



Serum Sclerostin Level Among Egyptian Rheumatoid Arthritis Patients: Relation to Bone Mineral Density, Disease Activity and Radiological Grading

Thesis

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ABSTRACT

Background: Bone loss in rheumatoid arthritis (RA) is caused by increased bone resorption, however, there is no increased bone formation. The Wnt pathway is important in the control of bone formation through regulation of osteoblast activity. Sclerostin is an important regulator of the Wnt pathway by blocking Wnt binding to its receptor and thereby inhibiting bone formation.

Aim of the work: This work aimed to study serum sclerostin level in a group of Egyptian rheumatoid arthritis patients and to correlate its level with bone mineral density, disease activity and radiological grading.

Patients and methods: Forty patients (70% females and 30% males) diagnosed according to The 2010 American College of Rheumatology/ European League Against Rheumatism classification criteria for rheumatoid arthritis and 40 age and sex matched apparently healthy subjects were included. All patients were subjected to full history taking and clinical examination. Routine laboratory investigations and testing for serum sclerostin level were done. Plain radiographs of hands & feet and dual-energy x-ray absorptiometry test were done for all patients.

Results: No significant difference was found between RA patients & healthy controls as regard mean value of serum sclerostin level. Postmenopausal women had higher levels of serum sclerostin than premenopausal, however, it was statistically significant on comparing healthy postmenopausal to healthy premenopausal only. Serum sclerostin had significantly positive correlations with age of RA onset and weight of RA patients and negative correlation with ESR in RA patients, but has no correlation with BMD disease activity or radiographic grading.

Conclusion: Serum sclerostin level in RA patients did not differ significantly from healthy subjects. Serum sclerostin levels have no correlation to disease activity, radiographic joints damage or BMD in RA.

Key words: Bone mineral density - Rheumatoid arthritis - Sclerostin.

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LIST OF ABBREVIATIONS

ACPA	Anti- citrullinated peptide antibodies
ACR	American College of Rheumatology
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AP	Antero-posterior
APC	Adenomatous polyposis coli
APCDD1	adenomatosis polyposis coli down- regulated 1 protein
ASBMR	American Society for Bone and Mineral Research
AST	Aspartate aminotransferase
BMC	Bone mineral content
BMD	Bone mineral density
BMI	Body mass index
BMPs	bone morphogenetic proteins
BMU	Bone metabolic units
BSP	Bone sialoprotein
C3	Third component of complement
CBC	Complete blood count
CCP	Cyclic citrullinated peptides

CD	Cluster of differentiation
CFU-F	Colony forming unit-fibroblast
cm²	Centimeter square
COX	Cyclooxygenase
cPTH	Continous parathrmone
CRP	C-reactive protein
CT-1	Cardiotrophin 1
CT	Computed tomography
CTLA4	Cytotoxic T lymphocyte antigen 4
CyA	Cyclosporine A
DAN	Differential screening-selected gene aberrant in neuroblastoma
DAS 28	Disease Activity Score 28
DHEAS	dehydroepiandrosterone sulphate
Dkk1	dickkopf-1
dl	Deciliter
DM	Diabetes mellitus
DMARDs	Disease-modifying anti-rheumatic drugs
DPD	Deoxypyridinoline
Dsh	Disheveled
DXA	Dual-energy x-ray absorptiometry

DXR	Digital X-ray radiogrammetry
E2	Estradiol
ECM	Extracellular matrix
ELISA	Enzyme-linked immunosorbent assay
ESR	Erythrocyte sedimentation rate
ESRD	End-stage renal disease
FDA	Food and Drug Administration
FGF	fibroblast growth factor
Fig	Figure
FN	Femoral neck
Fn14	Fibroblast growth factor-inducible gene 14
FRAX	the fracture risk assessment tool
FZD	Frizzled
GCs	Glucocorticoids
GFRC	Garvan fracture risk calculator
GH	Growth hormone
GIO	Glucocorticoid-induced osteoporosis
GLA	Bone gama – carboxyglutamic acid
GM-CSF	Granulocyte-macrophage colony-stimulating activity
GnRH	Gonadotropin-releasing hormone

GSK 3	Glycogen synthase kinase 3
HB	Hemoglobin
HBM	High bone mass
HIV	human immunodeficiency virus
HLA	Human leukocyte antigen
HMG	high-mobility-group
HRDR	High-resolution digital radiology
HRP	Histidine-rich protein
HRqCT	high-resolution quantitative computer tomography
HSCs	hematopoietic stem cells
IFN-γ	interferon- γ
IGF	insulin-like growth factor
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IL	Interleukin
iPTH	intermittent parathrmone
IU	International Unit
IV	Intravenous
Kg	Kilogram
L	Liter

L1	Lumbar vertebra 1
L4	Lumbar vertebra 4
l	Liter
LDL	low-density lipoprotein
LEF	lymphoid-enhancer binding factor
LIF	leukemia inhibitory factor
LRP	receptor- related protein
LS	Lumbar spine
m²	Square meter
μl	Microliter
mm	Millimeter
mm³	Cubic millimeter
mg	Milligram
μCT	Micro-computed tomography
MCP	Metacarpo-phalangeal
M- CSF	Macrophage colony-stimulating factor
μg	Micrograms
MHAQ	Modified Health Assessment Questionnaire
MMP	Matrix metalloproteinase
MRI	Magnetic resonance imaging
MTP	Metatarso-phalangeal

MTX	Methotrexate
n	Number
NO	Number
ng	Nanogram
NOF	National Osteoporosis Foundation
NTX	N-telopeptidases of type 1 collagen
NSAIDs	Nonsteroidal anti-inflammatory drugs
OA	osteoarthritis
OC	Osteocalcin
OP	Osteoporosis
OPG	osteoprotegren
OPPG	Osteoporosis pseudoglioma
OSM	Oncostatin M
P	Probability value
PADI2	Peptidyl arginine deiminase type 2
PCD	Programmed cell death
PG	Prostaglandins
PIP	Proximal interphalangeal
PLT	Platelet
pmol	Pico-mole
PTH	Parathormone

QCT	Quantitative computer tomography
QUS	Quantitative ultrasound
r	Correlation coefficient
RA	Rheumatoid Arthritis
RANK	Receptor activator of nuclear factor κ -B
RANKL	Receptor activator of nuclear factor κ -B ligand
RANTES	Regulated upon Activation Normal T Cell Expressed and Secreted
RBCs	Red blood cells
REC	Research Ethics Committee
RF	Rheumatoid factor
rhPTH	Recombinant human parathyroid hormone
RNA	Ribonucleic acid
RP	Raynaud's Phenomenon
Runx2	Runt- related transcription factor 2
SC	Subcutaneous
Scl	Sclerostin
Scl-Ab	Sclerostin- antibody
SD	Standard deviation
SFRP	Secreted frizzled-related protein
SLE	Systemic Lupus erythematosus

SPSS	Statistical Package for the Social Science
TBV	Trabecular bone volume
TCFs	T cell-specific transcription factors
Th1	T helper type 1
Th-17	T helper type 17
TLC	Total Leucocytic count
TNF- α	Tumor necrosis factor - α
β-TrCP	β -transducin repeat-containing protein
T_{REG}	Regulatory T cells
TRAP	Tartrate-resistant acid phosphatase
TWEAK	Tumor necrosis factor -related weak inducer of apoptosis
U	Unit
Ub	Ubiquitin
ULN	Upper limit of normal
US	ultrasound
USA	United States of America
UV	ultraviolet
VF_s	Vertebral fractures
VFA	Vertebral fracture assessment
WBC	White blood cells

WHO	World Health Organization
WIF	Wnt inhibitory factor
Wnt	Wingless nt
1,25 (OH)₂D	1,25 dihydroxy vitamin D
11β-HSDs	11 β -hydroxysteroid dehydrogenases

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