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Serum Soluble CD163 as a Marker of activity in MS Patients

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Serum Soluble CD163 as a Marker of Activity in MS patients

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Serum Soluble CD163 as a Marker of Activity in MS patients

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Abstract

Background: Multiple sclerosis (MS) is a chronic autoimmune disease that affects the central nervous system. Microglia and macrophages have a substantial role in myelin and axonal degeneration by causing neuro-inflammatory damage. Soluble CD163 one of the myeloid linage biomarkers, showed a better correlation with monocyte count in the CSF of MS patients. **Objective:** In the current case control observational study, we aimed to assess serum level of sCD163 as an immunological non-invasive marker for MS activity. **Patients and methods:** Sixty relapsing remitting multiple sclerosis (RRMS) patients were included and divided into 2 groups based on disease activity. Twenty-eight matched healthy controls were included and all subjects' serum levels of sCD163 were measured using ELISA. **Results:** We demonstrated a highly significant difference between the whole patients compared to controls with a concomitant no statistically

significant difference between the patients' groups. **In conclusion:** We emphasized the relevance of serum level of sCD163 as a non-invasive immunological biomarker in the diagnostic panel of MS reflecting the inflammatory process rather than the activity status of the patients.

Key words: Multiple sclerosis, sCD163, RRMS.

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List of Abbreviations

Abbreviations	Full term

Ab: ..... Antibody
ADAM: ..... A disintegrin and metalloproteinase
Ag: ..... Antigen
APCs: ..... Antigen presenting cells
AUC: ..... Area under curve
BBB: ..... Blood brain barrier
BCR ..... B cell receptor
CAMs: ..... Cell adhesion molecules
CCL: ..... CC chemokine ligand
CCR: ..... CC chemokine receptor
CD: ..... Cluster of Differentiation
cDCs: ..... Conventional dendritic cells
CIS: ..... Clinically isolated syndrome
CNS: ..... Central nervous system
COVID-19: ..... Corona virus disease 2019
CSF: ..... Cerebrospinal fluid
CXCL: ..... C-X-C motif ligand
DCs: ..... Dendritic cells
DMTs: ..... Disease-modifying therapies
DNA: ..... Deoxyribonucleic acid
EAE: ..... Experimental autoimmune encephalomyelitis
EBNA-1: ..... Epstein Barr nuclear antigen A-1
EBV: ..... Epstein Barr Virus
EC: ..... Epithelial cell
Ecto-CD163: ..... Ectodomain CD163
EDSS: ..... Expanded Disability Status Scale
ELISA: ..... Enzyme linked immunosorbent assay
EV-CD163: ..... Extracellular vesicles CD163
FasL: ..... Fas ligand
FoxP3: ..... Fork head box P3
GM-CSF: ..... Granulocyte-macrophage colony stimulating factor

List of Abbreviations (Cont...)

Abbreviations	Full term

GWASs: ..... Genome-wide association studies
Hb: ……Hemoglobin
HBV: ..... Hepatitis B virus
HCC: ..... Hepatocellular carcinoma
HCV: ..... Hepatitis C virus
HIV: ..... Human immunodeficiency virus
HLA: ..... Human leukocyte antigen
HRP: ..... Horseradish Peroxidase
HS: ..... Highly significant
ICAM-1: ..... Intercellular adhesion molecule 1
ICU: ..... Intensive care unit
IFN: ..... Interferon
IFNβ: ..... Interferon beta
Ig: ..... Immunoglobulin
IL: ..... Interleukin
IM: ..... Intramuscular
IQR: ..... Inter-quartile range
iTreg: ..... Inducible T regulatory
IV: ..... Intravenous
LPS: ..... Lipopolysaccharide
MBP: ..... Myelin basic protein
mCD163: ..... Membrane CD163
M-CSF: ..... Macrophage-colony stimulating factor
MHC: ..... Major histocompatibility complex
MMPs: ..... Matrix metalloproteinases
mo-DCs: ..... Monocyte-derived dendritic cells
MOG: ..... Myelin oligodendrocyte glycoprotein
MPO: ..... Myeloperoxidase
MRI: ..... Magnetic resonance imaging
MS: ..... Multiple sclerosis
NA: ..... Not available

List of Abbreviations (Cont...)

Abbreviations	Full term
NAFLD:	Non-alcoholic fatty liver disease
NASH:	Non-alcoholic steatohepatitis
NE:	Neutrophil elastase
NEO:	Neopterin
NETs:	Neutrophil Extracellular Traps
NfL:	Neurofilament light polypeptide
NK:	Natural killer
NMSS:	National Multiple Sclerosis Society
NPV:	Negative predictive value
Nrf2:	Nuclear factor (erythroid-derived 2)-like 2
NS:	Non-significant
nTreg:	Natural T regulatory
nVDR:	Nuclear vitamin D receptor
OCBs:	Oligoclonal bands
OD:	Optical density
OPN:	Osteopontin
pDCs:	Plasmacytoid dendritic cells
PLP:	Proteolipid protein
PMA:	Phorbol 12-myristate13-acetate
PPMS:	Primary-progressive MS
PPV:	Positive predictive value
PRMS:	Progressive- relapsing MS
RA:	Rheumatoid arthritis
ROC:	Receiver operating characteristic curve
RORγt:	Retinoic acid related orphan receptor
ROS:	Reactive oxygen species
RRMS:	Relapsing-remitting MS
S:	Significant
s:	Soluble
SC:	Schwann cell

SC: ..... Subcutaneous

List of Abbreviations (Cont...)

Abbreviations	Full term

sCD14: ..... Soluble CD14
sCD163: ..... Soluble CD163
sCD206: ..... Soluble CD206
SD: ..... Standard deviation
SLE: ..... Systemic lupus erythematosus
SPMS: ..... Secondary-progressive MS
SPSS: ..... Statistical Package for Social Science
SRCR: ..... Scavenger receptor cysteine rich
TACE: ..... Tumor necrosis factor (TNF) converting enzyme
TCR: ..... T cell receptors
TGF-β: ..... Transforming growth factor beta
Th: ..... T helper
TMB: ..... Tetramethyl benzidine
TNF: ..... Tumor necrosis factor
Treg: ..... T regulatory
TWEAK: ..... Tumor necrosis factor (TNF)-like weak inducer of apoptosis
VCAM: ..... Vascular cell adhesion molecules
VLA-4: ..... Very late antigen 4

INTRODUCTION

Multiple sclerosis (MS) is considered as a chronic autoimmune-mediated demyelinating disease that affects the central nervous system (CNS) ***(Bjornevik et al., 2022)*** which is usually associated with different degrees of progressive disabilities ***(Mahad et al., 2015).*** Diagnosis of MS depends mainly on clinical picture, magnetic resonance imaging (MRI) findings and cerebrospinal fluid (CSF) oligoclonal bands (OCBs) ***(Lo Sasso et al., 2019).***

Microglia and macrophages are the dominant immune cell type that are involved in MS lesions as they interact with adaptive immune cells to initiate demyelination and play role in both destruction and repair ***(Kamma et al., 2022)***. Activated macrophages are derived from peripheral monocytes and secrete proinflammatory cytokines that mediate demyelination and axonal damage, on the other hand, activated resident microglia clear cellular debris and thus promote tissue recovery ***(Harris et al., 2017).***

Biomarkers of myeloid lineage, such as soluble cluster of differentiation 163 (sCD163) and soluble CD14 (sCD14), were found to be elevated in the CSF of MS patient ***(Komori et al., 2015).*** Soluble CD163 showed a better correlation with monocyte count in MS CSF, and previous studies have suggested that it may be a biomarker of macrophage activity ***(Harris et al., 2017).***