ANEMIA AS A PREDICTOR OF DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Mohammad Omar Heiba

List of contents

List of abbreviations

Abbreviation Abbreviation	Meaning
ACD	Anemia of chronic disease
ACR	American College of Rheumatology
AIHA	Autoimmune hemolytic anemia
ANA	Antinuclear antibodies
Anti-ds DNA	Anti-double stranded deoxyribonucleic acid
Anti-HLA	Anti- human leukocyte antigen
Anti-SSA/Ro and anti-SSB/La	Anti-Sjögren's-syndrome-related antigen A and B
AOSD	Adult-onset Still's disease
APS	Anti-phospholipid syndrome
BFU-E	Burst forming units-erythroid
BILAG	British Isles Lupus Assessment Group
BM	Bone marrow
C3, C4	Complement 3,4
CBC	Complete blood count
CFU-E	Colony forming units- erythroid
CNS	Central nervous system
CRP	C-reactive protein level
CSA	Cyclosporine-A
CT	Computed tomography
CYC	Cyclophosphamide
DHEA	Dehydro-epiandrosterone
DNA	deoxyribonucleic acid

List of abbreviations (Cont.)

ds-DNA	Double-stranded deoxyribonucleic acid
EBV	Epstein-Barr virus
ECLAM	European Consensus Lupus Activity Measurement
ELISA	Enzyme-linked immunosorbent assay
EPO	Erythropoietin
ESR	Erythrocyte sedimentation rate
FcR	Fc receptor
fL	Femtoliters
GCs	glucocorticoids
GM-CSF	Granulocyte macrophage colony-stimulating factor
GP	Membrane glycoproteins
GWAS	Genome-wide association studies
Hb	Hemoglobulin
hCRH	Human corticotropin releasing hormone
HCT	Hematocrit
HGB	Hemoglobin concentration
HLH	Hemophagocytic lymphohistiocytosis
HS	Highly significant
IC	Immune complex
ICAMs	Intercellular adhesion molecules
IDA	Iron deficiency anemia
IDMS	Isotope dilution mass spectrometry
IFN	Interferon
IGF	Insulin growth factor

List of abbreviations (Cont.)

IIF	Indirect immunofluorescence
IL	Interleukin
ISN/RPS	International Society of Nephrology/ Renal Pathology Society
ITP	Immune thrombocytopenia
IVIg	Intravenous immunoglobulin
LAI	Lupus Activity Index
LDH	Lactate dehydrogenase
LFA	Lymphocyte function-associated antigen
LN	Lupus nephritis
MAHA	Microangiopathic hemolytic anemia
MAS	Macrophage activation syndrome
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
MMF	Mycophenolate mofetil
NK	Natural killer
NPSLE	Neuropsychiatric syndromes associated with SLE
NS	Non-significant
pg	picograms
PLT	Platelets
PRCA	Pure red cell aplasia
PNH	Paroxysmal nocturnal hemoglobinuria
RA	Rheumatoid arthritis
RBC	Red blood cell

List of abbreviations (Cont.)

RCM	Red blood cell mass
RDW	Red cell volume distribution width
RNA	Ribonucleic acid
S	Significant
SCF	Stem Cell Factor
±SD	Mean standard deviation
SLAM	Systemic Lupus Activity Measure
SLE	Systemic Lupus Erythematosus
SLEDAI	Systemic Lupus Erythematosus Disease Activity Index
SLICC	The Systemic Lupus International Collaborating Clinics
snRNPs	Small nuclear ribonucleic proteins
TGF-beta	Transforming growth factor-beta
TIBC	Total iron-binding capacity
TLRs	Toll-like receptors
TNF	Tumor necrosis factor
TTP	Thrombotic thrombocytopenic purpura
UV	Ultraviolet
VCAM	Vascular cell adhesion molecule
VWF	von Willebrand factor
WHO	World Health Organization

List of Tables

Table	Title	Page
1	International Society of Nephrology/ Renal Pathology Society classification of LN.	25
2	Indications for renal biopsy in patients with systemic lupus erythematosus.	26
3	Neuropsychiatric syndromes associated with SLE.	27
4	Clinical and immunologic criteria used in the SLICC.	43
5	Systemic Lupus Activity Measure (SLAM) Index.	49
6	SLICC/ACR damage index for SLE.	50
7	Normal values of red blood cell parameters.	54
8	Classic Distinguishing Features of IDA and ACD.	69
9	Description of age, disease duration, SLAM score, SLICC/ACR index and Hb concentration among patients.	84
10	Description of demographic and some lab data among group (1) anemic cases (IDA).	86
11	Description of CBC and iron profile among group (1) anemic cases (IDA).	87
12	Description of Retics, LDH and Coombs test among group (1) anemic cases (IDA).	88

List of Tables *(Cont.)*

List of Tables *(Cont.)*

List of Figures

Figure	Title	Page
1	Mechanism of autoantibody production and tissue injury in lupus.	15
2	Butterfly rash of SLE.	22
3	Erythema annulare centrifugum.	23
4	Livedo reticularis more pronounced in an upright posture.	24
5	Dependence of erythroid progenitor cells to EPO and SCF at different stages of erythropoiesis.	56
6	Showing gender distribution among patients.	84
7	Percentages of types of anemia among patients.	85
8	Comparison between three study groups as regards 24-Hrs urinary protein.	96
9	Correlation between Hb and C3.	101
10	Correlation between Hb and C4.	102
11	Correlation between Hb and SLAM activity.	102
12	Correlation between Hb and 24-Hrs urinary protein.	103
13	Correlation between Hb and SLICC/ACR damage score.	104

Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder that results from a combination of genetic, hormonal and environmental factors *(Nuttall et al., 2013).* It is an unusually heterogeneous disease, characterized by autoantibody production and immune complex (IC) deposition leading to multi-organ damage *(Chung et al., 2011).*

It is a chronic, usually lifelong, potentially fatal autoimmune disease characterized by unpredictable exacerbations and remissions with protean clinical manifestations *(Hung et al., 2005).*

SLE affects the joints, skin and blood in over 80% of patients and affects the kidneys, central nervous system and cardiopulmonary system in 30%-50% of patients. Between 10% and 30% of patients have anticardiolipin antibodies that are associated with arterial and venous thrombosis. The majority of patients demonstrate systemic manifestations, which may include fatigue, malaise, fever, anorexia, nausea and weight loss *(Chang et al., 2002).*

1

Haematological abnormalities are common findings in SLE. Anemia is found in about 50% of patients, the most common forms of anemia in these patients are: anemia of chronic disease (ACD), iron deficiency anemia (IDA), autoimmune hemolytic anemia (AIHA), anemia of chronic renal insufficiency, and cyclophosphamide-induced myelotoxicity. It is noteworthy that ACD often coexists with anemia caused by other mechanisms. Iron deficiency is common in patients with SLE as a result of menorrhagia and increased gastrointestinal blood loss, caused by the use of non-steroidal anti-inflammatory drugs, aspirin, and oral anticoagulants *(Giannouli et al., 2006)*.

Other causes of SLE associated anemia include: nutritional deficiencies (folate and B12), immune mediated, red cell aplasia, hemophagocytosis, aplastic anemia, pernicious anemia, myelofibrosis, uremia, treatment induced, hypersplenism, infection, and myelodysplasia *(Giannouli et al., 2006)*.

As a chronic disease, SLE can exhibit a wax and wane course that, oftentimes, cannot be predicted or corroborated by serological tests. The predictive value that many biomarkers have in the disease course, including anti-ds-