1.1 Introduction

Bronchial asthma is a common clinical condition characterized by airway inflammation, airway obstruction, and airway hyperresponsiveness to avariety of stimuli. About 300 million subjects are currently having asthma, with estimates suggesting that asthma prevalence is increasing worldwide. (Masoli *et al*,. 2004) The prevalence among Sudanese adults is approaching 10% in many areas of the Sudan. (Magzoub *et al*,. 2010)

In the recent studies, free oxygen radicals were accused for the pathogenesis of bronchial asthma. (Jarjour, Calhoun ,.1994) There are some defense mechanisms to escape from the effects of oxidant radicals. The most important antioxidant endogen systems are mitochondrial cytochrome oxidase, superoxide dismutase (SOD), catalase and glutathione peroxidase (GSH-Px) systems.Also albumin, seruloplasmin, ferritin and hemoglobin which are found in the extracellular space have antioxidant properties. (Halliwell B,.1994) Chromium induced the protein expression of Mn-superoxide dismutase,Cu/Zn-superoxide dismutase, catalase, glutathione peroxidase, and heme oxygenase-1 (HO-1).(J Biomed 2010) Chromium also significantly increased the activity of glutathione peroxidase (p<0.05). (J Clin Biochem Nutr *et al*,. 2008).Magnesium is directly involved in the mechanisms of cellular antioxidant defense by increasing the activity of important glutathione enzyme glutathione peroxidase (GPx). Decreasing of these trace elements causes the effects of antioxidant systems to be lower and this leads to hyperactivity and inflammation in the respiratory tract . (Pucheu *et al*,. 1995; Raeve,.1997) In this study, we aimed to define the relation between bronchial asthma and serum levels trace elements (Chromium and Magnesium).

1.2 Literature review

1.2.1 Bronchi

The bronchus(from Greek bronkhos "windpipe")is the part of the respiratory system that connects the trachea to the lung parenchyma. It is composed of an extensive branching system of airway passages that transmit the air from the atmosphere to the alveoli(the gas-exchange units).(Barrett *et al*,. 2009)

1.2.2 Anatomy

The bronchial tree begins when the trachea divides into the right and left mainstem bronchi at the level of the T5 vertebra. The right mainstem bronchus is shorter,wider,and more vertical than the left mainstem bronchus.The right and left mainstem bronchi divide first into lobar bronchi and subsequently into segmental(or tertiary)bronchi.Arteries,veins,and lymphatics also enter the lungs at the hilum along with the bronchi.Abronchopulmonary segment is a portion of lung that is supplied by a segmental bronchus and its adjacent blood vessels.The bronchial wall is made up of mucosa,lamina propria,smooth muscle,and submucosa with interspersed cartilage.The initial generations of the bronchi are similar to each other in their histologic structure,except for the amount of hyaline cartilage.In the trachea,the cartilage encircles the lumen,but in subsequent divisions of bronchi,it is replaced by diminishing quantities of cartilage plates.The bronchial mucosa is made of pseudostratified ciliated columnar epithelium with goblet cells and basal cells.The rhythmic movement of the cilia promotes the flow of the superficial liquid lining of the epithelium,along with mucin and other particulate material (eg, cells and debris)from within the lung to the pharynx. Goblet cells are devoid of apical cilia and have mucus granules in the cytoplasm

and are responsible for secretion of mucin.The density of goblet cells progressively decreases from the periphery and disappears at the level of terminal bronchioles.(West JB 2008) The bronchial submucosa contains mixed compound tubuloacinar glands,composed largely of mucin-secreting cells and some serous-secreting cells,that secrete mucin,water,and electrolytes into the bronchial lumen.Mucin is a complex glycoprotein that is responsible for trapping particulate material in the bronchi.(Adams *et al,*. 2010)

1.2.3.1 Bronchial Asthma

Is a chronic inflammatory disease characterized by hyper-responsiveness of airways to various stimuli.This complex disease affects patients of all ages.(Smith *et al,*. 2012)

1.2.3.2 Signs and Symptoms of Bronchial Asthma

One or more of the following signs and symptoms:

Shortness of breath,Tightness of chest,Wheezing,Excessive coughing or a cough that keeps you awake at night.(NHLBI/WHO 1995)

1.2.3.3 Causes and risk factors

Asthma comprises a range of heterogeneous phenotypes that differ in presentation,etiology and pathophysiology.The risk factors for each recognized phenotype of asthma include genetic,environmental and host factors.Although a family history of asthma is common,it is neither sufficient nor necessary for the development of asthma.(Sears *et al,*. 2003)

A. Genetics: Family and twin studies have indicated that genetics plays an important role in the development of asthma and allergy,likely through several genes of moderate effect(i.e.,genes associated with relative risks in the range of1.2–2). (Lawrence S *et al*,. 1994)

B.Prenatal risk factors

Risk factors in the prenatal period are multifactorial. Assessment is complicated by the variety of wheezing conditions that may occur in infancy and childhood, only some of which evolve to classical asthma.

B.1 Prenatal tobacco smoke

Prenatal maternal smoking has been consistently associated with early childhood wheezing, and there is a dose–response relation between exposure and decreased airway calibre in early life.Prenatal maternal smoking is also associated with increased risks of food allergy,cytokine responses in the cord blood and concentrations of nitric oxide in exhaled air in newborns.(Frey *et al*,. 2004)

B.2 Diet and nutrition

Several studies have demonstrated that higher intake of fish or fish oil during pregnancy is associated with lower risk of atopic disease(specifically eczema and atopic wheeze)up to age 6 years. Similarly,higher prenatal vitamin E and zinc levels have been associated with lower risk of development of wheeze up to age5years. (Willers *et al*,. 2007)

B.3 Stress Although there is a correlation between caregiver stress early in the infant's life and higher levels of immunoglobulin E in the infant and early

wheezing, no studies to date have shown an association with asthma.(Lin *et al*,. 2004)

B.4 Antibiotic use Longitudinal cohort studies examining any antibiotic use showed a greater risk of persistent wheeze and asthma in early childhood, and a dose–response relation between number of antibiotic courses and risk of wheeze or asthma.(Jedrychowski *et al*,. 2004)

B.5 Mode of delivery

Development of atopy was 2 to 3 times more likely among infants delivered by emergency cesarean section,although no such association occurred with elective cesarean section.(Kero *et al*,. 2002)

C. Risk factors in childhood

Phenotypes of asthma

Although some50%of preschool children have wheezing,only10%–15%have a diagnosis of"true"asthma by the time they reach school age. Commonly described phenotypes in early infancy and childhood are transient wheezing, non atopic wheezing,late-onset wheezing and persistent wheezing. Only transient wheezing in early infancy has been well characterized,with decreased airflow rates on pulmonary function testing at birth.The other 3 phenotypes have been described primarily by age of onset in cohort studies,and their genesis in early infancy is largely unknown.The majority of children with persistent wheezing(in whom asthma will subsequently be diagnosed)experience their first symptoms before age 3.By 3 years,they have abnormal lung function that persists to adulthood, and by adolescence,most have atopy.Of children with non atopic and late-onset

wheezing,some experience remission,whereas others experience persistent symptoms and atopy. (Lowe *et al,*. 2005)

C.1 Breastfeeding

Some studies have shown protection, whereas others have reported higher rates of allergy and asthma among breastfed children. A meta-analysis and several individual studies, showed that exclusive breastfeeding for at least 3 months was associated with lower rates of asthma between2and5years of age,with the greatest effect occurring among those with a parental history of atopy.One of the difficulties in interpreting these data lies in differentiating viral-associated wheeze in childhood from development of atopic asthma.In a longitudinal birth cohort study,breastfeeding was associated with a higher risk of atopic asthma in later childhood,with the greatest in fluence occurring among those with a maternal history of atopy. (Sears *et al,*. 2002)In some studies,exclusion of milk,eggs and fish from the maternal diet was associated with decreased atopic dermatitis in infancy, but other studies found no association. Studies following children to4years of age have demonstrated no effect of maternal dietary restriction during lactation on the subsequent development of atopic diseases,including asthma. (Muraro *et al,*. 2004)

C.2 Lung function

Decreased airway calibre in infancy has been reported as a risk factor for transient wheezing, perhaps related to prenatal and postnatal exposure to environmental tobacco smoke. Furthermore, the presence of airways with decreased calibre has been associated with increased bronchial responsiveness and increased symptoms of wheeze. Several studies have suggested an association between reduced airway

function in the first few weeks of life and asthma in later life. (Haland *et al*,. 2006)

Children with wheezing (and diagnosed asthma) persisting to adulthood have a fixed decrement in lung function as early as age7or 9 years. Recent studies of preschool children have documented abnormal lung function in children with persistent wheezing as young as age3years. However,some infants in whom persistent wheezing develops have normal lung function shortly after birth,which suggests a critical period of exposures within the first few years of life,before the development of these persistent abnormalities in expiratory flows. In contrast, infants who exhibit early transient wheezing have decreased airflow shortly after birth. Maternal smoking with in utero nicotine exposure has been correlated with this type of lung dysfunction, but the effects of other exposures have been less well studied . (Martinez *et al*,. 1995)

C.3 Family structure

The hygiene hypothesis posits that exposure of an infant to a substantial number of infections and many types of bacteria stimulates the developing immune system toward nonasthmatic phenotypes.

Although this theory has been supported by some studies of allergy prevalence, it has been partially refuted by recent studies of asthma prevalence suggesting that although large family size (more than 4 children) is associated with a decreased risk of asthma, birth order is not involved. Furthermore, doubt has been cast on simplistic renditions of this hypothesis, in that infections per se cannot explain some epidemiologic patterns (e.g., prevalence rates for allergy and asthma are high in some South American countries, where exposures to infection are higher than in

some countries with lower rates of asthma).In addition,not only allergic but also autoimmune and other chronic inflammatory diseases are increasing, a trend that is difficult to explain by the hygiene hypothesis alone, since allergic and autoimmune diseases are associated with competing immunologic phenotypes. (Matricardi *et al,*. 1995)

C.4 Socio-economic status

Children of parents with lower socio-economic status have greater morbidity from asthma, but findings with respect to the prevalence of asthma are mixed. Some studies have reported associations of lower socio-economic status with greater airway obstruction and symptoms but not with a diagnosis of asthma. Parental stress has also been prospectively associated with wheezing in infancy, and family difficulties have been linked to asthma. Children whose caregivers report high levels of stress and who have difficulties parenting are at greatest risk for asthma. (Klinnert *et al,*. 1995)

C.5 Antibiotics and infections

The use of antibiotics has been associated with early wheezing and asthma in several studies, One suggested mechanism for this association is immunologic stimulation through changes in the bowel flora,but Kummeling and associates found no coincident increase in eczema or atopy,despite increased wheezing rates,which would argue against this mechanism.Greater antibiotic use might also represent a surrogate marker for a higher numbers of infections(perhaps viral)in early life. (Kummeling *et al,*. 2007)

Viral infections of the lower respiratory tract affect early childhood wheezing. Whether lower respiratory tract infection promotes sensitization to aeroallergens

causing persistent asthma is controversial:childhood viral infections might be pathogenic in some children but protective in others. Infants of mothers with allergy or asthma have a relatively persistent maturational defect in Th1 cytokine synthesis in the first year of life,which may play a role in the development of persistent or severe viral infections. Severe viral infection of the lower respiratory tract in genetically susceptible infants who are already sensitized to inhalant allergens may lead to deviation toward Th2 responses promoting asthma.It is unclear whether these effects of lower respiratory tract infection are virus-specific(e.g.,respiratory syncytial virus,rhinovirus)or whether synergistic exposures to allergens can induce asthma even in individuals who are not genetically susceptible.Interactions of genes with environmental exposures(including allergens,air pollution,environmental tobacco smoke and diet) modulate the host response to infections. It remains controversial whether the occurrence or timing of childhood infection is pathogenic or protective for the development and long-term outcome of asthma and allergy and of nonallergic wheeze phenotypes.This controversy relates in part to small sample size,cross-sectional analysis,lack of precise case definition and incomplete microbial assessment in studies of this phenomenon. (Friedlander *et al*,. 2005)

Respiratory infections in early childhood are associated with early wheezing, but it is unclear whether infection alone has a role in the development of persistent asthma. Repeated lower respiratory tract infection may affect infants who are already at risk for asthma because of family history or atopy. Severe infection with certain viruses such as respiratory syncytial virus and rhinovirus may play a role in persistent wheezing,although other studies have suggested no effect. Considered as

a proxy for viral infections, daycare attendance is associated with greater incidence of early wheeze but lower incidence of persistent wheeze. (Martinez, Holt ,.1999)

C.6 Allergic sensitization Total serum immunoglobulin E level, a surrogate for allergen sensitivity, has been associated with the incidence of asthma. High levels of immunoglobulin E at birth were associated with greater incidence of both atopy and aeroallergen sensitivity but not necessarily asthma. However, sensitization to aeroallergens, particularly house dust mite, cat and cockroach allergens ,is well documented as being associated with asthma.

Immune responses in the developing infant and young child may affect the development of asthma .For example, impairment in interferon γ production at 3 months was associated with a greater risk of wheeze. Immaturity in neonatal immune responses may promote the persistence of the Th2 immune phenotype and development of atopy, but an association with persistent asthma is as yet unproven. More recent work has focused on the role of the innate immune system in handling and presentation of antigens and suggests that polymorphisms in Toll-like receptors may play a greater role than previously recognized in the development of the skewed immune responses associated with persistent asthma. (Sears *et al,*. 1991)

C.7 Exposure to environmental tobacco smoke

Postnatal exposure to environmental tobacco smoke, especially from maternal smoking, has been consistently associated with respiratory symptoms of wheezing. Exposure to environmental tobacco smoke also consistently worsens asthma symptoms and is a risk factor for severe asthma. (Stein *et al,*. 1991)

C.8 Exposure to animals

Although several studies have demonstrated a lower risk of development of atopy and asthma with exposure to farm animals in early life, the findings of studies of the influence of exposure to domestic cats and dogs have been inconsistent. (Simpson,Custovic *et al*,. 2005)

C.9 Gene-by-environment interactions

Epigenetic modification of DNA is believed to be responsible for the phenotypic differences that develop over time between monozygotic twins. It has been suggested that it is principally through epigenetic modification of DNA that lifestyle and chemical exposures affect susceptibility to diseases. (Qiu ,. 2006)

C.10 Sex and gender

Until age 13–14 years, the incidence and prevalence of asthma are greater among boys than among girls. Studies through puberty have shown a greater incidence of asthma among adolescent and young adult females and a greater proportion of males with remission of asthma. Before age12,boys have more severe asthma than girls, with higher rates of admission to hospital. In contrast, adult females have more severe asthma than males, with more hospital admissions, slower improvement, longer hospital stays and higher rates of readmission. Most authors have attributed these changes in prevalence and severity to events of puberty, although mechanisms for differences between the sexes have not been established. (Meurer *et al*,. 2000)

In childhood, airway hyperresponsiveness is more common and more severe among males; however, airway hyperresponsiveness increases in females during

adolescence, such that by adulthood it is both more common and more severe among adult women. Similar findings have been reported from studies of atopy, which is more common in males before age 13; during adolescence, the rate of new-onset atopy is higher among females, so that by young adulthood the prevalence of atopy is almost equal

In one study of adults,18%of women with asthma, but only2.3%of men with asthma, had normal results on common tests related to atopy(negative skin prick tests, immunoglobulin E< 100 IU / mL and eosinophilia < 5%),which suggested different disease mechanisms between the sexes. Interactions have been found between maternal and paternal history of atopy, breastfeeding and sex of the child in terms of the risk of asthma and atopy.(Sears *et al*,. 1993)

D. Adult-onset asthma

Asthma in adults may have persisted from childhood, may have occurred as a relapse of earlier childhood asthma(whether or not recalled by the individual)or may be true adult-onset asthma with no symptoms in earlier life. New-onset asthma in adulthood may have environmental(especially occupational)causes with or without allergen sensitization. Although adult asthma may develop in relation to specific drug treatments(e.g., β-blockers, nonsteroidal anti-inflammatory drugs)or, in women, the use of hormone replacement therapy, occupational exposure to sensitizing agents or irritants is more common. (Eagan *et al*,. 2000)

D.1 Occupational asthma: Asthma related to workplace exposures has been documented in many occupational settings .Commonly associated occupations and exposures include car painting (isocyanates) ,hairdressing (various chemicals),domestic and commercial cleaning(cleaning solutions),health care

professions(latex)and baking(flour dust),among many others. The relation between exposure to substances in the work-place and new-onset adult asthma was explored among participants with no previously reported asthma symptoms in phase I of the European Community Respiratory Health Study. (Kogevinas *et al*,. 2007)

D.2 Other risk factors for adult asthma

Smoking tobacco or marijuana may give rise to symptoms suggesting asthma, although symptoms of cough and sputum production, suggesting chronic bronchitis, are more common .As in childhood, the differential diagnosis should include other forms of airway inflammation and other causes of intermittent dyspnea and wheezing, such as cardiac failure. However, new-onset asthma can occur at any age, without prior illness or concomitant disease. Atopy as a risk factor for asthma is less common with increasing age, but occasionally it is the dominant trigger. Air pollution may affect adult asthma, but more often it is a factor worsening pre-existing asthma rather than a cause of incident asthma. (McCreanor *et al*,. 2007)

1.2.3.4 Complications

- Symptoms that interfere with sleep, work or recreational activities
- Sick days from work or school during asthma flare-ups
- Permanent narrowing of the bronchial tubes (airway remodeling) that affects how well you can breathe
- Emergency room visits and hospitalizations for severe asthma attacks.

- Side effects from long-term use of some medications used to stabilize severe asthma.Proper treatment makes a big difference in preventing both short-term and long-term complications caused by asthma. (Christine,. 2007)

1.2.3.5 Pathophysiology

The pathophysiology of asthma is complex and involves the following component

A. Airway inflammation

The mechanism of inflammation in asthma may be acute, sub acute, or chronic, and the presence of airway edema and mucus secretion also contributes to airflow obstruction and bronchial reactivity. Varying degrees of mononuclear cell and eosinophil infiltration, mucus hypersecretion, desquamation of the epithelium, smooth muscle hyperplasia, and airway remodeling are present.– Some of the principal cells identified in airway inflammation include mast cells, eosinophils, epithelial cells, macrophages, and activated T lymphocytes. T lymphocytes play an important role in the regulation of airway inflammation through the release of numerous cytokines. Other constituent airway cells, such as fibroblasts, endothelial cells, and epithelial cells, contribute to the chronicity of the disease. Other factors, such as adhesion molecules (eg, selectins, integrins), are critical in directing the inflammatory changes in the airway. Finally, cell-derived mediators influence smooth muscle tone and produce structural changes and remodeling of the airway. (Busse *et al*,. 1993)

The presence of airway hyperresponsiveness or bronchial hyperreactivity in asthma is an exaggerated response to numerous exogenous and endogenous stimuli. The mechanisms involved include direct stimulation of airway smooth muscle and indirect stimulation by pharmacologically active substances from mediator-

secreting cells such as mast cells or nonmyelinated sensory neurons. The degree of airway hyperresponsiveness generally correlates with the clinical severity of asthma.

A study by Balzar et al reported changes in airway resident mast cell populations from a large group of subjects with asthma and normal control subjects. A greater proportion of chymase-positive mast cells in the airways and increased prostaglandin D2 levels were identified as important predictors of severe asthma as compared with other steroid-treated subjects with asthma.

Chronic inflammation of the airways is associated with increased bronchial hyperresponsiveness, which leads to bronchospasm and typical symptoms of wheezing, shortness of breath, and coughing after exposure to allergens, environmental irritants, viruses, cold air, or exercise. In some patients with chronic asthma, airflow limitation may be only partially reversible because of airway remodeling (hypertrophy and hyperplasia of smooth muscle, angiogenesis, and sub epithelial fibrosis) that occurs with chronic untreated disease.

Airway inflammation in asthma may represent a loss of normal balance between two "opposing" populations of Th lymphocytes. Two types of Th lymphocytes have been characterized: Th1 and Th2. Th1 cells produce interleukin (IL)-2 and IFN-α, which are critical in cellular defense mechanisms in response to infection. Th2, in contrast, generates a family of cytokines (IL-4, IL-5, IL-6, IL-9, and IL-13) that can mediate allergic inflammation. A study by Gauvreau et al found that IL-13 has a role in allergen-induced airway responses. (Gauvreau et al ,. 2011)

The current "hygiene hypothesis" of asthma illustrates how this cytokine imbalance may explain some of the dramatic increases in asthma prevalence in westernized

countries. This hypothesis is based on the concept that the immune system of the newborn is skewed toward Th2 cytokine generation (mediators of allergic inflammation). Following birth, environmental stimuli such as infections activate Th1 responses and bring the Th1/Th2 relationship to an appropriate balance. (Anderson, Watson 2001)

B. Airflow obstruction

Airflow obstruction can be caused by a variety of changes, including acute bronchoconstriction, airway edema, chronic mucous plug formation, and airway remodeling. Acute bronchoconstriction is the consequence of immunoglobulin E-dependent mediator release upon exposure to aeroallergens and is the primary component of the early asthmatic response. Airway edema occurs 6-24 hours following an allergen challenge and is referred to as the late asthmatic response. Chronic mucous plug formation consists of an exudate of serum proteins and cell debris that may take weeks to resolve. Airway remodeling is associated with structural changes due to long-standing inflammation and may profoundly affect the extent of reversibility of airway obstruction. Airway obstruction causes increased resistance to airflow and decreased expiratory flow rates. These changes lead to a decreased ability to expel air and may result in hyperinflation. The resulting overdistention helps maintain airway patency, thereby improving expiratory flow; however, it also alters pulmonary mechanics and increases the work of breathing. (Sears MR 2000)

C. Bronchial hyperresponsiveness

Hyperinflation compensates for the airflow obstruction, but this compensation is limited when the tidal volume approaches the volume of the pulmonary dead

space; the result is alveolar hypoventilation. Uneven changes in airflow resistance, the resulting uneven distribution of air, and alterations in circulation from increased intra-alveolar pressure due to hyperinflation all lead to ventilation-perfusion mismatch. Vasoconstriction due to alveolar hypoxia also contributes to this mismatch. Vasoconstriction is also considered an adaptive response to ventilation/perfusion mismatch.In the early stages, when ventilation-perfusion mismatch results in hypoxia, hypercarbia is prevented by the ready diffusion of carbon dioxide across alveolar capillary membranes. Thus, patients with asthma who are in the early stages of an acute episode have hypoxemia in the absence of carbon dioxide retention. Hyperventilation triggered by the hypoxic drive also causes a decrease in $PaCO_2$. An increase in alveolar ventilation in the early stages of an acute exacerbation prevents hypercarbia. With worsening obstruction and increasing ventilation-perfusion mismatch, carbon dioxide retention occurs. In the early stages of an acute episode, respiratory alkalosis results from hyperventilation. Later, the increased work of breathing, increased oxygen consumption, and increased cardiac output result in metabolic acidosis. Respiratory failure leads to respiratory acidosis. (Bousquet *et al*,. 2000)

1.2.3.6 Diagnosis of Bronchial Asthma

A. Physical examination

To rule out other possible conditions — such as a respiratory infection or chronic obstructive pulmonary disease (COPD) — your doctor will do a physical exam and ask you questions about your signs and symptoms and about any other health problems.

B. Tests to measure lung function

- Spirometry : This test estimates the narrowing of your bronchial tubes by checking how much air you can exhale after a deep breath and how fast you can breathe out.

- Peak flow: A peak flow meter is a simple device that measures how hard you can breathe out. Lower than usual peak flow readings are a sign your lungs may not be working as well and that your asthma may be getting worse. Your doctor will give you instructions on how to track and deal with low peak flow readings.

Lung function tests often are done before and after taking a bronchodilator (brong-koh-DIE-lay-tur),such as albuterol, to open your airways .If your lung function improves with use of a bronchodilator ,it's likely you have asthma.

C. Additional tests of Bronchial Asthma

Other tests to diagnose asthma include:

- Methacholine challenge**:** Methacholine is a known asthma trigger that, when inhaled, will cause mild constriction of your airways. If you react to the methacholine, you likely have asthma. This test may be used even if your initial lung function test is normal.

- Nitric oxide test**:** This test, though not widely available, measures the amount of the gas, nitric oxide, that you have in your breath. When your airways are inflamed — a sign of asthma — you may have higher than normal nitric oxide levels.

- Imaging tests: A chest X-ray and high-resolution computerized tomography (CT) scan of your lungs and nose cavities (sinuses) can identify any structural abnormalities or diseases (such as infection) that can cause or aggravate breathing problems.

- Allergy testing: This can be performed by skin test or blood test. Allergy tests can identify allergy to pets, dust, mold and pollen. If important allergy triggers are identified, this can lead to a recommendation for allergen immunotherapy.

- Sputum eosinophils: This test looks for certain white blood cells (eosinophils) in the mixture of saliva and mucus (sputum) you discharge during coughing. Eosinophils are present when symptoms develop and become visible when stained with a rose-colored dye(eosin).

- Provocative testing for exercise and cold-induced asthma **:**In these tests, your doctor measures your airway obstruction before and after you perform vigorous physical activity or take several breaths of cold air.

1.2.3.7 Asthma classification

- Mild intermittent **:**Mild symptoms up to two days a week and up to two nights a month.

- Mild persistent :Symptoms more than twice a week, but no more than once in a single day.

- Moderate persistent: Symptoms once a day and more than one night a week.

- Severe persistent: Symptoms throughout the day on most days and frequently at night.(NHLBI 2007)

1.2.3.8 Medication Summary

Asthma medications are generally divided into 2 categories:

- Quick relief (also called reliever medications)
- Long-term control(also called controller medications)

A. Quick relief

Quick relief medications are used to relieve acute asthma exacerbations and to prevent exercise-induced asthma (EIA) or exercise-induced bronchospasm (EIB) symptoms.These medications include short-acting beta agonists(SABAs), anticholinergics(used only for severe exacerbations),and systemic corticosteroids ,which speed recovery from acute exacerbations.(Dhuper *et al*,. 2011)

B. Long-term control

Long-term control medications include inhaled corticosteroids(ICSs), cromolyn sodium, nedocromil,long-acting beta agonists(LABAs),combination inhaled corticosteroids and long-acting beta agonists ,methylxanthines,and leukotriene antagonists.Inhaled corticosteroids are considered the primary drug of choice for control of chronic asthma ,but unfortunately the response to this treatment is characterized by wide variability among patients .A study by Tantisira et al showed the glucocorticoid-induced transcript1gene(*GLCCI1*)to be the cause of this decrease in response.(Guilbert *et al*,. 2006)

1.2.4 Trace elements

The term trace element was originallv used to describe the - residual amount of inorganic analyte quantitatively determined in a sample. More sensitive analytical methods now provide more accurate determination of most inorganic micronutrients present at very low concentrations in body fluids and tissue. Those present in body fluids (pg/dL) and in tissue (mglkg) are, however, still widely referred to as "trace elements" and those found at ng1dL or pg/kg as the "ultra trace elements." The corresponding dietary requirements are quoted in mglday or pglday, respectively. An element is considered essential when the signs and symptoms induced by a deficient diet are uniquely reversed by an adequate supply of the particular trace element. (Burtis *et al*,. 2008)

1.2.4.1 Chromium

Chromium (Cr),from the Greek word chroma (“color”),makes rubies red and emeralds green.Chromium is used in the manufacture of stainless steel.Chromium exists in two main valency states:trivalent and hexavalent.Chromium(VI)is better absorbed and more toxic than chromium(III)and has also been listed as a carcinogen implicated in lung cancer. Occupational exposure to chromium occurs in wood treatment, stainless steel welding, chrome plating, the leather tanning industry, and the use of lead chromate or strontium chromate paints. (Bishop *et al*,. 2010)

A. Dietary sources:

Chromium is widely distributed in the food supply, but most foods provide only small amounts (less than 2 micrograms [mcg] per serving). Meat and whole-grain products, as well as some fruits, vegetables, and spices are relatively good sources .

In contrast, foods high in simple sugars (like sucrose and fructose) are low in chromium .(Anderson *et al*,. 1992)

B. Health Effects: Cr(III),an essential dietary element, plays a role in maintaining normal metabolism of glucose, fat, and cholesterol. Chromium nutritional role has not been thoroughly explained. The estimated safe and adequate daily intake of chromium for adults is in the range of50–200g/day, although data are insufficient to establish are commended daily allowance. (Milne 1996)

C. Absorption, Transport, and Excretion of Chromium

Cr(VI)compounds, which are powerful oxidizing agents and thus tend to be irritating and corrosive, appear to be much more toxic systemically than Cr(III)compounds, given similar amounts and solubilities. Although mechanisms of biological interaction are uncertain, this variation in toxicity may be related to the ease with which Cr(VI)can pass through cell membranes and its subsequent intracellular reduction to reactive intermediates .Once absorbed ,chromium in the blood is bound to transferrin. Studies have shown that transferrin has two binding sites :A and B. Chromium binds exclusively to the B site. Both transferrin and albumin are involved in chromium absorption and transport.Transferrin binds the newly absorbed chromium, while albumin acts as an acceptor and transporter of chromium, if the transferrin sites are saturated. Other plasma proteins, including -and-globulins and lipoproteins, bind chromium. Research indicates that when transferrin is saturated with iron ,chromium is not efficiently bound to plasma protein. (Sargent *et al*,. 1979)

D. Deficiency

Dietary chromium deficiency is reactively uncommon; most cases occur in persons with special problems such as total parenteral nutrition ,diabetes, or malnutrition. Chromium deficiency is characterized by glucose intolerance, glycosuria, hypercholesterolemia, decreased longevity, decreased sperm counts, and impaired fertility.

E. Toxicity

Severe dermatitis and skin ulcers can result from contact with Cr(VI)salts .Up to20%of chromium workers develop contact dermatitis .Allergic dermatitis with eczema has been reported in printers, cement workers, metal workers, painters, and leather tanners. Data suggest that a Cr(III)protein complex is responsible for the allergic reaction. When inhaled, Cr(VI)is a respiratory tract irritant, resulting in airway irritation, airway obstruction, and possibly lung cancer .The target organ of inhaled chromium is the lung; the kidneys, liver, skin, and immune system may also be affected .Low-dose ,chronic chromium exposure typically results only in transient renal effects .Elevated urinary 2-microglobulin levels(an indicator of renal tubular damage)have been found in chrome platers ,and higher levels have generally been observed in younger persons exposed to higher Cr(VI)concentrations. (Milne 1996)

F. Reference Intervals for Chromium

Chromium in whole blood: 0.7–28.0 _g/L

Chromium in serum: _0.05–0.5 _g/L

Chromium in urine: 0.1–2.0 _g/24 hr (Painter *et al*,. 1996)

1.2.4.2 Magnesium

Is a chemical element with symbol Mg and atomic number 12 .It is a shiny gray solid which bears a close physical resemblance to the other five elements in the second column(Group2,or alkaline earth metals)of the periodic table: they each have the same electron configuration in their outer electron shell producing a similar crystal structure. (Housecroft and Sharpe,. 2008)

A. Dietary sources:

The common nutritional sources of magnesium are green leafy vegetables, legumes, nuts, and animal protein. (Whang *et al*,. 1994)

B. Magnesium Physiology

Magnesium (Mg2) is the fourth most abundant cation in the body and second most abundant intracellular ion. The average human body(70 kg)contains1mole(24 g)of Mg2.Approximately53%of Mg2 in the body is found in bone,46% in muscle and other organs and soft tissue, and less than1%is present in serum and red blood cells. Of the Mg2 present in serum, about one third is bound to protein, primarily albumin. Of the remaining two thirds,61%exists in the free or ionized state and about5%is complexed with other ions, such asPO4 and citrate. Similar to Ca2,it is the free ion that is physiologically active in the body. The role of Mg2 in the body is widespread. It is an essential cofactor of more than 300 enzymes, including those important in glycolysis,transcellular ion transport, neuromuscular transmission, synthesis of carbohydrates, proteins, lipids, and nucleic acids, and release of and response to certain hormones. The clinical usefulness of serum Mg2 levels has greatly increased in the past 10 years as more information about the analyte has been discovered. The most significant findings are the relationship between

abnormal serum Mg2 levels and cardiovascular, metabolic, and neuromuscular disorders. Although serum levels may not reflect total body stores of Mg2,serum levels are useful in determining acute changes in the ion. (Polancic 1991)

C. Absorption ,Transport ,and Excretion of Magnesium

Rich sources of Mg2_ in the diet include raw nuts, dry cereal,and“hard”drinking water; other sources include vegetables, meats, fish, and fruit. Processed foods, an ever-increasing part of the average U.S. diet, have low levels of Mg2 that may cause an inadequate intake. This in turn may increase the likelihood of Mg2 deficiency. The small intestine may absorb 20%–65% of the dietaryMg2,depending on the need and intake. The overall regulation of body Mg2 is controlled largely by the kidney, which can reabsorb Mg2 in deficiency states or readily excrete excess Mg2 in overload states. Of the non protein-bound Mg2 that gets filtered by the glomerulus,25%–30%is reabsorbed by the proximal convoluted tubule(PCT),unlike Na, in which60%–75%is absorbed in the PCT. Henle’s loop is the major renal regulatory site,where50%–60%of filtered Mg2 is reabsorbed in the ascending limb. In addition,2%–5% is reabsorbed in the distal convoluted tubule. The renal threshold for Mg2 is approximately0.60–0.85mmol/L(1.46–2.07mg/dL).Because this is close to normal serum concentration, slight excesses of Mg2 in serum are rapidly excreted by the kidneys. Normally, only about6%of filtered Mg2 is excreted in the urine per day. Mg2 regulation appears to be related to that of Ca2and Na. Parathyroid hormone(PTH)increases the renal reabsorption of Mg2 and enhances the absorption of Mg2 in the intestine.However,changes in ionized Ca2_have a far greater effect on PTH secretion.Aldosterone and thyroxine

apparently have the opposite effect of PTH in the kidney, increasing the renal excretion of Mg2. Normal range: 0.7–1 mmol/L (1.5–2 mEq/L;1.7–2.4 mg/dL). (Bringhurst *et al*,. 2012)

D. Hypomagnesemia

Hypomagnesemia is most frequently observed in hospitalized individuals in intensive care units or those receiving diuretic therapy or digitalis therapy. These patients most likely have an overall tissue depletion of Mg2 as a result of severe illness or loss, which leads to low serum levels. Hypomagnesemia is rare in non hospitalized individuals. There are many causes of hypomagnesemia;however,it can be grouped into general categories. Reduced intake is least likely to cause severe deficiencies in the United States. An Mg2-deficient diet as a result of starvation, chronic alcoholism, or Mg2deficient IV therapy can cause a loss of the ion. Various GI disorders may cause decreased absorption by the intestine, which can result in an excess loss of Mg2 via the feces. Malabsorption syndromes; intestinal resection or bypass surgery; nasogastric suction; pancreatitis; and prolonged vomiting, diarrhea, or laxative use may lead to an Mg2 deficiency. Neonatal hypomagnesemia has been reported as a result of various surgical procedures. A primary deficiency has also been reported in infants as a result of a selective malabsorption of the ion. A chronic congenital hypomagnesemia with secondary hypocalcemia(autosomal recessive disorder)has also been reported; molecular studies have revealed a specific transport protein defect in the intestine. (Schlingman *et al*,. 2002)

Mg2 loss due to increased excretion by way of the urine can occur as a result of various renal and endocrine disorders or the effects of certain drugs on the kidneys. Renal tubular disorders and other select renal disorders may result in excess amounts of Mg2 being lost through the urine because of decreased tubular reabsorption. Several endocrine disorders can cause a loss of Mg2.Hyperparathyroidism and hypercalcemia may cause increased renal excretion of Mg2 as a result of excessCa2 ions. Excess serum Na levels caused by hyperaldosteronism may also cause increased renal excretion of Mg2.A pseudohypomagnesemia may also be the result of hyperaldosteronism caused by increased water reabsorption. Hyperthyroidism may result in an increased renal excretion of Mg2 and may also cause an intracellular shift of the ion. In persons with diabetes, excess urinary loss of Mg2 is associated with glycosuria. Hypomagnesemia can aggravate the neuromuscular and vascular complications commonly found in this disease. Some studies have shown a relationship between Mg2 deficiency and insulin resistance;however,Mg2 is not thought to play a role in the pathophysiology of diabetes mellitus. The American Diabetes Association has issued a statement regarding dietary intake of Mg2 and measurement of serum Mg2 in patients with diabetes.Several drugs, including diuretics,gentamicin,cisplatin,and cyclosporine,increase renal loss of Mg2 and frequently result in hypomagnesemia. The loop diuretics, such as furosemide, are especially effective in increasing renal loss of Mg2.Thiazide diuretics require alonger period of use to cause hypomagnesemia.Cisplatin has a nephrotoxic effect that inhibits the ability of the renal tubule to conserve Mg2.Cyclosporine,an immunosuppressant,severely inhibits the renal tubular reabsorption of Mg2 and has many adverse effects, including nephrotoxicity,hypertension,hepatotoxicity,and neurologic symptoms such as seizures and tremors.Cardiac glycosides ,such as

digoxin and digitalis, can interfere with Mg2 reabsorption. The resulting hypomagnesemia is a significant finding because the decreased level of Mg2 can amplify the symptoms of digitalis toxicity. Excess lactation has been associated with hypomagnesemia as a result of increased use and loss through milk production. Mild deficiencies have been reported in pregnancy, which may cause a hyperexcitable uterus, anxiety, and insomnia. (Polancic 1991)

E. Symptoms of hypomagnesemia Apatient who is hypomagnesemic may be asymptomatic until serum levels fall below0.5mmol/L. A variety of symptoms can occur.The most frequent involve cardiovascular,neuromuscular,psychiatric,and metabolic abnormalities.The cardiovascular and neuromuscular symptoms result primarily from the ATPase enzyme's requirement for Mg2.Mg2 loss leads to decreased intracellular K levels because of a faulty Na-K pump (ATPase).This change in cellular RMP causes increased excitability that may lead to cardiac arrhythmias.This condition may also lead to digitalis toxicity.Muscle contraction also requires Mg2and ATPase for normal Ca2uptake following contraction.Normal nerve and muscle cell stimulation requires Mg2 to assist with the regulation of acetylcholine,apotent neurotransmitter.Hypomagnesemia can cause a variety of symptoms from weakness to tremors,tetany,paralysis,or coma.The CNS can also be affected,resulting in psychiatric disorders that range from subtle changes to depression or psychosis.Metabolic disorders are associated with hypomagnesemia.Studies have indicated that approximately 40% of hospitalized patients with hypokalemia are also hypomagnesemic. In addition,20%–30%of patients with hyponatremia,hypocalcemia,or hypophosphatemia are also hypomagnesemic. Mg2 deficiency can impair PTH release and target tissue response,resulting in hypocalcemia.Replenishing any of these deficient ions

alone,often does not remedy the disorder unless Mg2 therapy is provided.Mg2therapy alone may restore both ion levels to normal;serum levels of the ions must be monitored during treatment.

F. Hypermagnesemia

Hypermagnesemia is observed less frequently than hypomagnesemia. (Polancic JE 1991) Causes for elevated serum Mg2 levels the most common is renal failure(GFR,_30 mL/min).The most severe elevations are usually a result of the combined effects of decreased renal function and increased intake of commonly prescribed Mg2-containing medications,such as antacids,enemas,or cathartics.Nursing home patients are at greatest risk for this occurrence.Hypermagnesemia has been associated with several endocrine disorders.Thyroxine and growth hormone cause a decrease in tubular reabsorption of Mg2,and a deficiency of either hormone may cause a moderate elevation in serum Mg2.Adrenal insufficiency may cause a mild elevation as a result of decreased renal excretion of Mg2.MgSO4 may be used therapeutically with preeclampsia,cardiac arrhythmia,or myocardial infarction.Mg2_is a vasodilator,and can decrease uterine hyperactivity ineclampsic states and increase uterine blood flow.This therapy can lead to maternal hypermagnesemia,as well as neonatal hypermagnesemia due to the immature kidney of the newborn.Premature infants are at greater risk to develop actual symptoms. Studies have shown that IV Mg2_therapy in myocardial infarction patients may reduce early mortality. Dehydration can cause a pseudohypermagnesemia,which can be corrected with rehydration.Because of increased bone loss,mild serum Mg2_ elevations can occur in individuals with multiple myeloma or bone metastases. (Elin RJ 1994)

G. Symptoms of hypermagnesaemia

Symptoms of hypermagnesemia typically do not occur until the serum level exceeds 1.5mmol/L. The most frequent symptoms involve cardiovascular, dermatologic, GI ,neurologic, neuromuscular, metabolic, and hemostatic abnormalities .

Mild to moderate symptoms ,such as hypotension ,bradycardia ,skin flushing, increased skin temperature ,nausea ,vomiting ,and lethargy may occur when serum levels are 1.5–2.5mmol/L. Life-threatening symptoms ,such as electrocardiogram changes ,heart block, asystole, sedation ,coma, respiratory depression or arrest, and paralysis, can occur when serum levels reach5.0 mmol/L. Elevated Mg2_ levels may inhibit PTH release and target tissue response. This may lead to hypocalcemia and hypercalcuria. Normal hemostasis is a Ca2_-dependent process that may be inhibited as a result of competition between increased levels of Mg2_ and Ca2_ ions.Thrombin generation and platelet adhesion are two processes in which interference may occur. (Polancic 1991)

1.2.5 Trace elements and bronchial asthma:

Trace elements are essential micronutrients that exist in very low concentrations in the body, forming 0.01% of the total body weight.(Laker M 1982)They play an important role in various physiological processes,and are crucial for proper functioning of the immune system.Deficiency of trace elements and infectious diseases are often concomitantly observed and result in complex interactions.The major trace elements have imunomodulatory effects and thus influence susceptibility and the course of a variety of infections.This is mainly due to the fact that these elements are part of the structure of antioxidant enzymes.These enzymes

act as antioxidant defense and are able to regulate the host immune system,and alter viral enome.(Lukac, Massanji 2007)

Chromium induced the protein expression of Mn-superoxide dismutase,Cu/Zn-superoxide dismutase, catalase, glutathione peroxidase, and heme oxygenase-1 (HO-1).(J Biomed 2010) Chromium also significantly increased the activity of glutathione peroxidase (p<0.05). (J Clin Biochem Nutr *et al*., 2008).Magnesium is directly involved in the mechanisms of cellular antioxidant defense by increasing the activity of important glutathione enzyme glutathione peroxidase (GPx).This enzyme speeds up the reaction between glutathione and free radicals, particularly toxic hydrogen peroxide.Magnesium also increased the activity of other important antioxidants – superoxide dismutase (SOD) and catalase. (Yavuz, Mollaoglu ; 2013)

There is increasing evidence that reactive oxygen species can be of particular importance in the pathophysiology of several lung diseases.Changes in the level of these trace elements decrease the efficiency of antioxidant systems and this leads to hyper-reactivity and inflammation in the respiratory tract. (Pucheu *et al*,. 1995)

1.3 Rationale:

Trace elements play an important role in various physiological processes, and are crucial for proper functioning of the immune system.Chromium and Magnesium have a major value in the antioxidant mechanisms which protect the respiratory tract against reactive oxygen species can be of particular importance in causes of hyper-reactivity and inflammation of bronchi.

Studies have been established on this topic in the western countries of world (Ermis *et al*,.2004; Vural ,2000; Picado *et al*,. 2001),few published studies were found regarding the level of trace elements among Sudanese with bronchial asthma. (Hussein, Yousif and Saeed,. 2008)

In view these facts it is important to determine the levels of trace elements(Chromium and Magnesium) in patient of bronchial asthma ;to clarify their status.

1.4 Objectives:

1.4.1 General objective

To Assess levels of serum chromium and magnesium among sudanese with bronchial asthma.

1.4.2 Specific objectives:

- To compare serum chromium and magnesium levels between case and control group.
- To correlate between serum chromium and magnesium levels and BMI, age and duration of the disease.

2.1. Materials

2.1.1 Study design:

This is acase-control study to determine chromium and magnesium levels in bronchial asthmatic patients.

2.1.2 Study area:

Blood sample were collected from Alshaab Teaching Hospital, asthma room patient, in Khartoum state.

2.1.3 Sample size:

A total of 100 samples were collected to perform this study (50 samples collected from diagnosed bronchial asthmatic patients as case group, and 50 samples collected from normal individuals as control group).

2.1.4 Study duration:

The study took time from 18 may to 18 June 2015

2.1.5 Sample type:

Serum blood samples were used in this study.

2.1.6 Sample collection:

5 ml of venous blood was drawn from each volunteer in this study using a disposable plastic syringe. The blood is poured in a plain container and then centrifuged after clotted. The Serum is kept at -20°C in sterile condition till estimation.

2.1.7 Study population:

In this study, bronchial asthmatic patients was tested for trace elements (chromium, and magnesium)

2.1.8 Exclusion criteria:

We excluded patients have diabetes mellitus and also hypertensive patients

2.1.9 Inclusion criteria:

We included patients with bronchial asthma

2.1.10 Ethical consideration:

The objectives of the study were explained to all individuals Participating in this study. All participants who agreed were included as volunteer.

2.2 Methods

2.2.1 chromium measurement:

The estimation of serum chromium were performed in environment and natural resources and desertification research institute in Khartoum by using buck scientific atomic absorption spectrophotometry (AAS) model 210 VGP apparatus(appendix2), D2 corrector nitrous oxide burner, conditions N2O/Acetylene flame (temperature range : 2650-2800č)

2.2.1.2 Principle of AAS

The principle based on estimation of chromium by measuring the amount of absorbed light of unknown concentration of these element. The diluted sample aspirated, aerosolized and mixed with acetylene/ nitrous oxide gas. The mixture is

ignited in the flame. During the combustion, atoms of the elements of interest in the sample are reduced in free, un excited ground state atoms which absorb light at a characteristic wavelengths , the characteristic wavelengths are element specific ((Cr: 357.8nm). To provide elements specific wavelengths, a light beam from a lamp (hollow cathode lamp) whose cathode is made of the element being determined in passed through the flame. A device such as photomultiplier detector can detect the amount of reduction of the light intensity due to absorption by the analyte, and this can be directly related to the amount of the element in the sample. The electronic convert the amount of light absorbed to the actual sample concentration.

2.2.2 Magnesium measurement:

The estimation of serum Magnesium were performed in International Hospital in Khartoum by using Mindary BS 200. (appendix3).

2.2.2.2 Principle

Magnesium forms a purple coloured complex in alkaline solution. in the presence of EGTA ,the reaction is specific . The intensity of the purple colour is proportional to the magnesium concentration .

2.2.3 Calculation of BMI

BMI obtained by calculation according to formula:

$$\text{weight(kg)} \div \text{hight}^2\text{(m)}$$

2.2.4 Quality control:

Control sera were used to detect the accuracy of methods give result agree with the acceptable limit for normal and also give result agree with the acceptable limit for pathological.

2.2.5 Statistical analysis

All data were analyzed by SPSS software version 11.5.

3. Result

A hundred samples were collected to evaluate the level of Chromium and Magnesium and BMI , 50 healthy apparently as control group and 50 bronchial asthmatic patients as case, males account 30(60%) and female 20 (40%) with ratio 0f 1.5:1.the patients samples age ranges from (18-90) years also for control group. Statistical analysis is was done by spss and results were as follow :

Table 3.1 Shows mean of serum levels of chromium was significantly lower among asthmatic patients compared to control group (p value 0.000), and no significantly difference in serum levels of magnesium between asthmatics and control group p .value 0.314.

Table 3.2 Shows no significantly difference in serum levels of chromium and magnesium between asthmatics and control group in both sex male and female with P-value = 0.135&0.102

Figure 3.3 Personal correlation results shows no correlation between chromium and age with r-value - 0.067 and P-value 0.644

Figure 3.4 Personal correlation results shows no correlation between magnesium and age with r-value - 0.035 and P-value 0.808

Figure 3.5 Personal correlation results shows no correlation between chromium and duration of disease with r-value- 0.191 and P-value 0.0.184

Figure 3.6 Personal correlation results shows no correlation between magnesium and duration of disease with r-value 0.087 and P-value 0.0.550

Figure 3.7 Personal correlation results shows no correlation between chromium and BMI with r-value- 0.006 and P-value 0.968

Figure 3.8 Personal correlation results shows no correlation between magnesium and BMI with r-value - 0.092 and P-value 0.524

3.1 Comparison of trace elements levels between asthmatic patients and control group

Elements	Mean±SD Case	Mean±SD Control	P value
Chromium Mg/l	0.060±0.051	0.107±0.025	0.000*
Magnesium Mg/dl	0.087±0.047	0.077±0.047	0.314

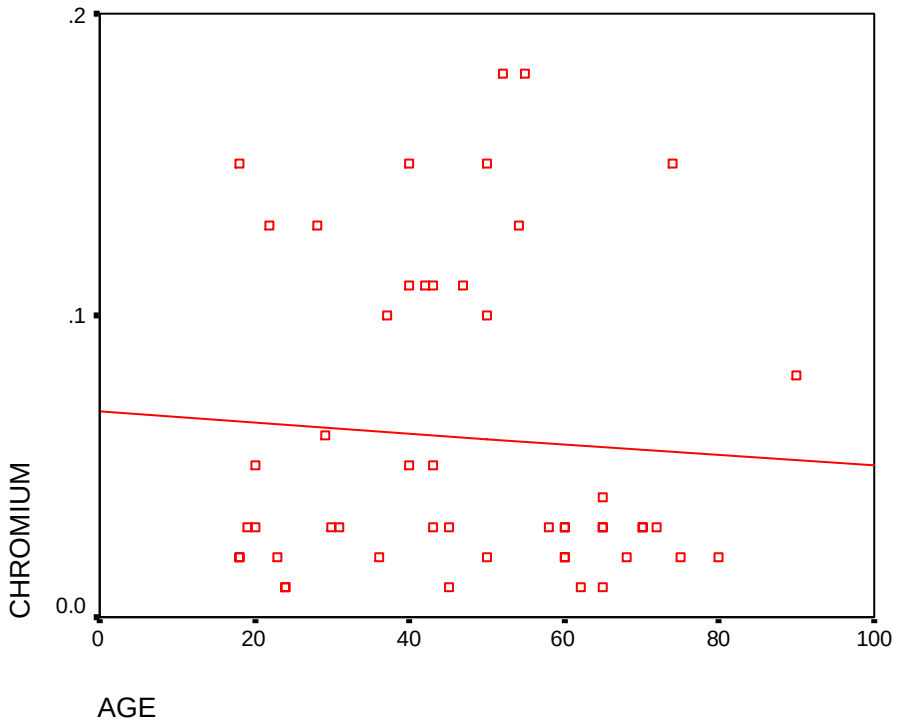
- Independent T Test
- * P-value $\leq$ 0.05 considered significant

3.2 Comparison of trace elements levels between male and female

Elements	Mean±SD Male	Mean±SD Female	P value
Chromium Mg/l	0.068±0.055	0.047±0.043	0.135
Magnesium Mg/dl	2.44±0.280	2.31±0.204	0.102

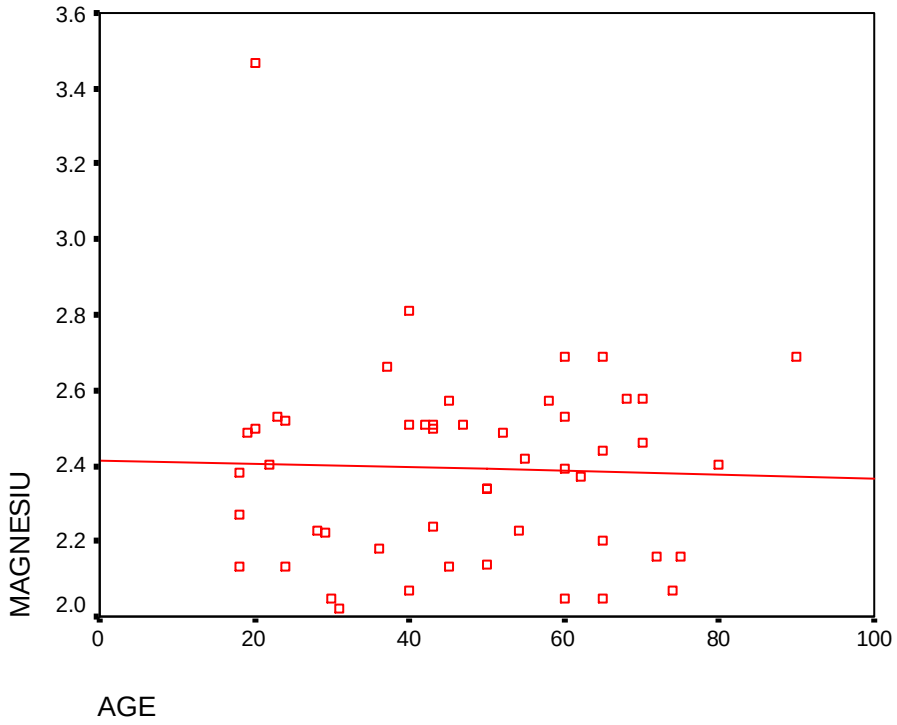
- Independent T Test
- * P-value $\leq$ 0.05 considered significant

3.3 correlation between age and chromium levels



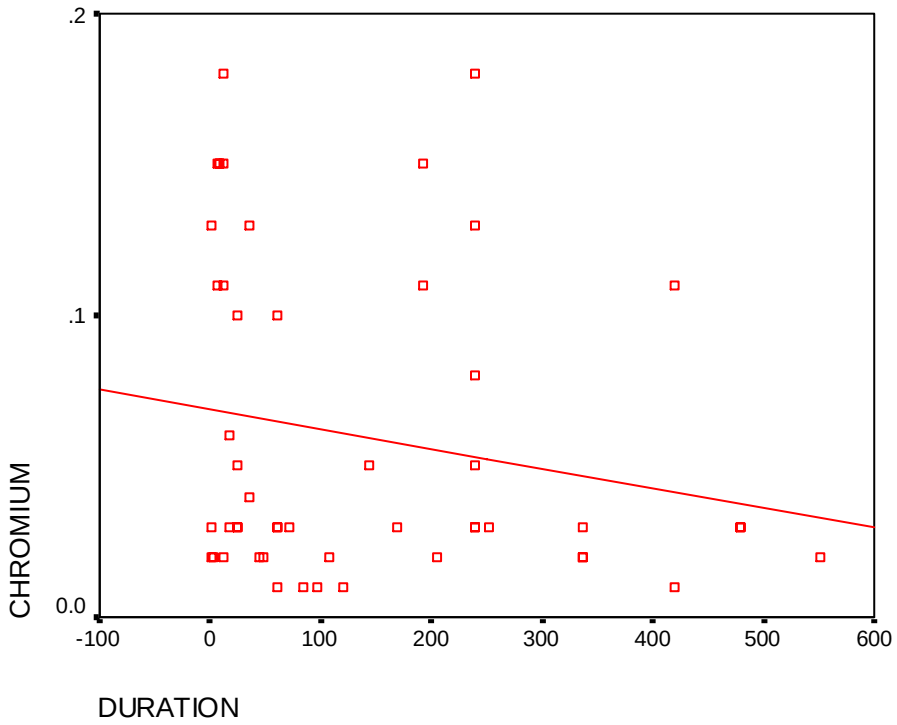
- Correlation test (bivirate) scatter
- r-value -0.067 = no correlation.
- P-value 0.644 = strength of correlation.

3.4 correlation between age and magnesium levels



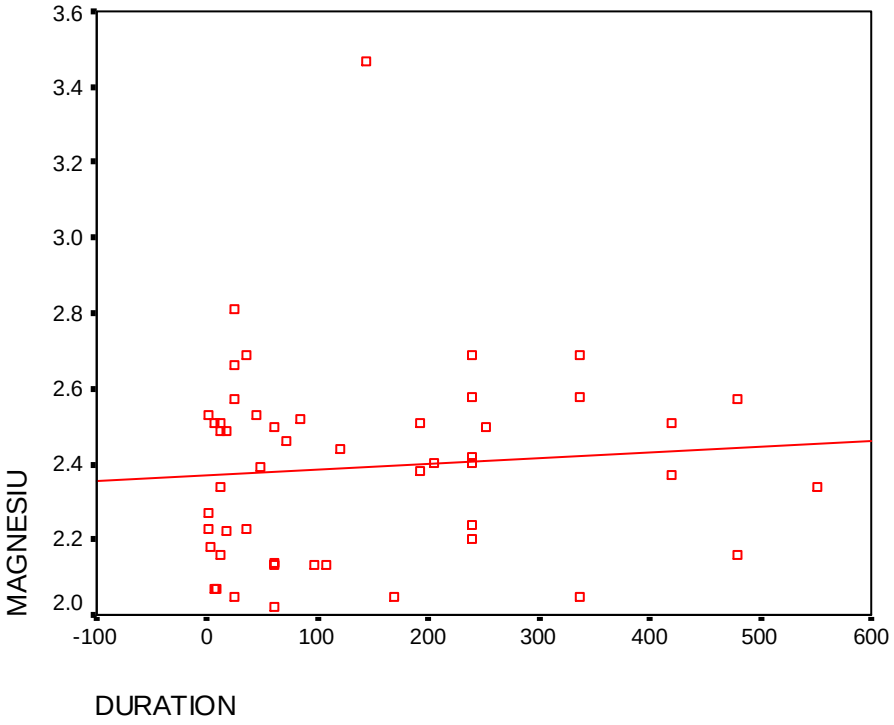
- Correlation test (bivirate) scatter
- r-value -0.035 = no correlation.
- P-value 0.808 = strength of correlation.

3.5 correlation between duration of disease and chromium levels



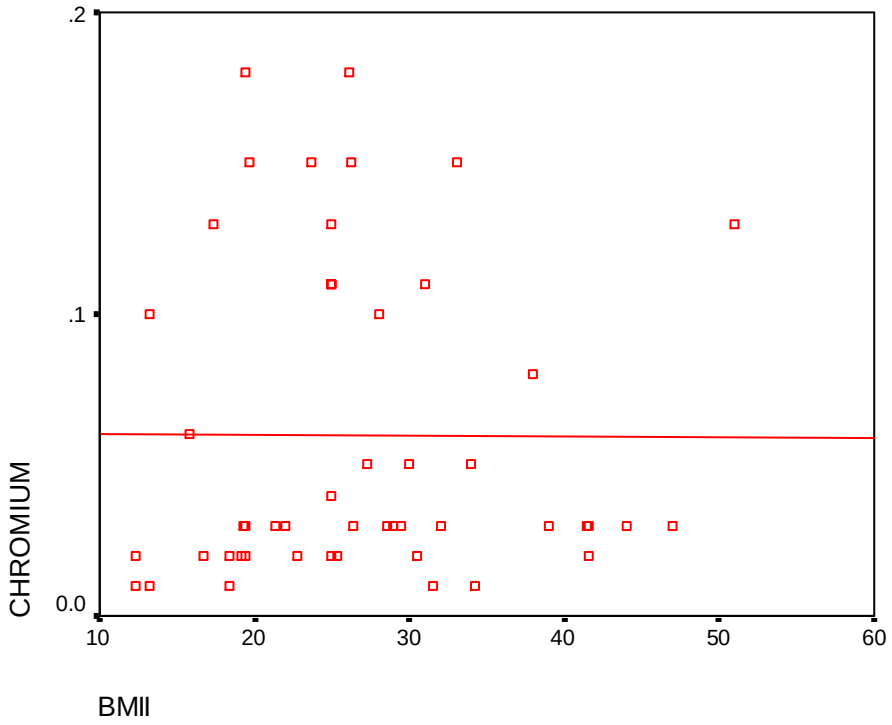
- Correlation test (bivirate) scatter
- r-value -0.191 = no correlation.
- P-value 0.184 = strength of correlation.

3.6 correlation between duration of disease and magnesium levels



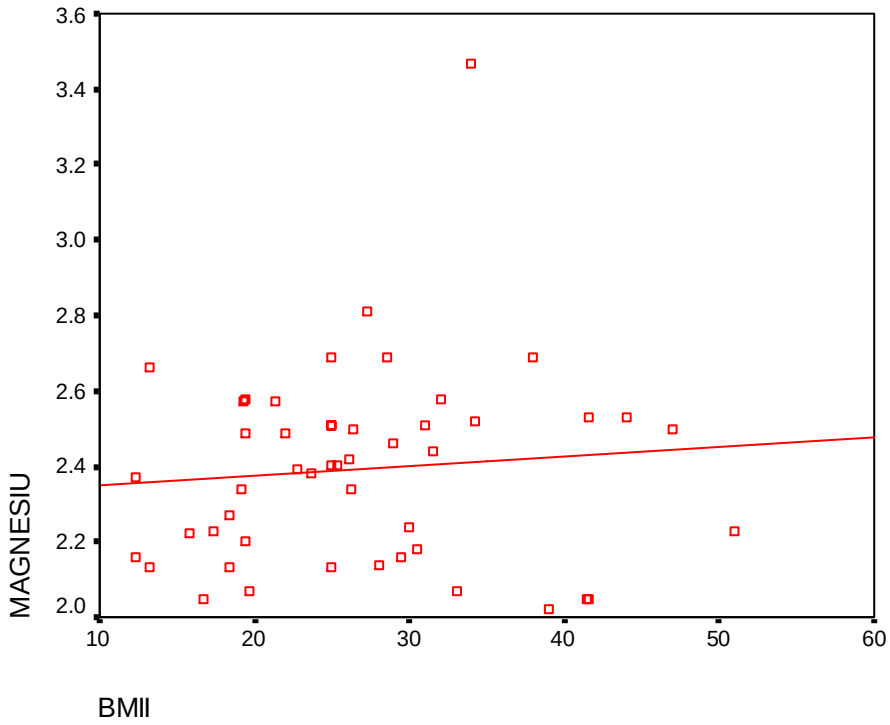
- Correlation test (bivirate) scatter
- r-value 0.087 = no correlation.
- P-value 0.550= strength of correlation.

3.7 correlation between BMI and chromium levels



- Correlation test (bivirate) scatter
- r-value -0.006= no correlation.
- P-value 0.968= strength of correlation.

3.8 correlation between BMI and magnesium levels



- Correlation test (bivirate) scatter
- r-value 0.092= no correlation.
- P-value 0.524= strength of correlation.

4.1 Discussion

One of the factors contributed to more severe asthma may be an increased susceptibility to the effects of reactive oxygen species (ROS) generated by inflammatory cells recruited into the lungs. The potentially damaging effects of oxidative stress are normally limited by antioxidants that scavenge ROS in the respiratory tract lining fluid. (Wood *et al,*. 2003; Cross 2003). Due to the role of free oxygen radicals in pathogenesis of asthma, most studies have recently paid attention to the role of antioxidant defense systems.The antioxidant mechanisms that protected the lung against these oxidants include: three superoxide dismutases (SODs) and Glutathione peroxidase (GSH-Px). (Vuokko *et al,*.2003). The results of present study revealed that, there was a significant decrease in mean concentration of serum chromium in bronchial asthma patients when compared with control group (*p*-value 0.000).This results agreed with chromium significantly increased the activity of glutathione peroxidase ($p<0.05$). (J Clin Biochem Nutr *et al,*. 2008). The chromium (III) when complexed with Metformin has succeeded in elevating antioxidant capacities in diabetic patients.(El-Megharbel *et al,*. 2015). No difference in serum levels of magnesium between asthmatics and controls was obtained in this study. This result was similar to some reports in the literature (Ermis *et al,*.2004; Vural ,.2000; Picado *et al,*. 2001) and differ from other ones.(Anetor *et al,*.2003).

Magnesium significantly increased the activity of antioxidants enzymes.(Luo *et al,*.2002; Sheirli *et al,*.2003; Howard ,. 1999). Increased dietary magnesium has been shown to be associated with an independent beneficial effect on lung function, airway responsiveness, and wheezing in the United Kingdom population

(Britton *et al*,.1994). Another study showed that a low intake of magnesium,which is involved in the relaxation of smooth muscle, is associated with reduced lung function, bronchial hyper-reactivity and self reported wheezing (Baker *et al*,. 1999).When given intravenously magnesium can lead to broncho- dilatation in acute severe asthma(Hill *et al*,. 1996). The current study showed mean of chromium and magnesium in male and female there is no variation in mean of chromium and magnesium levels in male and female p value(chromium 0.135,magnesium0.102) .also in our study there is no correlation between chromium level and age with R-value 0.067 and P-value 0.644 and magnesium R-value 0.035 and P-value 0.808 .the result also express there is no correlation with duration of disease with R-value 0.191 and P-value 0.184 for chromium and with R-value 0.087 and P-value 0.550 for magnesium. Also the current study showed that there is no correlation between chromium and magnesium level with body mass index of patients with R-value 0.006 and P-value 0.968 for chromium and with R-value 0.092 and P-value 0.524 for magnesium . This result differ from other study reported that asthma subjects had significantly lower magnesium intakes when they were overweight (P= 0.004) and obese (P= 0.001) than did normal-weight asthma subjects.(Kazaks *et al*,. 2006)

4.2 Conclusion

- The decrease of blood chromium level in BA patients seems to have an important role in induction of asthma but the serum level of magnesium was not difference in asthmatic compared to healthy people.
- According to this study there is no effect of age, BMI, and duration of disease on the serum trace elements levels.

4.3 Recommendation

1- Measurement of chromium level is recommended in asthmatic patients to monitoring antioxidants enzymes system .

2- More studies include estimation for more trace elements in asthmatic patients is recommended to be done.

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