of Medicine, Tanta University, Tanta, Egypt

3 Physiology Department, Faculty of Medicine, Tanta University, Tanta, Egypt

4 Clinical Pathology Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Abstract:

Background:

Diabetic Nephropathy (DN) is serious diabetic complication affecting the structure and function of the kidney. This study assessed the stimulator of interferon genes/ Interferon regulatory factor 3 (STING/IRF3) signaling pathway roles and inflammasome-activation mediated pyroptosis, being imperative pathways of inordinate importance in disease progression, in DN throughout its different stages.

Methods:

45 Diabetic cases were categorized into three groups based on their albuminuric status as follow: Normoalbuminuric, Microalbuminuric and Macroalbuminuric diabetic groups and 15 healthy subjects as controls were included. We evaluated STING and absent in melanoma 2 (AIM2) messenger RNA (mRNA) expressions from whole blood using quantitative RT-PCR. Additionally, Serum levels of STING, AIM2, IRF3, Nod like receptor pyrins-3 (NLRP3), interleukin-1β (IL-1β) and caspase-1 were assessed by ELISA technique.

Results:

The study documented that STING and AIM2 mRNA expressions had significantly increased in DN cases with highest value in macroalbuminuric diabetic groups ($p < 0.001$*). Parallel results were observed concerning serum STING, AIM2, IRF3, NLRP3, Caspase-1 in addition to IL-1β levels ($p < 0.001$*).

Conclusion:

The study documented the forthcoming role of STING in DN progression and its positive correlation with inflammasome-activation mediated pyroptosis biomarkers throughout its three different stages; launching new horizons in DN pathogenesis by highlighting its role as a reliable prognostic biomarker.