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TRENDS OF SEVERITY, PROGRESSION AND BURDEN OF DISEASE IN THE "ATTIKON" SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) COHORT: EVIDENCE FOR THE RULE OF "ONE THIRD" IN DISEASE SEVERITY

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Background: SLE phenotype, severity and prognosis varies widely, while its course, prognosis and pattern of severity cannot be predicted with confidence.

Objectives: We analyzed the phenotype and severity patterns of a SLE cohort in the Attica area of Greece, based in "Attikon" University Hospital, and assessed whether these patterns change over the course of the disease.

Methods: Retrospective cohort study of 512 Caucasian SLE patients fulfilling the ACR 1997 and/or SLICC 2012 criteria. Data on clinical course, pattern of severity and SLICC damage index (SDI) were recorded for each patient at the time of diagnosis and at last evaluation. Severity of disease was stratified based on BILAG manifestations and patients were assessed for progression to a more severe phenotype over their disease course. Patients with disease duration < 12 months were excluded. Binary logistic regression was performed to identify independent predictors of such progression.

Results: More than half patients (53.7%, 275/512) presented with mild disease, while in approximately 20% (20.8%, n=106) lupus presented with severe manifestations at diagnosis. Median (IQR) follow-up was 96.5 (144) months. Of 246 patients with initially mild disease, 126 (56.4%) retained their mild phenotype, 73 (29.7%) progressed to a moderate phenotype, while the remaining 47 (19.1%) eventually developed severe lupus. Also, 30 patients (29.4%, 30/102) who initially manifested moderately severe manifestations progressed to severe disease over time. At last evaluation, a nearly equal distribution in severity patterns was evident (mild 30%, moderate 34% and severe 36%). Independent factors for disease progression were older age at diagnosis (OR: 0.97 per 1-year, 95% CI 0.95-0.98), disease duration (OR: 1.10 per 1-year, 95% CI 1.06-1.13), positive anti-dsDNA (OR: 2.20, 95% CI 1.38-3.49) and presence of fever at diagnosis (OR: 1.67, 95% CI 1.00-2.77). By multivariate regression, only disease duration (OR: 1.09, 95% CI 1.05-1.12) and anti-dsDNA (OR: 1.73, 95% CI 1.05-2.85) were independently associated with disease progression.

Ninety-two subjects (18%) had organ damage at the time of diagnosis, mainly due to neuropsychiatric and thrombotic events. At last visit, mean (SE) SDI was 0.67 (0.57). Two-hundred eight patients (59.8%) had no damage (SDI=0), while high damage (SDI ≥ 3) was measured in 25 subjects (7.2%).

Conclusion: In this SLE cohort of Caucasian patients, almost half of cases have mild disease at presentation, yet with significant damage accrual. Of patients with disease duration ≥1 year, 43.1% progressed to more severe phenotypes, with patients distributed evenly in the mild, moderate and severe categories. These data reiterate the rule of one third for severity observed in other autoimmune diseases.

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IMPACT OF IL34, IFNA AND IFN-λ1 ON DISEASE ACTIVITY OF SLE PATIENTS IN EGYPT

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Background: SLE is a systemic inflammatory and autoimmune disease. IL-34 plays pivotal roles in the proliferation and differentiation of mononuclear phagocyte cells, osteoclastogenesis and inflammation [1]. IFN-α play

an important role in SLE pathogenesis [2] and proportion of patients displays increased serum IFN-α and IFN-λ1 [3]. Interestingly, the gene signatures of IFN-λ1 and IFN-α overlap [4].

Objectives: Assessment of IL34, IFN-λ1 and IFN-α in SLE with relationship to clinical, laboratory parameters, treatment response and disease progression. We hypothesized a subgroup of patient with a concordance of high level of these cytokines that could have a different disease behavior.

Methods: 82 newly diagnosed SLE Egyptian patients. History, examination and laboratory investigation with assessment of disease activity. Pretreatment assessment of IL34, IFN-α and IFN-λ1 level by ILIZA. Patients started treatment (antimalarial ±Steroid ±immunosuppressive drugs) with response evaluation after six months.

Results: 14 male (17.1%) and 68 female (82.9%), age mean±SD (48.6 ±8.2). Mean±SD of IL34, INFα and INF-λ1 were 175.9±125.9 pg/mL, 109.3±32.5 pg/mL and 227.9±144.8 pg/mL respectively. 21 patients (25.6%) had lupus nephritis, 32 patients (39%) with SLAM >6 and 22 patients (26.8%) with SLEDAI >6.

IL34 was positively correlated with anti-dsDNA (P= 0.002) but inversely correlated with C3 level (P = 0.009). IL34 was highly presented with lupus nephritis (P 0.005), SLAM>6 (P 0.03), SLEDAI>6 (P 0.007) and poor responder to treatment (P 0.02).

IFNα was inversely correlated with C3 (P 0.001). IFNα was highly presented with lupus nephritis (P 0.02) and poor responders (P 0.01) however no relation with SLAM>6 nor SLEDAI>6.

INF-λ1 was positively correlated with anti-dsDNA (P= 0.02) but inversely correlated with C3 (P = 0.01). INF-λ1 was highly presented with lupus nephritis (P 0.001), with SLAM>6 (P 0.04), with SLEDAI>6 (P 0.02).

Accumulation of ≥3 clinical features during follow up was associated with high IL34 (P 0.001), high IFNα (P 0.001) and high INF-λ1 (P 0.001).

We assigned high levels (i.e., ≥ 75% or third quartile) of each cytokine. Triple high (IL34^{high}, IFNα^{high} and IFN-λ1^{high}) found in 17 patients (20.7%) and were positively correlated with anti-dsDNA (P= 0.001) but inversely correlated with C3 (P = 0.001). Triple cytokines level was highly presented with lupus nephritis (P 0.001), SLAM>6 (P 0.02), SLEDAI>6 (P 0.03) and poor response to treatment (P 0.01) indicating these patients have aggressive disease. 28 patients developed (3 – 8) accumulated clinical features during the disease course, out of them 15 patients (53.5%) have high level of the triple cytokines indicating a poor prognosis of these subgroup.

Conclusion: High pretreatment IL-34 or IFN-λ1 has a prognostic significance in SLE. Patients with high IL-34 or IFNα or IFN-λ1 had more kidney affection and poor response to treatment. Triple cytokines elevation significantly associated with lupus activity, more kidney affection and poor response to treatment so, this aggressive phenotype may need combination of targets or multicytokines targeted therapy.

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