THE COMPARATIVE EVALUATION OF OUTCOMES OF ASTHMA TREATMENT THROUGH USE OF REGIMEN THAT CONTAIN FLUTICASONE VERSUS OTHER TYPES OF TREATMENT REGIMEN IN PRIVATE AND PUBLIC HOSPITALS IN ERBIL, IRAQ

KARWAN BAHRAM MAULOOD

UNIVERSITI SAINS MALAYSIA

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by

KARWAN BAHRAM MAULOOD

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LIST OF ABBREVIATIONS

KRI	Kurdistan Region of Iraq
QOL	Quality of life
AQLQ	Asthma quality of life questionnaire
KAP	Knowledge, attitudes, and practice
FEV1	Forced expiratory volume in 1 second
KRI	Kurdistan Region of Iraq
DALY	Disability-adjusted life years
SM	Sulfur mustard gas
ICS	Inhaled corticosteroids
BDP	Beclomethasone dipropionate
BUD	Budesonide
HRQL	Health related quality of life
COPD	Chronic Obstructive Pulmonary Disease
CP	Community Pharmacist
FVC	Forced Vital Capacity
FP	Fluticasone Propionate
HCP	Health Care Professionals
IL-37	Interleukin-37
PEF	Peak Expiratory Flow
SABA	Short-Acting β2 Agonists

LABA	Long Acting β2 Agonists
BHR	Bronchial hyperresponsiveness
HRQL	Health-related quality of life
WHO	World health organization
GHG	Greenhouse gases
HEI	Health education intervention

PENILAIAN PERBANDINGAN HASIL RAWATAN ASMA MENGGUNAKAN REGIMEN MENGANDUNGI FLUTICASONE DENGAN RAWATAN REGIMEN LAIN DALAM KALANGAN PESAKIT ASMA DI HOSPITAL AWAM DAN SWASTA DI ERBIL, IRAQ

ABSTRAK

Erbil adalah salah satu bandar di Iraq yang banyak terlibat dalam perang semasa konflik Iraq-AS. Perang ini menyebabkan berjuta-juta orang menderita asma kerana bahan kimia dan senjata yang digunakan semasa perang. Ribut debu di wilayah ini, yang membawa banyak pencemaran debu dan merupakan penyebab utama asma di wilayah ini, Kerana perang, rantaian bekalan dan sistem penjagaan kesihatan runtuh sepenuhnya, yang menjadikan rawatan sukar dan menyebabkan kualiti hidup yang buruk. Kajian ini bertujuan untuk menilai kualiti hidup (QOL) dan pengetahuan, sikap, dan praktikkan (KAP) pesakit asma mengenai asma bronkial dan untuk menyediakan rejim rawatan yang lebih baik dengan kortikosteroid yang dihirup (ICS) dan pendidikan kesihatan. Kajian ini dirancang dalam dua fasa. Pada fasa pertama, kajian kuasi eksperimen dilakukan untuk menilai QOL dan tiga ICS (Fluticasone, Budesonide, dan Beclomethasone) yang berbeza. 105 subjek direkrut dalam tiga kumpulan. Soal Selidik Kualiti Hidup Asma Mini (mini-AQLQ) digunakan untuk menilai QOL. FEV1 dilakukan dengan spirometri. Kiraan eosinofil dan ujian Vitamin D dilakukan pada darah serum. Kedua-dua data QOL dan ICS dikumpulkan pada selang waktu awal, 2 minggu, dan 12 minggu. Pada fasa II, 250 pesakit direkrut untuk penilaian KAP. Soal selidik yang tersusun dan disahkan digunakan untuk menilai KAP. Setelah penilaian pra KAP, program pendidikan kesihatan disampaikan

kepada pesakit dan penilaian dilakukan setelah 2 minggu dan 12 minggu. Pada peringkat awal, tidak ada perbezaan dalam QOL. Selepas 2 minggu dan 12 minggu rawatan, terdapat perbezaan yang signifikan (P = 0.001) yang terdapat di antara kumpulan, dengan min tertinggi dalam kumpulan fluticasone. Terdapat perbezaan ketara keseluruhan antara kumpulan ICS untuk nilai FEV1: F (2,96) = 71.07; (P < 0.001); Nilai Vit-D: F (2,96 74.77; (P < 0.001); dan nilai eosinofilia: F (2,95) = 166.88; (P < 0.001). Selepas 2 dan 12 minggu rawatan, kumpulan fluticasone menunjukkan nilai FEV1, Vit-D, dan eosinofilia yang lebih baik berbanding kumpulan lain. Selepas intervensi pendidikan kesihatan, responden mempunyai skor pengetahuan yang lebih tinggi (P < 0.001) dengan sikap positif yang lebih baik (P < 0.005). Kualiti hidup pesakit asma meningkat dengan ketara selepas rawatan dengan ICS, sementara fluticasone lebih berkesan berbanding dengan ICS lain. Program dalam pendidikan kesihatan meningkatkan pengetahuan, sikap, dan amalan pesakit asma terhadap asma.

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ABSTRACT

Erbil is one of the cities in Iraq that was heavily involved in war during the Iraq-USA conflicts. Due to the chemicals and weapons used in this war, millions of people now suffer from asthma. Another major contributor to asthma cases in this province is the dust storms that blow in a lot of dust pollution. War caused a total breakdown in supply chains and healthcare systems, making it difficult to get treatment and lowering people's quality of life overall. The goal of this study was to measure the quality of life (QOL) and knowledge, attitudes, and practices (KAP) of asthmatic patients with bronchial asthma and come up with a better treatment plan using inhaled corticosteroid (ICS) and health education. This study is designed in two phases. In the first phase, a quasi-experimental study was carried out to assess the QOL and clinical outcomes following treatment with three different ICS (Fluticasone, Budesonide, and Beclomethasone). For objectives 1 and 2, 105 and 250 patients for objective 3 were recruited, respectively. The Mini Asthma Quality of Life Questionnaire (mini-AQLQ) was used to assess the QOL. The clinical outcomes following ICH treatments include forced expiratory volume in 1 second (FEV1) from spirometry, eosinophil count and Vitamin D assay from serum blood. Both QOL and ICS data were collected at baseline, 2 week, and 12-week intervals. In phase II, 250 patients were recruited for KAP assessment. A structured, validated questionnaire was

used to assess the KAP. After the pre KAP assessment, a health education program was delivered to the patients and assessments were done after 2 weeks and 12 weeks. At baseline, there was no difference in QOL. After 2 weeks and 12 weeks of the treatment, there was a significant difference ($P < 0.001$) found between the groups, with the highest mean in the fluticasone group. There is an overall significant difference between the ICS group for the FEV1 value: $F(2,96) = 71.07$; (P 0.001); Vit-D value: $F(2,96) = 74.77$; (P 0.001); and eosinophilia value: $F(2,95) = 166.88$; ($P < 0.001$). After 2 and 12 weeks of the treatment, the fluticasone groups showed better FEV1, Vit-D, and eosinophilia values compared to another group. After health education intervention, respondents had a higher knowledge score ($P < 0.001$) with a better positive attitude ($P < 0.005$). Patients with asthma have a much better quality of life after being treated with ICS, and fluticasone is more effective than other ICS. Programs in health education significantly improved asthmatic patients' knowledge, attitudes, and practices towards asthma.

CHAPTER ONE

INTRODUCTION

1.1 Background

The Kurdistan Region of Iraq (KRI) [1] is a populous autonomous region in northern Iraq. Erbil is one of the cities in KRI heavily involved in war during Iraq- USA conflicts [2]. This war has caused millions of people to suffer not only from the catastrophic effects of the war, but also from post-war diseases [3] caused by the chemicals and weapons used during the conflict. Asthma is a chronic inflammatory condition marked by episodes of coughing, wheezing, shortness of breath, and chest tightness. Asthma is defined as “a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role: in particular, mast cells, eosinophils, neutrophils (especially in sudden onset, fatal exacerbations, occupational asthma, and patients who smoke), T lymphocytes, macrophages, and epithelial cells”. This inflammation produces recurring episodes of coughing, wheezing, dyspnea, and chest tightness in sensitive individuals. An airflow blockage that is widespread but varies in severity is generally reversible either naturally or by medical intervention "[2, 4]. There must be both symptoms (more than one of the following: wheezing, dyspnea, and chest tightness) and fluctuating airflow restriction in order to meet the guideline's standards. Air hyperresponsiveness (AHR) and inflammation of the airways are also included in more recent classifications [5].

Early in the history of asthma, reversible airflow restriction was defined as the defining characteristic [4]. The American Thoracic Society then added the feature of “hyperreactivity of the airways” to the list. The term "airway hyperresponsiveness (AHR)" refers to a condition in which the airways contract excessively upon the inhalation of certain stimuli [6]. There are a variety of airway challenge tests, such as histamine, cold air, methacholine, and exercise, which make it difficult to examine the airway [5]. Asthma can't be accurately assessed with a single test [6]. Asthma symptoms or a **physician**'s diagnosis are frequently sought in epidemiological studies, which is why questionnaires are so common [7, 8].

1.2 Epidemiology of asthma

Asthma's burden varies greatly from country to country. Asthma is a common respiratory disease that affects up to 235 million people worldwide. The prevalence of asthma varies due to the difficulty of assessing its severity. The reported worldwide prevalence is between 5.2% and 9.4%. In Malaysia, the prevalence is estimated to be 4.2% based on the third National Health and Morbidity Survey [30]. Asthma prevalence (as measured by the frequency of wheezing in the previous 12 months) is 15-16.2% in Iraq, according to data from phase three of the International Study of Asthma and Allergies in Childhood [31] [32, 33]. The World Health Survey sheds light on the prevalence of adult-onset asthma. In the Middle Eastern countries, the prevalence of asthma is lower than that in developed countries, while the prevalence of asthma and wheezing in Iraq is similar to that in developed and industrialized countries [34, 35]. There is no specific data of asthmatic patients in Erbil, Iraq. Although it’s the most common cause reported at the local health

care center. One in every 250 deaths worldwide is attributable to asthma, which affects an estimated 300 million people [36]. It's possible that by 2025, there will be an additional 100 million people suffering from asthma. Asthma, diabetes, cirrhosis of the liver, and schizophrenia all result in about the same number of disability-adjusted life years DALYs lost as a result of disability. According to a recent systematic review, there are now signs that the prevalence of asthma is decreasing overall (rather than plateauing) [37]. However, the prevalence of asthma continues to rise in many regions of the world.

1.3 Pathophysiology and pathogenesis of asthma

Asthma is a complex bronchial airway disorder that causes wheezing. Hippocrates created the name "asthma" from a Greek word that means "panting" [9, 10]. Asthma is marked by persistent inflammation, bronchial hyperresponsiveness (BHR), and airway obstruction [11]. Asthma is a complicated, multi-symptom disease, therefore, its pathophysiology and etiology continue to evolve [12]. Airway inflammation underlies asthma etiology regardless of phenotype [13]. Because inflammation changes the shape and function of the airways, asthma develops. Asthma symptoms often include wheezing, shortness of breath, tightness in the chest, and coughing [12, 14].

Airway inflammation in asthma is a multicellular process. Inhaling allergens and/or irritants induces mast cells, eosinophils, and TH2 lymphocytes, leading to a cascade of inflammation and systemic inflammatory responses such as acute bronchoconstriction [15]. The airway releases TH2-associated cytokines or key mediators such as IL-4, IL-5, and IL-13, as well as IgE, which govern many aspects of allergic inflammation [16]. IL-13 induces mast cell growth in the early inflammatory response to allergens, releasing

histamine, leukotrienes, and prostaglandins [17]. These mediators trigger smooth muscle cell contraction and mucus release, blocking asthmatics' airways [18]. Sensitized mast cells can be activated by osmotic stimuli to generate bronchoconstriction, as shown in exercise-induced bronchospasm (EIB)[19]. Mast cell mediators are responsible for late phase cellular responses, which produce bronchial wall edema and airway hyperresponsiveness [4] [18, 20]. IL-5 increases eosinophil development; eosinophils cause allergic asthma and airway dysfunction [16, 18]. In allergic asthma patients, these cells carry inflammatory mediators that induce airway epithelial cell death, AHR, and airway remodeling. "Eosinophilic asthma" involves bronchial eosinophils. Anti-IL-5 antibodies suppress airway eosinophils, highlighting their role in asthma pathogenesis [21, 22].

Neutrophils aren't pathogenic, unlike eosinophils. They are the main inflammatory leucocytes in the airways and sputum of people with severe asthma and are linked to airway blockage [23, 24]. Long-term inflammation from excessive IL-13 production may harm asthmatics' epithelium and airways. Errors in the injury-repair system can cause epithelial wall rebuilding and airway remodeling [25, 26]. Asthma patients with atopy had thicker basement membranes than non-atopy patients [27] . Our understanding of asthma's etiology is constantly growing, although TH2 cytokines and inflammation are crucial. Asthma is a TH2-cell-dependent, IgE-mediated allergic disease, as TH2 cytokines are higher in asthma patients' bronchoalveolar lavage [28][29].

1.4 Risk Factors of asthma

Exposure to cigarette smoke has been linked to an increased risk of developing asthma [38]. Particulate matter with an aerodynamic diameter of less than 10 nm (which is the component of air pollution small enough to penetrate the intrathoracic respiratory tract, abbreviated to (PM10) appears to be associated with the prevalence of childhood asthma [39]. Asthma hospitalizations in older adults have been linked to long-term exposure to air pollution, measured by the annual nitrogen dioxide (NO2) level [40]. The European Multicenter Allergy Study (MAS) found no correlation between early exposure to house dust mite and cat allergens and the development of asthma [41]. However, children with allergic asthma who are exposed to allergens indoors may experience a long-term decline in lung function [8]. Research has found a correlation between obesity and asthma. Overweight and obese men and women are more likely to develop asthma, per a meta-analysis of prospective epidemiological studies [42]. Another study that looked at gender effect modification found that asthma and obesity are linked to women but not in men [43, 44]. An investigation into the role of diet in asthma has been attempted, but dietary intake is hard to measure and susceptible to information bias. Studies in the Middle East conflict area have shown that asthma is linked to a higher rate of stress, Post-traumatic stress disorder (PTSD), and depression [45]. Sulfur mustard gas (SM), a chemical weapon, has been linked to asthma in the war-conflict region [45, 46].

1.5 Asthma management and Inhaled corticosteroids (ICS)

Asthma management aims to keep the disease under control while minimizing any negative effects that can be caused by the treatments that are being utilized. But

substantial, global, community-based surveys on asthma have indicated that the majority of patients have an alarmingly high prevalence of symptoms and disruption of life due to their disease, showing that this goal is not being met [3, 31] . Consequently, the "great majority" of patients may not be able to achieve the level of asthma control specified in the guidelines. Consider whether this insufficiency emerges from the refractory nature of the disease, existing therapy constraints, or an issue with treatment strategies and low physician and patient expectations and treatment compliance [47]. There are now guidelines from the National Institute of Health that encourage the daily use of anti-inflammatory drugs for the long-term management of chronic asthma. For mild, moderate, and severe chronic asthma, inhaled corticosteroids are the most effective anti-inflammatory drugs [48].

Asthma morbidity and health status have both decreased significantly since the widespread use of inhaled corticosteroids at the early onset of the disease's course. The use of inhaled corticosteroids (ICS) [49] is now the first-line treatment for all individuals with asthma [50]. ICS was also prescribed for asthmatic patients in Erbil according to guidelines. Inhaled corticosteroids are now available in a variety of forms, including topical and nasal sprays. Asthma patients of all ages and levels of severity can benefit from the use of ICS. For many patients, ICS increases the quality of their lives and allows for a return to a more normal way of life. It improves lung function, reduces the frequency of exacerbations, and may even help to prevent irreversible airway abnormalities. When oral corticosteroids were first introduced to individuals with severe asthma, many studies demonstrated that most patients could be weaned off oral corticosteroids [51, 52]. When compared to other corticosteroids, such as beclomethasone dipropionate, budesonide has

a higher topical-to-systemic action ratio. The effects of budesonide on plasma cortisol and urine free cortisol excretion in healthy volunteers are less pronounced than those of beclomethasone dipropionate [53, 54].

Different people require different doses of inhaled budesonide to reduce fasting plasma cortisol levels in adults. For short-term use, inhaled budesonide may affect biochemical markers of bone turnover less than equivalent doses of beclomethasone dipropionate and may be less harmful to bone metabolism than oral prednisolone doses expected to have the same anti-asthma effect [55]. The corticosteroid fluticasone propionate inhibits eosinophil activation and the subsequent release of inflammatory mediators. When salmeterol and fluticasone propionate are inhaled together, they have the same effects as when they are given separately, and in vitro studies suggest that they work well together or add to each other [56]. When comparing salmeterol/fluticasone propionate maintenance therapy to formoterol/budesonide maintenance therapy in adults and teens, the results have been mixed. Some studies have shown that both are equally effective, while others have shown that one is more effective than the other [56, 57]. Twice-daily ICS fluticasone propionate provided more effective control of asthma symptoms than twice-daily sustained-release theophylline. People with asthma who take fluticasone propionate twice a day have seen improvements in their **HRQL** from where they started. Asthma quality-of-life questionnaire scores improved more with ICS fluticasone propionate than with other ICS [58, 59].

1.6 The concept of Health-related quality of life (HRQL)

Health-related quality of life (HRQL) is defined as “the functional effects of an illness and its subsequent therapy on a patient, as perceived by the patient” [59]. HRQL is a component of the overall quality of life that is influenced by a person's health. In other words, the ability to function and enjoy a variety of roles [59, 60]. Disease, injury, treatment, or policy can alter the value assigned to life duration. The concept of “health-related quality of life” states that better health care can potentially improve a person's QoL[61]. What is defined as quality of life is an individual's "perception of their position in life in relation to their goals, expectations, standards, and concerns" by the World Health Organization's international collaborative Quality of Life Group [62]. To measure quality of life, the group devised a set of six domains: physical, psychological, level of independence, social relationships, environment and spirituality, and religious or personal beliefs [63]. A study of health-related quality of life models found that fewer than a quarter of the authors had a clear definition of the term. Subjective well-being, which includes cognitive judgments and positive and negative feelings, can be a way to conceptualize "quality of life"[64]. Disease-specific instruments have been developed because different aspects of HRQL are more or less important for different conditions. In comparison to generic instruments, they have the advantage of being more sensitive to changes in specific conditions [65]. However, generic instruments are less sensitive to specific conditions, but they can be used to compare results from different conditions. How well and reliably a quality-of-life indicator measures what it claims to be able to detect depends greatly on whether a measurement is considered adequate and robust, or adequacy and robustness, for that matter [14, 65].

Currently, there are no reported documents on HROL in Erbil city. The monetary crisis is a typical wartime complication. That factor is directly related to the degree of asthma management. HRQL is related to asthma management and is associated with more hospitalizations, emergency and unscheduled visits, and uncontrolled medicine sales [66]. About 80% of community pharmacies, wholesaler drug stores, and scientific bureaus do not adhere to the official pricing system set by Ministry of health (MoH) and the Syndicate of Iraqi pharmacists [67]. Furthermore, a large percentage of drugs (60% to 70%) in community pharmacies and drug stores do not meet the requirements of circulation in terms of approval or registration or drug testing [67, 68]. Iraq requires an effective policy for medicine regulation according to a report by WHO, where they mentioned that the private sector is largely out of the MoH's supervision and regulation[67, 69]. This is considered another key factor that affects the patient's quality of life.

1.7 Health Education for asthma patients

An organized learning experience involving teaching, counseling, and behavior modification strategies that influences patients' knowledge and health behaviors involves an interactive process that encourages patients to actively participate in their own health care. While most experts believe that asthma education increases patient understanding, the impact on other health outcomes varies widely [70]. Generally, asthma education programs teach participants how to manage their asthma with a **physician** (self-management), or both. There should be a self-management program for people with asthma. Asthma education can be accomplished in a variety of ways, but one of the

simplest and least expensive is to simply provide people with information on the disease and how to treat it. This can be done effectively in either a clinical or community setting [71]. An interactive or non-interactive method of delivering asthma information can be used. Lectures, audiovisual presentations, and group discussions are all examples of forms of interactive learning that may be used in either individual or group sessions with a teacher. Other examples include role-playing, project- or assignment-based learning, participatory learning, and the case method for developing problem-solving skills [72].

1.8 Problem Statements

Millions of people around the world suffer from asthma, making it a major public health issue. In the last few decades, the number of asthma cases has skyrocketed [36]. Asthma prevalence has risen sharply in recent decades as a result of environmental changes. Some of the most important external factors include pollution, diet, allergens, and climate [10]. External non-specific exposure factors include climate change, with its rapid rise in temperature and long-lived greenhouse gases (GHG), as well as the predicted increase in extreme events like thunderstorms and flooding . Most cities in Iraq had an average annual PM2.5 concentration of 112 g/m3, far exceeding the standard of 10 g/m3 [2]. In the aftermath of the 2003 war conflicts, people with asthma in Erbil were among those who suffered the most. Local asthma guidelines classify asthmatics who visit the Erbil public or private hospital respiratory clinic as moderate-to-severe asthmatics. Chemical weapon pollution is one of the known risk factors for asthma in war-conflict cities like Erbil. Chemical and weapon pollutants, including fine particulate matter [73], nitrogen dioxide (NOx), sulfur mustard gas (SM), and ozone, have been linked to both asthma exacerbations and the onset of asthma [2, 38, 45]. Summers are very hot and windy, and

the air is full of dry soil and dust. Temperatures range from 50°C in the summer to below 0°C in the winter. Another common environmental event in Erbil is a dust storm, which carries a lot of dust pollutants and is another major cause of asthma in this province [2]. The local language uses the words "Shamal" for northern seasonal dust and "sharqi" for eastern seasonal dust storms [74].

Stress and compromised living conditions in war-torn countries can increase the risk of asthma flare-ups and other complications for people with asthma [75]. There is evidence that conflict can lead to an increase in both military personnel's and civilians' symptoms of asthma. Studies found that 14% of soldiers serving in Iraq had spirometry abnormalities, compared to 1.8 percent of soldiers serving in the United States [76]. There was also an increase in asthmatic symptoms such as wheezing and a nighttime cough in both military and contractor personnel returning from Iraq, regardless of their diagnosed asthma status [77]. More than 70 percent of Syrians who went to an outpatient clinic reported having asthma after the war began [78].

A report from the local health center showed that, before the war, prednisolone and salbutamol were the most commonly prescribed drugs, with theophylline being the next [45]. During the 2003 war period, the supply chain and healthcare systems completely collapsed. Following the post-war in Erbil with new guidelines, the most common ICS used in asthma treatment are fluticasone, beclomethasone, and budesonide [5]. The availability and cost of these drugs also play a vital role in Erbil. Fluticasone is not supplied to the government hospital in Erbil, while it is available only in private pharmaceutical sales centers at a high cost. Other two ICS are also not available in

government hospitals, but they are less expensive and less effective, according to the literature [79, 80].

The health-related quality of life [62] of the asthmatic patients in Erbil is not documented yet. Although the high cost of inhaled corticosteroid medicine within healthcare systems makes it more complicated for most asthmatic patients. Data from the University Soleimani showed that, most of the asthmatic patients were male with young adult ages (less than 30 years). However, there is no other information reported yet to construct a frame of reference for the QOL of asthmatic patients in Erbil, which is why it's important to find out. The Knowledge, attitude, and perception [33] study sought to learn more about patients' knowledge of risk factors for developing asthma and worsening the disease, as well as ways to help those who suffer from it. These sessions should focus on improving patients' knowledge of asthma, reducing risk factors, and avoiding medication side effects [81]. A study showed that both asthma knowledge and social support had a significant positive relationship with asthma self-management behaviors and accounted for 14% of self-management behavior variability [82].

This study aimed to assess the quality of life and knowledge of asthmatic patients regarding bronchial asthma and to provide a better clinical outcome with available inhaled corticosteroid drugs and proper education in terms of improving their knowledge regarding the meaning, risk factors, signs and symptoms, diagnostic measures, management, and prevention of bronchial asthma.

1.9 Objectives

General objective

To compare the outcomes of asthmatic patients following management with three asthmatic drugs (Fluticasone, Beclomethasone, and Budesonide) and health education intervention in Erbil province, post-war Iraq.

Specific Objectives:

1. To compare the quality of life of asthmatic patients before and after management with three asthmatic drugs (Fluticasone, Beclomethasone, and Budesonide) in Erbil province, post-war Iraq.
2. To compare the clinical outcomes of asthmatic patients before and after management with three asthmatic drugs (Fluticasone, Beclomethasone, and Budesonide) in Erbil province, post-war Iraq.
3. To compare the knowledge, attitude and practice of asthmatic patients before and after health education intervention in Erbil province, post-war Iraq.

1.10 Research Question

1. What are the differences in quality of life of life of asthmatic patients before and after management with three asthmatic drugs (Fluticasone, Beclomethasone, and Budesonide) in Erbil province, post-war Iraq ?

2. Does management with three asthmatic drugs (Fluticasone, Beclomethasone, and Budesonide) provide different clinical outcomes in asthmatic patients before and after in Erbil province, post-war Iraq ?
3. What are the differences in knowledge, attitude and practice of asthmatic patients before and after health education intervention in Erbil province, post-war Iraq?

1.11 Research Hypothesis

Null Hypothesis:

1. There are no differences in the quality of life of asthmatic patients before and after management with three asthmatic drugs (fluticasone, beclomethasone, and budesonide) in Erbil province, post-war Iraq.

2. Management with three asthmatic drugs (fluticasone, beclomethasone, and budesonide) does not provide different clinical outcomes in asthmatic patients before and after the war in Erbil province, post-war Iraq.

3. There are no differences in knowledge, attitude, and practice among asthmatic patients before and after health education intervention in Erbil province, post-war Iraq.

Alternative Hypothesis:

1. There are differences in the quality of life of asthmatic patients before and after management with three asthmatic drugs (fluticasone, beclomethasone, and budesonide) in Erbil province, post-war Iraq.

2. Management with three asthmatic drugs (fluticasone, beclomethasone, and budesonide) provided different clinical outcomes in asthmatic patients before and after the war in Erbil province, post-war Iraq.

3. There are differences in knowledge, attitude, and practice among asthmatic patients before and after health education intervention in Erbil province, post-war Iraq.

CHAPTER TWO

LITERATURE REVIEW

2.1 General scope of literature review

This literature review's ultimate purpose was to explore the quality of life of asthmatic patients as well as diagnostic and management criteria, knowledge, attitudes, and practices surrounding improved asthma control. This chapter provides an overview of the condition known as asthma, including its pathophysiology and natural history, in addition to the operational definitions of asthma that are typically applied in epidemiological research. A description is given of the phenotypes and severity of asthma, in addition to the prevalence of asthma (both globally and locally). There is a presentation of literature that explains asthma and the risk factors that are related to it. Finally, we investigated the relationship between asthma and health quality of life as well as the efficacy of inhaled corticosteroids on asthma patients, using a variety of literature for health education programs geared toward asthma patients in order to improve their ability to avoid asthma attacks.

2.2 Searching methods

This study's literature review drew on information from a variety of sources, including peer-reviewed journal articles, textbooks, review articles, consensus recommendations, conference attendance, and internet resources. Updated searches were done, and the literature review was updated as needed. To discover research that analyzed asthma,

PubMed, Embase, Google Scholar, Science Direct, and Web of Science search engines were used. The scope of the search was expanded to include asthma severity and diagnostic patterns. combinations of key words like "war conflict," "Iraq," "Middle East," "endotoxin," "asthma," "severity," "phenotypes," "diagnostic patterns," "lung function," "FEV1," "FVC," "asthma risk factors," "burden of asthma," "asthma care and management," "access to care," "quality of life," and "Asthma quality of life questionnaire". The majority of the publications chosen were peer-reviewed, but technical reports, executive summaries, and hearings were also included if they contained relevant information. The following criteria were used to analyze the selected articles: studies written in English; studies containing data and materials relevant to any of the study objectives; and studies published within the last 50 years. Most of the papers that were chosen came from different countries and were either cohort studies or cross-sectional studies.

2.3 Natural course of asthma and wheeze

The natural history or course of the disease refers to the normal course of expression of symptoms of asthma over time, whether by remission, relapse, or increasing severity [83]. According to the existing longitudinal research, the symptoms of asthma and wheezy illnesses exhibit temporal patterns, altering significantly over time in the course of life. According to research, children who have asthma symptoms (such as wheezing) early in life may have a different experience with the condition later in life [84]. In rare circumstances, the illness may entirely resolve (known as remission), resolve temporarily and reoccur (known as relapse), or persist into adolescence and adulthood (known as

persistent) [85]. Each of these groups has different risk factors, and there is some overlap between them.

Longitudinal studies exploring the natural history of asthma and wheeze have revealed several phenotypes depending on the emergence of wheeze and asthma based on the life course patterns of asthma. The Tucson Children's respiratory birth cohort study, conducted from 1980 to 1984 in Arizona, USA, is one of these studies[86, 87]. This study included 826 children from the original 1,246 births between 1980 and 1984 who had complete follow-up data at three and six years of age. Based on their wheezing history, children were observed to fall into one of four clinically distinct wheezing categories (or three temporal patterns): never wheeze (51.5 percent); transient wheezing (19.9 percent) defined as children who had 1 lower respiratory tract illness (LRTI) with wheezing during the first 3 years but no wheeze at 6 years of age]; late-onset wheezing (15 percent) defined as children with no episodes of wheeze [88].In addition, compared to never wheezed children, persistent wheezing children were more likely to have allergic sensitization, maternal smoking, and mothers with asthma history during the first year of life, whereas transient wheezing children were more likely to have mothers who smoked but not mothers with asthma history. In two other cohort studies, the same thing was found: most kids who wheezed when they were young (preschool age) grew out of it by the time they were in school, but those who wheezed for a long time were more likely to get asthma when they were in school [89, 90].

While the majority of infants with wheezing are transient wheezers who will outgrow the condition by school age, other evidence from the Tucson study suggests that after infancy, both transient and persistent wheezing may continue to experience a significant decrease

in lung function into adolescence, signaling a negative respiratory outcome and a predisposition to asthma later in life [88]. Children were followed up on from the age of six to sixteen in this study, which was nested within the Tucson study. Late-onset and persistent wheezers were both more likely than never wheezing to continue wheezing from the age of 8 to 16 years {RRs = 3.12; 95 percent CI: 2.5-3.9 (late-onset wheezing) and 3.8; 95 percent CI: 3.1-4.7 (persistent wheezing)}The decreased lung function found in both transitory early wheezing and persistent wheezing at age 6 years in the Martinez et al study was maintained at ages 11 and 16, with these groups of children having significantly worse lung function compared to those who had never wheezed [88]. Furthermore, persistent wheezers were more atopic at ages 11 and 16 years, as previously shown at age 6.

These investigations, taken together, demonstrated a multitude of temporal patterns of asthma-related symptoms ranging from preschool to adulthood, implying a different etiology for wheeze and asthma in children. Although asthma can start at any age, most asthma-related symptoms (e.g., wheezing) occur in the first few years of life, particularly in infancy, and may be connected with allergic sensitization, whereas wheezing situations after preschool age are more likely to be non-atopic [91].

2.4 Risk factors for asthma patients

2.4.1 Gender and age

As was indicated earlier in the course of the conversation about the natural history of asthma, the vast majority of cases of asthma begin in early infancy, with children who have asthma having their first episodes prior to the age of six years old [92]. At this point

in life, the incidence and prevalence of asthma are higher in boys than in girls, although the difference is not statistically significant. This pattern persists until approximately the time of puberty, at which point it begins to reverse, with a larger prevalence of asthma being shown in females [1, 93]. Although the mechanisms that underlie the gender shift in the prevalence of asthma are not fully understood, some of the possible explanations that have been proposed include an increase in the incidence of asthma coupled with a decrease in the remission of asthma in females compared with males during adolescence. This has been suggested as one of the possible explanations [49, 94].

2.4.2 Family history of asthma and allergy

Children who come from families with a history of asthma have a greater risk of developing the condition themselves. Other studies showed that the risk of developing early-onset persistent asthma was increased by a PR of 12.1, early-onset transient asthma by a PR of 7.51, and late-onset asthma by a PR of 5.38 when there was a family history of asthma and allergies [95]. Due to the fact that asthma tends to run in families, it is possible that a child's positive family history could be utilized to determine whether or not they are likely to get asthma [96].

2.4.3 Obesity

Obesity has been linked to asthma in adults, adolescents and children who are of school age. A five-year study conducted in Southern California found these correlations among all age groups [97]. Similarly, a study conducted in Germany indicated that the prevalence of asthma that was identified by a **physician** was 2.5% for normal weight, 5.8% for who were overweight, and 10.3% for who were obese [28]. In another study, obesity was found

to be linked with airway hyperresponsiveness [98]. Studies have shown that people who are obese are more likely to have asthma that is both more severe and more difficult to treat. This suggests that obesity may have a particularly significant role in severe asthma [99]. A recent study that looked at the relationship between asthma and obesity found that, in addition to making asthma symptoms more severe, being overweight or obese was related to less effective management of asthma symptoms and a reduced therapeutic response compared to people of normal weight [100].

2.4.4 Race/ethnicity and Socio-economic status

Multiple studies have found a connection between ethnicity and asthma as another probable risk factor. It is considered that patients who belong to a particular ethnicity or group have a higher prevalence, morbidity, and severity of asthma than patients who do not belong to that group[101, 102]. The low socioeconomic position of a community has led to further speculation that the association between underprivilege race and asthma may be complicated by socioeconomic status, resulting in a disproportionately high burden of asthma among the less privileged group [102]. It also suggests that certain ethnic groups may be disproportionately affected by asthma.

2.4.5 Pet exposures

There is a lack of consistency in the correlations between exposure to pets and asthma. Pet ownership has been shown in certain research to be protective against asthma [103]. while other research has shown it to be a risk factor for asthma [104](44). According to a pooled study of 11 birth cohort studies conducted in Europe, there was no correlation observed between having pets as young children and asthma in school-aged children

[105]. A comprehensive analysis [106] of 17 birth cohort studies of cat and 13 birth cohort studies of dog exposures during infancy found no effect on the development of asthma or wheezing symptoms .In addition, it was discovered that people who were exposed to dogs while they were infants were protected from acquiring sensitivity to aeroallergens . Early cat exposure was found to have a positive association with allergy sensitization to cats as well as wheeze in a large cross-sectional study that was conducted by Roost et al. and included 35 centers located in 16 different countries [105]. It may be difficult to demonstrate consistently connected links between owning a pet and respiratory disease due to the possibility of selection bias or the failure to analyze the effects of interaction.

Even though the effects of pet exposure on the development of asthma can be hard to predict, pet exposures are substantial risk factors for asthma severity in children who already have asthma and are susceptible to it [107].

2.4.6 Smoking

There has been a consistent link established between pregnant mothers' smoking and increased wheezing in children as well as the likelihood of developing food allergies [108]. A dose-response relationship exists between early-life exposure and a reduction in airway diameter, and this relationship is dose-dependent [109]. It has been shown that there is a connection between prenatal maternal smoking and cytokine response in the cord blood [110], as well as nitric oxide concentration in the exhaled air in infants [111]. The water pipe, sometimes called the hubbly-bubly or the narguile, is a method of inhaling cannabis that is exclusive to the Kurdistan area of Iraq [112]. The use of waterpipes is on the rise all over the world, but it is particularly prevalent in the Eastern Mediterranean

region [113]. In this part of the world, women and children are frequently encouraged to use waterpipes due to misguided beliefs regarding the safety and health risks associated with this practice [114]. There is preliminary evidence that water pipe smoking is linked to a variety of life-threatening conditions, including pulmonary disease, coronary heart disease, and pregnancy-related complications [115]. Another studies supported the hypothesis that[116]. There was also evidence that secondhand smoke, often known as SHS, played a significant part in the development of asthma. However, it is conceivable that the interplay between genes and the environment has a significant role in the impact of air pollution on the development of asthma. Recent research has shown that infants whose mothers smoked during pregnancy were more likely to have an unfavorable genetic predisposition to asthma, and this susceptibility also depended on the infant's ancestry. PM10 exposure was also related to a higher risk of asthma in infants [117].

There may be a transgenerational impact of prenatal tobacco smoke exposure on the development of asthma, as evidenced by the fact that a grandmother's smoking during pregnancy with the mother raises the risk of asthma in the grandchild regardless of whether or not the mother smokes herself [118]. In addition, prenatal paternal smoking exposure was associated with the development of childhood asthma at the age of 6, and this association appeared to be mediated by a mechanism independent of IgE. Through cytosine-phosphate-guanine (CpG) methylation, prenatal paternal smoking leads to epigenetic alterations in some genes, such as LIM Domain Only 2 (LMO2) and interleukin-10 (IL-10), and these modifications are connected to the development of asthma in children [119]. There is a lack of consistency in research that focuses purely on postnatal exposure, which is one of the constraints associated with the investigation of the

effect of postnatal exposure. The fact that the majority of parents smoke during both the prenatal and postnatal periods is another disadvantage. A recent study found that the smoking habits of fathers before their children reached the age of 15 increased the risk of asthma in those children, even if the children did not suffer from nasal allergies. This finding suggests that the pre-adolescent environments of fathers have an effect on the subsequent generation [120].

2.4.7 Stress

Studies have led researchers to the conclusion that maternal prenatal stress lowers the infant's cortisol level via regulating the offspring's hypothalamic–pituitary–adrenal–axis. This modulation may be linked to the formation of an allergic phenotype. Although there is a link between caregiver stress, an elevated level of immunoglobulin (Ig) E in babies, and early wheezing [121]. Rosenberg and colleagues demonstrated that there is substantial evidence to support a connection between the presence of chronic psychosocial stress and the development and progression of asthma [122]. Alterations in neuroendocrine pathways, in addition to immunologic mechanisms, are likely to be involved in these effects, and specific signal transduction pathways through which stress modulates epigenetic and transcriptional activity in asthma-relevant cells have been suggested. Both of these mechanisms are likely to be at play [122, 123].

In spite of the fact that the disruption of the hypothalamic-pituitary-adrenal [36] axis is the one that has received the most attention from researchers, recent findings reveal that hormonal or neuroendocrine abnormalities are not necessary for autonomic imbalance or dysfunction to exist. The disruption of these key stress systems in the mother as a result