Anti-IFNα antibodies in SLE: Association with organ involvement, disease activity and infections

Introduction:

Systemic Lupus Erythematosus (SLE) is a multi-systemic chronic autoimmune disease, predominantly affecting women in the reproductive age group. The disease pathogenesis involves a complex interaction between genetic, environmental and host factors leading to immune dysregulation and autoimmunity. Apart from the considerable morbidity associated with SLE, it ranks among the leading causes of mortality in young females. Concomitant infections mostly due to immune suppressive therapy, the disease activity, accelerated cardiovascular disease and malignancy are the various factors responsible for the morbidity and mortality associated with lupus disease.

The relationship of infection and SLE disease activity is a bidirectional one, with studies showing both variables driving each other. The similarity of presenting manifestations, lack of reliable biomarkers and diametrically opposite treatment options for SLE disease activity and infections possesses a great challenge for physicians across the globe. Additionally, a high burden of tropical and parasitic infections, and lack of access to health care resources in developing countries like ours make SLE patients more vulnerable to infections.

Anti-cytokine antibodies (ACAA) by reducing or augmenting cytokine signalling pathways or by altering the half-life of cytokine in circulation plays an important role in disease severity and predisposition to infection. IFNα is a key cytokine driving SLE severity and blockade of IFN pathways have been a landmark development in disease management. Anti IFN-α antibodies have been associated with less severe disease at the same time predispose to severe infections in SLE. This pilot study is designed to measure the levels of anti-IFNα antibodies in SLE patients, and to study its functional characteristics, its association with disease activity and ultimately its association with severe concomitant infections.

Objectives:

1. Estimate the levels of anti-IFNα antibodies in the serum of SLE patients.
2. Functional characterisation of anti-IFNα antibodies, including their IFNα neutralising capacity.
3. Association of antibody titres with clinical and disease activity metadata.
4. Association of antibody titres with Infections.

Methodology:

Patients and matched controls:-
Inclusion Criteria:
SLE patients (n=50) fulfilling SLICC criteria admitted to the Department of Clinical Immunology and Rheumatology at SCB Medical College and Hospital, Cuttack, Odisha with fever as the presenting manifestation will be included after taking an informed consent.Patient details will be entered into a predesigned study proforma.

Exclusion Criteria:
Overlap Syndrome
Comorbidity like Diabetes, CKD, CLD

Controls:
Age and sex matched 50 healthy controls will be recruited.

Type of Study:
Cross-sectional, case control, hospital-based study

ELISA:
IFNα concentration and Anti-IFNα antibody titres levels will be measured by ELISA as per vendor recommended protocols.

IFN Gene Signature:
Interferon stimulated gene expression using a three gene biomarker for MX1, ISG15, IFIT1 to know the effect on downstream signalling pathways will be measured.

Neutralisation Assay:
In patients with Anti-IFNα antibodies in serum, neutralising effect of these antibodies will be studied using ELISA.

Anticipated Outcomes:
1. Study will lead to better understanding of IFNα pathway in cohort of Indian SLE patients.
2. If there is a correlation between anti-IFNα levels, disease severity and concomitant infections. This assay can be further developed as a biomarker to differentiate infection versus disease flare which is very important for routine clinical practice.

Timelines:

	0-3 Months	3-6 Months	6-9 Months
Patient Recruitment	Yes	Yes	No
Laboratory Tests	Yes	Yes	No
Data Analysis	No	No	Yes
Manuscript Preparation and Final Report	No	No	Yes

Key References:

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