

SERUM LEVEL OF BONE MORPHOGENIC PROTEIN-7 IN RHEUMATOID ARTHRITIS

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿يَرْفَعُ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ

وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ﴾

صدق الله العظيم

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To

*My
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List of Abbreviations

ACR:	American College of Rheumatology.
ALK-1:	Activin Like Kinase -1.
ALT:	Alanine Transaminase.
Anti-CCP:	Anti –Citruillinated Protein antibodies.
Anti RA-33:	A highly specific protein antibody for Rheumatoid Arthritis.
AP-1:	Activator Protein -1.
AS:	Ankylosing Spondylitis.
ASOT:	Anti-streptolysin titer.
AST:	Aspartate Amino-Transferase.
A-V block:	Arterio-ventricular block.
BAMBI:	Bone morphogenic protein and Active Membrane – Bound Inhibitor.
BMP:	Bone Morphogenic Protein.
BSA:	Bovine Serum Albumin.
C1-3:	Cervical vertebrae 1-3.
CD :	Cluster of Differentiation.
CDMPs :	Cartilage –Derived Morphogenic Proteins.
CIA:	Collagen Induced Arthritis.
COPD:	Chronic Obstructive Pulmonary Disease.
CO-Smad:	Common Smad.
CPT:	Corticosteroid pulse therapy.

CRP:	C-reactive protein.
DAN:	Differential screening –selected gene aberrative in neuroblastoma.
DAS:	Disease Activity Score.
DIP:	Distal Interphalangeal .
DMARDS:	Disease Modifying Anti-Rheumatic Drugs.
DM:	Diabetes Mellitus.
DNA:	Deoxy ribonucleic acid.
DVT:	Deep Venous Thrombosis.
EBNA:	Epstein-Barr Nuclear Antigen.
ELISA:	Enzyme Linked Immuno-Sorbent Assay.
ESR:	Erythrocyte Sedimentation Rate.
Fc:	Fc portion of immunoglobulin.
GC:	Glucocorticoid.
GDFs:	Growth Differentiation Factor.
GIT:	Gastro-Intestinal Tract.
IBM:	International Business Machine .
IBM-PC:	International Business Machine Personal Computer.
Ig:	Immunoglobulin.
IGF-1:	Insulin like Growth Factor -1.
INF:	Interferone.
ILD:	Interstitial Lung Disease.
IL-1RI:	Interleukin 1 receptor type 1.

<i>I-Smad:</i>	Inhibitory Smad.
<i>HA:</i>	Hyalouronic Acid.
<i>HAQ:</i>	Health Assessment Questionnaire.
<i>Hb:</i>	Hemoglobin.
<i>HLA-DR:</i>	D-related Human Leukocyte Antigen.
<i>hnRNP-A2:</i>	Hetrogenous nuclear Ribonucleoprotein complex.
<i>HTN:</i>	Hypertension.
<i>hTNFtg:</i>	Human Tumor Necrosis Factor Transgene (animal model for RA).
<i>KDa:</i>	Kilodalton.
<i>MCP:</i>	Metacarpo-phalangeal.
<i>MHAQ:</i>	Modified Health Assessment Questionnaire.
<i>MMP:</i>	Matrix Metalloproteinase Protein.
<i>MRI:</i>	Magnetic Resonance Imaging.
<i>MTP:</i>	Metatarso-phalngeal.
<i>MTX:</i>	Methotrexate.
<i>NF-KB:</i>	Nuclear Factor Kappa Beta.
<i>NSAIDs:</i>	Non-Steroidal Anti-Inflammatory Drugs.
<i>OA:</i>	Osteoarthritis.
<i>OP-1:</i>	Osteogenic Protein-1.
<i>PG:</i>	Prostaglandin.
<i>PIP:</i>	Proximal Interphalangeal.
<i>PLT:</i>	Platelet Count Test.

<i>P-Smad:</i>	Phosphorylated Smad.
<i>q</i> :	Quaque=Each,every
<i>RA:</i>	Rheumatoid Arthritis.
<i>RA33:</i>	Nuclear auto-antigen with an apparent molecular mass33.
<i>RF:</i>	Rheumatoid Factor.
<i>RNA:</i>	Ribonucleic Acid.
<i>ROM:</i>	Range of Motion.
<i>R-Smad:</i>	Receptor-Smad.
<i>SD:</i>	Standard Deviation.
<i>SEM:</i>	Standard Error of Mean.
<i>SLE:</i>	Systemic Lupus Erthematosus.
<i>SPSS:</i>	Statically Package for time Social Solution.
<i>STNFR-IG:</i>	Stand for soluble TNF receptor immunoglobulin.
<i>TB:</i>	Tuberculosis.
<i>TGF-β:</i>	Transforming Growth Factor beta.
<i>TLC:</i>	Total Leukocytic Count.
<i>TNF:</i>	Tumor Necrosis Factor.
<i>WBCs:</i>	White Blood Cells.

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Introduction

Bone morphogenic proteins (BMPs) are polypeptides discovered by ***Marshall Urist*** in 1965 and later defined by his co-workers as multifunctional cytokines involved in osteoinduction. They are members of the transforming growth factor- β (TGF- β) superfamily with the exception of the BMP-1. More than 20 BMPs have identified and studied , But only BMP-2,4, and 7 have been able in vitro to stimulate the entire process of stem cell differentiation into osteoblastic mature cells (***Boden et al., 2000***).

BMP-7 (osteogenic protein -1) is expressed by human adult articular chondrocytes and plays a crucial role in the maintenance of cartilage matrix integrity and the promotion of repair process (***Chubinskaya et al. , 2000 ; Soder et al., 2005***).

It has a potent anabolic effect on articular cartilage and other connective tissues .It stimulates the synthesis of major cartilage matrix components (***Chubinskaya and Kuettner , 2003***) ,promoting matrix assembly and serving as an antagonist to the deleterious effects of catabolic mediators (***Huch et al., 1997 ; Im et al., 2003***) without inducing chondrocyte hypertrophy and proliferation (***Flechtenmacher et al ., 1996 ; Chubinskaya et al ., 2002***).

BMP-7 gene expression and protein expression have been detected in all of the connective tissues of the joint, cartilage , meniscus, synovium , ligament and tendon (***Rueger and Chubinskaya , 2004***).

It was found that the level of BMP-7 in synovial fluid of Osteoarthritis (OA) and Rheumatoid arthritis (RA) patients is higher than normal asymptomatic donors (***Chubinskaya et al., 2006***).

Overproduction of BMP-2 and BMP-7 was also noted in serum of Ankylosing Spondylitis (AS) and RA patients, and serum BMP-7 level reflected radiographic damage observed in AS patients. However , previous data was unable to find significant correlation between BMP level and DAS28 and Larsen scores in RA patients (***Park et al., 2008***). Thus it is worth studying the level of BMP-7 in order to confirm or contradict the previous results.

Aim of The Work

The aim of the study is to estimate the level of BMP-7 in the serum of patients with RA in order to detect its possible correlation with disease activity or severity.