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**CLINICAL UTILITY OF SERUM SOLUBLE
CTLA-4 ASSAY IN BRONCHIAL
ASTHMA PATIENTS**

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَقُلْ رَبِّ
زِدْنِي عِلْمًا

صدق الله العظيم

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LIST OF ABBREVIATIONS

Abbrev.	Full term
3uTR	Three prime untranslated region
aa	Amino acid
AchR	Acetylcholine receptor
AHR	Airway hyper-responsiveness
AITD	Autoimmune thyroid disease
AP-1	Activator protein 1
APC	Antigen presenting cells
BTLA	B and T lymphocyte attenuator
CCR3	Chemokine receptor 3
CD4	Cluster of differentiation
CTLA-4	Cytotoxic T-lymphocyte associated antigen-4
DCs	Dendritic cells
EDTA	Ethylenediamine tetra-acetic acid
FDA	Food and Drug Administration
FITC	Fluorescein isothiocyanate
FWSC	Forward scatter
GD	Graves disease
GM-CSF	Granulocyte macrophage colony stimulating factor
HLA	Human leukocyte antigens
ICOs	Inducible co-stimulator
IgE	Immunoglobulin E
IL2R	Interleukin 2 receptor
IL-4	Interleukin 4
IL-5	Interleukin 5
IL7R	Interleukin 7 receptor
LABA	Long acting beta adrenoreceptor agonists
LTC4	Leukotriene C4
MCP-4	Monocyte chemotactic protein 4
MDIs	Metered dose inhaler
MG	Myasthenia gravis

LIST OF ABBREVIATIONS (Cont...)

Abbrev.	Full term
MHC	Major histocompatibility
MoAb	Monoclonal antibody
NAEPP	National Asthma education and prevention program
NK-k- β	Nuclear factor K- β
PBS	Phosphate buffer saline
PCR-RFLP	Polymerase chain reaction restriction fragment length polymorphism
PD1	Programmed death 1
PE-Cy7	Pheoerythrin-canin 7
PEF	Peak expiratory flow
Per CP	Peridinin chlorophyll
RAST	Radioallergosorbent test
RBM	Reticular basement membrane
RT	Reverse transcriptase
SABA	Short acting beta 2 adrenoreceptor agonists
SD/SA	Splice donor/splice acceptor
SLE	Systemic lupus erythematosus
SNP	Single nucleotide polymorphism
SSc	Systemic sclerosis
SSC	Side scatter
T1D	Type 1 diabetes
TCA	Tricyclic antidepressants
TCR	T-cell receptor
Th	T-helper
TNF- α	Tumor necrosis factor alpha
uRTIs	Upper respiratory tract infections
VCAM-1	Vascular cell adhesion molecule-1
VEGF	Vascular endothelial growth factor
VEV1	Forced expiratory volume in one second
WHO	World Health Organization

INTRODUCTION

Bronchial asthma is a chronic disease that has increased in prevalence over the past two decades (*Janson et al., 2001*). The disease is characterized by reversible airway obstruction, airway hyper-responsiveness, and airway inflammation (*LaRochelle et al., 2007*). It is usually manifested by recurrent episodes of wheezing, coughing and shortness of breath. The disease process is usually multifactorial and is associated with genetic, allergic, environmental, infectious and nutritional components (*Bhulani et al., 2011*).

Inflammation plays a pivotal role in the pathogenesis of bronchial asthma. The disease phenotypes are usually triggered by CD4+T lymphocytes generating the T helper 2- associated cytokines IL-4 & IL-5 (*Oh et al., 2010*). T cell activation requires the delivery of at least two signals to T cells by the antigen presenting cells. One signal is provided by the ligation of T- cell receptor by the complex of antigen and major histocompatibility complex, while the second co-stimulatory signal is generated by the interaction between CD28 on T cells and its ligands on the antigen presenting cells, B7.1 and B7.2 (*Sato et al., 2004 and Oh et al., 2010*).

Cytotoxic T lymphocyte associated antigen-4 (CTLA-4) is a member of the immunoglobulin gene superfamily. It is expressed on activated T cell and shares sequence homology with CD28 and therefore binds with higher affinity to B7.1 and

B7.2 molecules (*Chan et al., 2010*). CTLA-4 can engage inhibitory signal resulting in the down- regulation of T cell responses and induction of apoptosis and immunological anergy (*Botturi et al., 2011*).

Recent studies have revealed an alternative transcript of the CTLA-4 gene encoding a protein that lacks a transmembrane region and probably represents a native soluble form of CTLA-4 (*Ryden et al., 2012*). High levels of soluble CTLA-4 have been reported in some autoimmune diseases as systemic lupus erythematosus, myasthenia gravis and Sjogren's syndrome; this in turn pointed to the immunoregulatory functions of this molecule (*Wang et al., 2012*).

AIM OF THE WORK

The aim of the present study is to determine the level of serum soluble CTLA-4 in bronchial asthma patients and to assess the relationship between its level and the degree of the disease severity in a trial to clarify the diagnostic and prognostic value of this marker in bronchial asthma.