STUDY OF GENETIC AND ENVIRONMENTAL INTERACTIONS IN ACUTE CHEST SYNDROME IN ASTHMATIC PATIENTS WITH SICKLE CELL DISEASE

By

Hanan Saad Ibrahim

M.Sc. Internal Medicine, Faculty of Medicine

Ain Shams University1998

A Thesis Submitted In Partial Fulfillment

Of

The Requirement for the Degree of Doctor of Philosophy

In

Environmental Medical Science

Department of environmental medical sciences

Institute of environmental studies and research

Ain Shams University

2013

APPROVAL SHEET

STUDY OF GENETIC AND ENVIRONMENTAL INTERACTIONS IN ACUTE CHEST SYNDROME IN ASTHMATIC PATIENTS WITH SICKLE CELL DISEASE

By

Hanan Saad Ibrahim

M.Sc. Internal Medicine, Faculty of Medicine

Ain Shams University1998

A Thesis Submitted In Partial Fulfillment of the Requirement for the Degree of Doctor of Philosophy in Environmental Medical Science has been approved by:

Signature

Prof. Dr Mahmoud Serry Al-Bokhary ……

Prof. of chest diseases Head of department of environmental Medical Sciences Institute of environmental studies & Research

Ain Shams University.

Prof. Dr. Howaida Mohamed Kamal ……..

Prof. of clinical and chemical pathology Faculty of Medicine

Banha University

Prof. Dr. Talaat Abdel Aziz Arafa ……

Prof. of chest diseases, Faculty of Medicine , El Azhar University

Prof. Dr. Mahmoud Abdullah El Azouni …….

Prof. of clinical and chemical pathology, Faculty of Medicine

Banha University.

Date of examination: 12/9/2013.

2013

STUDY OF GENETIC AND ENVIRONMENTAL INTERACTIONS IN ACUTE CHEST SYNDROME IN ASTHMATIC PATIENTS WITH SICKLE CELL DISEASE

By

Hanan Saad Ibrahim

M.Sc. Internal Medicine, Faculty of Medicine

Ain Shams University1998

A Thesis Submitted In Partial Fulfillment

Of

The Requirement for the Degree of Doctor of Philosophy

In

Environmental Science

Department of Environmental Medical Science

Under the Supervision of

Prof. Dr. Mahmoud Serry Al-Bokhary

Prof. of chest diseases and head of department of environmental Medical sciences, Institute of environmental studies & research

Ain Shams University

Prof. Dr. Howaida Mohamed Kamal

Prof. of clinical and chemical pathology Faculty of Medicine

Banha University

2013

ABSTRACT

Asthma and sickle cell disease (SCD), are common conditions that both may result in pulmonary complications. Asthma is a common co morbidity in SCD with a reported prevalence of 30-70 %. We are trying to investigate the patients with SCD and concomitant asthma have an increased risk of acute chest syndrome. This study aimed to assess the effect of bronchial asthma on the rate of acute chest syndrome in patients with sickle cell anemia. A 2-year prospective analysis was performed including 30 patients with asthma and SCD and 30 patients with SCD alone. Hospital admissions were recorded for acute chest syndrome in all patients and Chi square analysis was used to assess differences between the groups.

All selected patients were subjected to detailed history and medical examination, complete laboratory investigations, hemoglobin electrophoresis and x ray chest. It was shown that patients with SCD and asthma had significantly more episodes of acute chest syndrome (p= 0.02) compared to patients with sickle disease without asthma. In conclusion patients with diagnoses of concomitant asthma and SCD have increased episodes of acute chest syndrome. Whether aggressive asthma therapy can reduce this complication in this subset of patients is unknown and requires further research.

Keywords: Bronchial asthma–Acute chest syndrome – sickle cell anemia

ACKNOWLEDGEMENT

First and foremost, thanks to Allah who allowed and helped me to accomplish this work.

No words can express the magnitude of appreciation and respect I carry to the eminent ***Prof. Dr. Mahmoud Seri El Bokhari*** Professor of chest diseases, faculty of medicine, Ain Shams University, whom I am very fortunate to be one of his students; I feel greatly indebted for his kind advice, constant help and generous support throughout every step of this work.

My sincere gratitude and the unlimited thanks is addressed to ***Prof. Dr. Howaida Mohamed***. Professor of Hematology, faculty of medicine, Ain Shams University, for her faithful suggestions, constant advice, encouragement and sincere remarks helped me to finish this work.

I am also grateful to ***Dr. Mostafa Hussein***, consultant of Gastroenterology and Endoscopy - Police Hospital, for his unforgettable assistance, continuous advice, constructive discussion, and critical reading for every minute detail in this work, and support me to continue this work.

Lastly, I am endlessly grateful to my children specially the elder one Sherif, the guiding Light for every progress I make and every step I take. With all the love and gratitude in the world I dedicate this work to them.

List of abbreviations

SCD: Sickle Cell Disease

ACS : Acute Chest Syndrome

SCA : Sickel Cell Anemia

MCV: Mean Corpuscular Volume

MCHC : Mean Corpuscular Hemoglobin Concentration

OPSI : Overwhelming Post Splenectomy Infection

RSV : Respiratory Syncytail Virus

VOC : Volatile Organic Compounds

BBzP : Butyl Benzyl Phthalate

SNP : Single Nucleotide Polymorphism

NAEPP : National Asthma Education and Prevention Program

ACE : Agniotensin-Converting Enzyme

COPD : Chronic Obstructive Pulmonary Disease

SABA : Short Acting Beta- Adrenoceptor

LABA : Long Acting Beta-Adronceptor

WHO : World Health Organization

Contents

LIST OF TABLES

LIST OF FIGURES

Introduction and aim of the work

Asthma is a common pulmonary condition that involves the heightened bronchial hyper responsiveness and reversible broncho-constriction together with acute – on – chronic inflammation that leads to decreased air exchange, ventilation – perfusion mismatch and subsequent hypoxemia (Boyd et, al. 2006), (Vendamini et, al. 2006).

Asthma is also a common co-morbidity in sickle cell disease (SCD). Similar to sickle cell disease, mechanisms that contribute to asthma are complex and multifactorial, and influenced by genetic polymorphism environmental factors and infections triggers. The association of asthma with inflammation, oxidative stress, and hypoxemia contribute to a vasculopathy in SCD, and the known consequence of there factors on sickle erythrocytes, co-morbid asthma would likely contribute to a vicious cycle of sickling and subsequent complications of SCD, (Phillips et, al. 2008), (Bernaudin et al., 2008).

Acute chest syndrome (ACS), a common complication of SCD, has the potential to progress to severe pulmonary disease or death. Also patients with concomitant asthma and sickle cell disease have increased episodes of acute chest syndrome (Boyd et, al. 2004 and Boyd et, al. 2006).

Further, ACS is the leading cause of premature death in this population and affects approximately 50% of patients with sickle-cell anemia at least once in their lifetime (Koumbourlis et, al. 2001), (Knight-Madden et al.2005).

It may be a presenting diagnosis but often develops after acute infections, painful episodes, rib or bone marrow or pulmonary infarction, surgery, and fat embolism. Previous episodes of acute chest syndrome increase the likelihood of repeated acute pulmonary events and subsequent pulmonary hypertension. Asthma and airway hyper reactivity seem to be associated with recurrent acute chest syndrome and pain (Stuart and Setty, 2001), (Nordness et al.2005).

Asthma is a risk factor for acute chest syndrome and cerebral vascular accidents in children with sickle cell disease. (Nordness et al. 2005).

AIM TO WORK:-

This study aimed to assess the effect of bronchial asthma on the rate of acute chest syndrome in patients with sickle cell anemia.

Bronchial Asthma

Definition of Asthma:-

Asthma is a chronic, persistent airways disease distinguished by exacerbation of coughing, wheezing, chest tightness and difficult breathing. It is characterized by airway inflammation and variable airflow obstruction that is usually reversible, but may be life threatening. (Traidl-Hoffmann et al. 2003).

History:-

Asthma was recognized in Ancient Egypt and was treated by drinking an incense mixture known as kyphi Officially recognized as a specific respiratory problem separate from others was first recognized and named by Hippocrates circa 450 BC. During the 1930s–50s, asthma was considered as being one of the 'holy seven' psychosomatic illnesses. Its aetiology was considered to be psychological, with treatment often based on psychoanalysis and other 'talking cures'.

As these psychoanalysts interpreted the asthmatic wheeze as the suppressed cry of the child for its mother, they considered that the treatment of depression was especially important for individuals with asthma. Among the first papers in modern medicine published on the subject are one published in 1873, which tried to explain the pathophysiology of the disease and one in 1872, which concluded that asthma can be cured by rubbing the chest with chloroform liniment. (Chandran G et al. 2007)

Some of the first references to medical treatment include one in 1880, when Dr. J. B. Berkart used IV therapy to administer doses of a drug called pilocarpin. In 1886, F.H. Bosworth theorized a connection

between asthma and hay fever. Epinephrine was first referred to in the treatment of asthma in 1905, and again for acute asthma in 1910. (Jenkins M et al. 1997).

Epidemiology:-

As of 2009, 300 million people worldwide were affected by asthma leading to approximately 250,000 deaths per year. It is estimated that asthma has a 7-10% prevalence worldwide. As of 1998, there was a great disparity in the prevalence of asthma across the world, with a trend toward more developed and westernized countries having higher rates of asthma, with as high as a 20 to 60-fold difference. Westernization however does not explain the entire difference in asthma prevalence between countries, and the disparities may also be affected by differences in genetic, social and environmental risk factors. Mortality however is most common in low to middle income countries, while symptoms were most prevalent (as much as 20%) in the United Kingdom, Australia, New Zealand, and Republic of Ireland; they were lowest (as low as 2–3%) in Eastern Europe, Indonesia, Greece, Uzbekistan, India, and Ethiopia. (Phillips KL et al. 2008)

Asthma affects approximately 7% of the population of the United States and 5% of people in the United Kingdom. Asthma causes 4,210 deaths per year in the United States. In 2005 in the United States asthma affected more than 22 million people including 6 million children. It accounted for nearly 1/2 million hospitalizations that same year. More boys have asthma than girls, but more women have it than men. In England, an estimated 261,400 people were newly diagnosed with asthma in 2005; 5.7 million people had an asthma diagnosis and were prescribed 32.6 million asthma-related prescriptions. (Nordness ME et al. 2005).