Original Article

DESCRIPTION OF RISK FACTORS AMONGST ASTHMA PATIENTS WHO WERE INTUBATED IN CWM HOSPITAL FROM JANUARY 2012 TO DECEMBER 2014

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ABSTRACT

Introduction

Risk factors for life-threatening asthma resulting in intubation and ventilation are well documented in the international literature. Patients and health systems differ and it is not known whether such risk factors apply to the Fijian population. This study documents the prevalence of risk factors and describes the outcomes of patients who were intubated for severe asthma in Suva, Fiji.

Methods

Retrospective descriptive study of patients intubated for asthma at the Colonial War Memorial Hospital between December 2012 and January 2014

Results

There were 53 patients with 64 intensive care admission episodes. There were equal numbers of males and females. Regarding the risk factors identified from other studies, 75% of our study population reported increased beta agonist use and 32% reported increased inhaled steroid use. 68% had previous hospital admissions for asthma and 23% had been previously intubated. Twenty-one percent of the patients died during admission. Most deaths were due to hypoxic brain injury following cardio-respiratory arrest on presentation to hospital. At one year follow up, 15% of the discharged patients had died and 4 % had suffered another severe asthma attack resulting in intubation.

Conclusion

Internationally-reported risk factors were present in similar proportions in our study population. This suggests similar strategies should be employed to reduce morbidity and mortality from asthma in Fiji. These include: improving asthma education among patients and clinicians, increasing utilization of preventer medications, use of a spacer devices and asthma action plans.

Keywords: Severe Asthma, Risk Factors for Intubation

INTRODUCTION

It is estimated by the Global Initiative for Asthma (GINA) that as many as 300 million people of all ages and all ethnic backgrounds suffer from asthma and that the economic burden of this disease is increasing worldwide(1). The American Lung Association has reported a decline in the mortality rate from asthma in the United States of America, as asthma care has improved through use of evidence-based asthma patient education, use inhaled quidelines, of corticosteroids and outpatient follow-up care(2) Similar trends have been noted in other developed countries, such as Australia, where asthma remains prevalent but where the mortality rate has declined from 4.8 (1980's) to 1.5(2011) per 100 000(3).

Asthma is no longer considered a disease of high income countries as was once thought, with high prevalence and mortality rates being found in low and middle-income countries(4). There is no published literature documenting prevalence and mortality rates due to asthma in adults in the South Pacific Region. A study carried out in 1994 by Flynn et Al (5) found out that the prevalence of wheeze was approximately 20% amongst children in Fiji. They investigated ethnic based differences in asthma prevalence amongst children in Suva, with no significant differences reported. How this relates to asthma prevalence in adults in Fiji is uncertain. A recent report by the Global Asthma Network in 2014(6) revealed that Fiji has an alarmingly high age-standardized mortality rate for asthma, which is the third highest in the world.

The presence of asthma stations at all the health facilities across Fiji, suggests that the disease is omnipresent across the population. Symptoms of asthma are often downplayed by patients. In addition, health care practitioners frequently do not manage asthma according to evidence-based guidelines. Asthma stations have allowed for the establishment of a "help yourself

nebulizer culture." Patients will present to health facilities, request medication and return home, without a thorough assessment and without management being tailored specifically to them. This leads to suboptimal disease control, with patients at high risk for rebound attacks, sometimes resulting in tragedy. This is despite evidence that timely clinician-directed medical intervention, together with patient education at emergency departments and discharging patients with asthma action plans, improves quality of life, reduces hospital admissions and reduces mortality rates (7) which was found in countries across Europe, Asia and America. Patients who are intubated for severe asthma, have a 10% to 20% higher mortality rate when compared with other causes of mortality amongst intubated patients in the Intensive Care Unit (8). Identification of risk factors associated with intubations provides clinicians with a valuable tool to predict at-risk patients, and thus target management strategies to prevent mortality.

Lack of continuity of care, non-compliance with medical treatment, previous hospital admissions and a history of intubations are some of the risk factors for intubation which have been found elsewhere in the world (9)(10). However, despite the high prevalence of asthma, the prevalence of these risk factors in the Fijian population was not previously known.

Since the conception of the Emergency Medicine program in 2012, the emergency department at CWMH, under the guidance of program director Dr. Anne Creaton, has attempted to shift towards the utilization of evidencebased guidelines for common conditions. Asthma is one such disease that results in large numbers of patients presenting to the emergency department. As such, in 2013 an asthma care pathway was developed and approved for implementation by the National Clinical Services Network committee for Emergency Medicine. The pathway aimed to standardize triage to ensure accurate classification of asthma severity, management in accordance to severity classification and the early administration of systemic corticosteroids. Patients were also referred to a physiotherapist for asthma education and follow-up.

Patients presenting to the emergency department with severe life-threatening asthma bypass triage and are rushed to the resuscitation area, where they receive immediate maximal therapy. A small number of patients (n = 21/year) deteriorate despite maximal therapy, requiring intubation and mechanical ventilation. The decision to intubate is a clinical one. Indications include: respiratory or cardiac arrest, altered conscious state and fatigue. Intubated patients are then transferred to the intensive care unit for ongoing management.

The implementation of the asthma clinical pathway has assisted with the classification of asthma severity at

triage, the early administration of oral prednisolone and the identification of those patients that need to be reviewed by doctors immediately. This has been a change from previous practice where nurses would give the nebulisers and allow patients to leave as they please without insisting to be assessed by a medical officer. Another significant change in the management of the patients is the use of magnesium sulphate, which is reserved for severe asthma episodes only. With improved emergency management of asthma exacerbations, the department began to look into factors that may prevent future attacks, such as poor inhaler technique and lack of an asthma action plan.

To further strengthen these initiatives in the fight against asthma, the identification of risk factors which predispose individuals to intubation is vital. A history of hospital admissions for asthma, lack of inhaled corticosteroid use and recent increased salbutamol use are some of the risk factors found amongst intubated patients in other countries(10)(9)(12) This study looked at the prevalence of these risk factors amongst patients with severe asthma that were intubated in Fiji.

Problem Statement

The death rate from asthma in Fiji is shockingly high. The 2014 Global Asthma Network (6) has ranked Fiji as having the third highest age-standardized death rate in the world for the age group of 5 to 34 years.

Asthma can be described as the "forgotten noncommunicable disease" in Fiji. This is because it is overshadowed in public health policy and resource allocation by diabetes, hypertension, obesity and heart disease. This is further compounded by the fact that symptoms and severity are underplayed by patients and clinicians alike, leading to under-recognition and underreporting of the extent of the problem (13). Lack of readily available data means that policy makers fail to prioritize asthma care in strategic initiatives and resource allocation. We believe that the combination of these factors contributes to the high mortality rates from asthma in Fiji.

Data from the three largest hospitals in Fiji (CWM Hospital, Lautoka and Labasa) (14) indicate that a total of 2285 patients were admitted with asthma from 2011 to 2014. The inpatient mortality rate for these patients was 6.6%. Asthma deaths in Fiji reached 170 patients (4.15% of total deaths) in 2011.

Risk factors for asthma mortality have been described in previous studies, in both high and middle income countries. It is not known whether these risk factors are present in the same proportions in our population. In order to be able to predict which patients are at a high risk of dying due to severe asthma in Fiji, documentation of these risk factors is a crucial first step. This will inform the development of a tool that will enable frontline clinicians to be able to predict which patients are at a high risk of dying due to asthma and thus be able to take necessary actions to avert bad outcomes.

This study will describe those risk factors amongst asthma patients who required intubation due to severe asthma in CWM Hospital between the periods of January 2012 to December 2014.

AIMS & OBJECTIVES

In the cohort of patients intubated for asthma and admitted to the intensive care unit of CWM Hospital between January 2012 and December 2014 to:

1. Describe the socio-demographics of this group

2. Describe the prevalence of internationally-documented risk factors for life-threatening asthma.

3. Describe the outcomes of these patients (hospital length of stay, mortality rate and ate of readmission to ICU)

METHODOLOGY

A consecutive sample of all patients aged 18 and above who were admitted in the Intensive Care Unit with a diagnosis of asthma at CWM for the period of January 2012 to December 2014 were included.

This information was cross checked with information from the Patient Information System (PATIS.)

Admission episodes for asthma were screened for exclusion criteria

Patients with a diagnosis other asthma were excluded as stated in Table 2. Some patients had more than one admission episode in the study period and only patients

Table 1.Inclusion and Exclusion Criteria				
Inclusion Criteria	Exclusion Criteria			
Age > 18 years Primary Diagnosis of Asthma Intubated	Not Intubated Hypertension Ischemic Heart Disease Diabetes Mellitus Chronic Kidney Disease Chronic Obstructive Pulmonary Disease Congestive Cardiac Failure			

were studied.

Patient folders containing the medical record) of identified patients were obtained from the medical records department. Parameters obtained from the medical record such as demographics and risk factors are listed below

A preformed data sheet was used to record variables found in the medical record and data was transferred to an excel spreadsheet.

Outcome parameters were also recorded. These included outcome at discharge from ICU (dead or alive) and status at one year (dead, readmission to hospital, readmission to ICU).

Information that was not able to be identified from the patient record was obtained by contacting the patient and/or relative, for example information regarding employment status and previous medication usage.

Parameters Collected From the Patient Record

- Age
- Gender
- Ethnicity
- Employment status

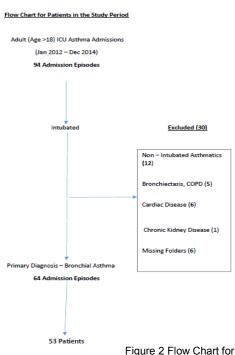
Clinical Parameters

- Previous intubation due to asthma
- Any hospitalization due to asthma
- Increased use of beta agonist (> 1 inhaler per month)
- Increased steroid use (inhaled or oral)
- Increased use of oral theophylline

Outcome Parameters

- Discharge and death
- Readmissions within one year

The data forms were stored securely and the information was stored in an excel spreadsheet. Proportions were calculated and the data is presented as tables and s.



Patients in the study period

Table 2: Patient Characteristics of Intubated Patients				
	N (%)			
Age				
18 – 23	4(7%)			
24 - 39	22(41.5%)			
40 – 55	25(47.1%)			
>55	2(3.7%)			
Gender				
Male	26(49%)			
Female	27(51%)			
Employment				
Yes	28(52%)			
No	25(48%)			
Ethnicity				
iTaukei	25(48%)			
Indian	21(40%)			
Others	7(12%)			

RESULTS

The ICU register contained 94 admissions with a diagnosis of asthma during the study period. Of these, 12 were not intubated and were excluded.

12 patients were excluded as they were found to have a diagnosis other than asthma.

6 folders were missing

10 patients had been readmitted thus 53 patients were included in the study.

Risk Factors

Prevalence of Risk Factors is shown in table 3

68% of the study population had been admitted previously for asthma.21% had been previously intubated at CWM hospital.

Medication Usage

75% of the patients had used more than one canister of beta agonist inhalers in the month prior to intubation. For 13%, beta agonist use was not known due to missing data.32% of patients were taking oral corticosteroids 23% were taking inhaled corticosteroids. In 30%, steroid use was not known.

At the time of intubation, 4% were taking theophylline, 55% were not taking theophylline and for 41% it was not known.

Outcome Parameters

Figure 2 shows outcomes following ICU admission.

21 %(n= 11) of the study population died in ICU during their admission. 6 patients had CPR prior to intubation and 5 patients had hypoxic brain injury which was diagnosed by patients not waking up after cessation of sedation

Of 79 %(n=42) of the patients that were discharged, 4 %(n=2) were readmitted to ICU within the same year whereas 24% of the patients were admitted to the general ward within one year of being discharged home.

	-		
Risk Factor	Yes N (%)		Not Known N (%)
Previous Hospitalization	36(68%)	17(32%)	1(0.1%)
Previous Intubation	11(21%)	42(79%)	0(0%)
Increased use of Beta Agonist (> 1 per month)	40(75%)	6(11%)	7(13%)
Oral steroid Used	17(32%)	20(38%)	16(30%)
Increased inhaled Corticosteroid use	12(23%)	25(47%)	16(30%)
Increased use of oral Theophylline	2(4%)	29(55%)	22(41%)

Table 3: Prevalence of risk factors in Intubated Patients

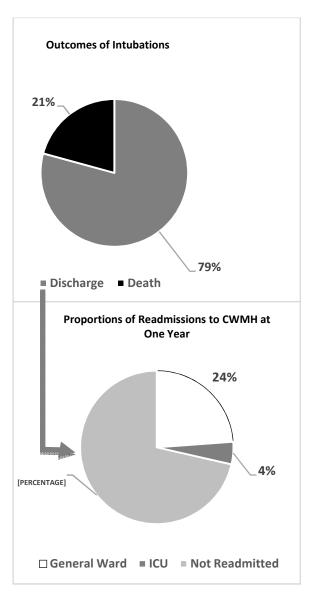


Figure 3: Outcome Parameters of Intubated Patients Readmissions to CWMH at one year

DISCUSSION

This study is the first to describe the sociodemographics, risk factor prevalence and the outcomes for patients intubated for asthma in Fiji at the CWM Hospital.

The study group contained an equal number of males and females. The international literature is conflicting with several studies reporting an increased prevalence amongst females (28) other studies reporting a male predominance (29) and others showing no difference (30).

The prevalence of different ethnic groups in this study reflected that of the general Fiji population.

The majority (85%) of the study participants lived in the Suva-Nasinu area which is an urban centre with one of

the highest population densities in Fiji. Overcrowding with concomitant higher exposure to infectious pathogens such as respiratory viruses, and air pollution are known to trigger asthma attacks in susceptible individuals.

88% were aged under 55 year (the age of retirement from public service in Fiji) with 46% aged less than 40.52% were employed at the time of ICU admission. These findings allude to the effect of asthma on the workforce. When a disease affects young, working adults it represents an important economic burden to the country.

Asthma care and management worldwide incurs significant healthcare expenditures associated with both direct costs such as the cost of hospitalization and cost of medications and indirect costs such as loss of work days and productivity annually (31).

75% of the intubated patients admitted to the ICU at CWMH in this study were found to have an increased use of beta agonists prior to admission which was defined as using more than one canister of inhaled beta agonist in one month. D.A Campbell et al (32) carried out a comparison between the severe asthmatics presenting to the emergency departments and those that died of asthma within a period of 5 years They found that both the groups studied had significantly high proportions (88% and 82% respectively)had an increased beta agonist use. Similarly, Al-Dorzi et al (29) who studied risk factors amongst asthma patients admitted with severe asthma who required intubation and mechanical ventilation in Riyadh, found that there was a high proportion of rapid acting beta agonist use in both the intubated patients (86.4%) and the patient group (72.1%) who were admitted in the ward for asthma within a period of 4 years. Increased use of reliever medication has been associated with deteriorating asthma control and an increased risk of severe asthma exacerbations. The Global Initiative for Asthma (GINA) has therefore included the frequency of beta agonist use as one of the indicators in the classification of deteriorating asthma control. The introduction of inhaled corticosteroids is vital in controlling the airway inflammation even in mild intermittent asthma. Doses of corticosteroids are increased in a stepwise manner until asthma is controlled i.e. less than 3 episodes of asthma exacerbation per week. This is highly effective in reducing the risk of asthma exacerbations, hospitalization and death if used daily in low doses (6).

This study found that only 23% of the intubated patients had been using inhaled corticosteroids in the 3 months preceding the episode of life threatening asthma. Low rates of inhaled corticosteroid use have been demonstrated in other studies of life threatening asthma, (13.6%) in the study from Riyadh by Al-Dorzi (29).

Other medications commonly used in asthma are oral corticosteroids and oral theophylline. In this study the proportion taking oral corticosteroids was 32% which is greater than inhaled corticosteroid (23%) and theophylline (4%).In some cases, patients prefer oral over inhaled corticosteroids due to greater perceived benefit. There is often poor understanding of the importance of inhaled corticosteroids in preventing an attack and hence patients focus exclusively on reliever medication and oral corticosteroids during exacerbations. In some, worsening of symptoms despite inhaled corticosteroid use may have prompted oral steroid use. It may also indicate steroid dependency from ongoing airway inflammation even with therapy being stepped up which has been found to be a risk factor for intubation in a study by Dhuper et al (12).

Previous hospitalization and a history of intubations serve as markers for risk of near fatal and fatal asthma (33)(12)(10). In this study, both of these risk factors were found in significant proportions. Out of the 53 participants in the study, 67.9% were previously hospitalized for asthma exacerbations either in the general medical wards or ICU at a health facility in Fiji and 20.7% had previously been intubated. In a 10 year study of mechanically ventilated asthmatic patients conducted at Ben Taub General Hospital in USA, 55% of the population studied had a previous history of hospitalization from asthma exacerbations and 39% reported a history of intubation (9). These findings correspond with those of Dhuper et al (12) who found that in comparison to the non-intubated asthma patients, the intubated group had a higher proportion of previous intubations which led them to conclude that a history of previous intubations is a risk factor for another similar event. In contrast, Al-Dorzi et al (29) noted that only 2% of the intubated patients in their study had a history of previous intubations. This, they attributed to near fatal asthma with intubations being uncommon in Riyadh with only 30 admissions over a span of 5 years even though this was the main referral hospital within the area.

There were 11 deaths amongst the 53 intubations for asthma. The mortality rate of 21% is comparable to that of international studies in both high and middle income countries.(9). 6 of the 11 patients presented in cardiac arrest due to asthma and 5 patients had hypoxic brain injury which was defined as patients not waking up after the cessation of sedation, thus none of the deaths were ventilator related complications. Hypoxic brain injury has been reported in other studies as one of the common causes of death following intensive care admission for asthma (34)(10).

CONCLUSION

Asthma is a reversible airways disease that can be controlled with cost effective interventions and affects

mainly the economically productive population of the country. Fiji's asthma death rate is third highest in the world. Many of these deaths are avoidable. There is an overreliance on reliever medications and low utilization of preventer medications. Risk factors that identify patients at risk of intubations and death identified internationally include increased beta agonist use, low rates of inhaled corticosteroid use, previous hospital admission for asthma and previous intubation for asthma.

These risk factors are present in similar proportions in this study.

STRENGTHS & LIMITATIONS OF THE STUDY

This was a single centre study performed in an area of high population density which is not representative to the rest of the country. This may mean that results cannot be extrapolated to the nation as a whole. However, given the level of agreement with international studies this is unlikely to be the case.

The retrospective design and use of chart review is likely to have introduced information bias. The investigator relied upon interpreting what was written in the medical record which may not have reflected the true situation and data was incomplete for some patients. Much of the information recorded in the medical record relied on information from family members as intubated patients cannot be questioned. The quality of the information would be dependent on the knowledge and recall of the relatives.

The principal investigator performed all data extraction and coding and may have been a source of bias, as he was not blinded to outcomes and may have unknowingly introduced bias when interpreting what was written the medical record.

Ten percent of folders were missing and this may introduce selection bias. It must be noted however that a 90% folder retrieval rate is exceptionally high for a study of this type.

RECOMMENDATIONS

Three action areas address the risk factors identified in this study.

1. Asthma Education and Awareness

Education about asthma, prevention of attacks and the medications used to control symptoms should be disseminated at the community level. This has been started by celebrating world asthma day and disseminating information using radio and televisions talkback shows. Other avenues that should be explored include use of the internet. The Fiji ministry of health website now contains information about asthma.

Nursing initiatives should be implemented to empower and educate patients

2. Health Care Providers

The culture of 'three nebulisers' and the asthma stations needs to be eliminated to ensure all patients are assessed by appropriately-trained clinicians. Medical, nursing and nurse practitioners need to implement evidence based practice in the management of asthma. The use of spacers and asthma action plans need to be encouraged for all patients.

3. Policy Makers

More attention, resources and strategies need to be applied to the forgotten NCD. The high mortality rate, bed days and money spent is a substantial burden on our country's economy. There needs to be high level support for evidence based interventions and national asthma training for all levels of clinician's.

Data collection and reporting of asthma deaths should be implemented. Deaths from asthma could be added to other key performance indicators for non-communicable disease in the next Ministry of Health strategic plan.

REFERENCES

- Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. [Online].; 2016 [cited 2016 October 11. Available from: http://ginasthma.org/.
- Rebuck AS. The global decline in asthma death rates: can we relax now? Asia Pacific Allergy. 2013 March; 3(3).
- Australian Institute of Health and Welfare. Asthma in Australia with a focus chapter on chronic obstructive pulmonary disease. Publication. Canberra: Australian Institute of Health and Welfare, Australian Centre for Asthma Monitoring; 2011. Report No.: 1448-7594.
- The International Union Against Tuberculosis and Lung Disease. Asthma the Neglected Epidemic. In 44th World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease; 2013; Paris. p. 330 - 332.
- G FM. Respiratory symptoms of rural Fijian and Indian children in Fiji. Thorax. 1994 March; 49(12).
- Global Asthma Network. The Global Asthma Report 2014. Report. Auckland: Global Asthma Netowrk, The Global Asthma Network; 2014. Report No.: 978-0-473-29125-9.
- Gibson , Powell H, Wilson A. Self-management education and regular practitioner review for adults with asthma. Cochrane Database Systematic Review. 2002 July; 3(CD001117).
- Shapiro JM. Intensive Care Management of Status Asthmaticus. Chest. 2001 November; 120(5).
- Christina C, Jain S, Kalpalatha K, Bandi G. Mechanical Ventilation for Asthma: A 10 - year experience. Journal of Asthma. 2009 July; 45(7).
- Alvarez G, Schulzer M, Jung D, Fitzgerald J. A Systematic Review of Risk Factors associated with Near Fatal and Fatal Asthma. Canadian Respiratory Journal. 2005 July; 5(12).
- Ministry of Health and Medical Services. Annual Report. Annual Report. Suva: Fiji National University, Health Information Unit; 2014. Report No.: 25.
- 12. Dhuper S, Maggiore D, Shim C. Profile of Near-Fatal Asthma in an Inner-City Hospital. Chest. 2003 November; 124(5).
- Pierre L, Laberge A, Lebel , Boulet LP, Marie , Pierre , et al. Cartography of Emergency Department Asthma visits for Asthma -Targeting High Morbidity Populations. Canadian Respiratory Journal. 2004 November; 11(6).
- 14. Ministry of Health Fiji. The Fiji Islands Health System Review. Review. Suva: Fiji National University, Department of Health

Information; 2014. Report No.: ISBN 978 92 9061 543 9.

- Gupta D, Keogh B, Chung KF, Ayres JG, Harrison DA, Goldfrad, et al. Characteristics and outcome for admissions to adult, general critical care units with acute severe asthma: a secondary analysis of the ICNARC Case Mix Programme Database. Critical Care. 2005 September; 9(3).
- Omachi T, Iribarren C, Sarkar U, Tolstykh I, Yelin E, Katz P. Risk Factors For Death Among Adults with Severe Asthma. Annals Allergy Asthma Immnuology. 2008 August; 2(101).
- Comino E. Asthma mortality in Australia 1960 -2008. Report. Sydney: University of NSW, UNSW Research Centre for Primary Health Care and Equity; 2010.
- Ministry of Health, Fiji. Annual General Report 2011 13. Annual General Report. Suva: University of Fiji, Department of Health Information; 2013.
- Smith J, Mildenhall S, Noble M, Mugford M, Shepstone L, Harrison B. Clinician-Assessed poor compliance identifies adults with severe asthma who are at risk of adverse outcomes. Journal Of Asthma. 2005 May; 42(6).
- Lacasse Y, Archibald H, Ernst P, Boulet L. Patterns and determinants of compliance with inhaled steroids in adults with asthma. Canadian Respiratory Journal. 2005 May; 4(12).
- Mayo PH, Richman J, Harris W. Results of a program to reduce admissions for adult asthma. Annals of Internal Medicine. 1990 June; 112(11).
- Eder W, Markus J, Erika V. The asthma epidemic. New England Journal of Medicine. 2006 November; 4(355).
- Robertson C, Heycock E, Bishop J, Nolan T, Olinsky A, Phelan P. Prevalence of asthma in Melbourne school children : changes over 26 years. British Medical Journal. 1991 May; 302(6785).
- Reddel H, Cooper S, Guevara-Rattray E, Ampon R, Marks G. Asthma Control in Australia 1990 -2011. Research. Sydney: University of Sydney, Woolcock institute of Medical Research; 2013.
- Royal College of Physicians. Why asthma still kills. Confidential Enquiry Report. England: Royal College of Physicians, The National Review of Asthma Deaths(NRAD) ; 2014. Report No.: ISBN 978 1-86016-531-3.
- Ruben D, Peters J. Near-Fatal Asthma: Recognition and Management. Current Opinion Pulmonary Medicine. 2008 January; 1(14).
- Al-Ghamdi Badr R, Taklu Bayu G. Acute life threatening asthma in Asia central hospital. Journal of Family and Community Medicine. 1997 January; 1(4).
- Van der Merwe L, de Klerk A, Kidd M, Bardin PG, van Schalkwyk EM. Case-control study of severe life threatening asthma (SLTA) in a developing community. Thorax. 2006 September; 61(9).
- Al-Dorzi H, Haifa A, Arabi Y. Risk factors, management and outcomes of patients admitted with near fatal asthma to a tertiary care hospital in Riyadh. Annals of Thoracic Medicine. 2014 Jan; 9(1).
- Trawick D, Holm C, Wirth J. Influence of gender on rates of hosptalisation, hospital course, and hypercapnia in high risk patients admitted for asthma: a 10 year retrospective study at Yale - New Haven Hospital. Chest. 2001 March; 119(6).
- Bahadori K, Doyle-Waters MM, Carlo , Lynd L, Alasaly K, Swiston J, et al. Economic burden of asthma: a systematic review. BMC Pulmonary Medicine. 2009 May; 9(24).
- Campbell DA, Mclennan G, Coates JR, Frith PA, Gluyas PA, Latimer KM, et al. A comparision of asthma deaths and near -fatal asthma attacks in South Australia. European Respiratory Journal. 1994 March; 420(7).
- 33. Mcfadden ER, Warren EL. Observations on asthma mortality. Annals of Internal Medicine. 1997 July; 127(2).
- Zimmerman J, Dellinger R, Shah A, Taylor R. Endotracheal intubation and mechanical ventilation in severe asthma. Critical Care Medicine. 1993 November; 21(11).
- Ulrick C, Frederiksen J. Mortality and markers of risk of asthma death among 1075 patients with asthma. CHEST. 1995 October; 12(105).
- Fanta C, Rossing T, Mcfadden E. Emergency room treatment of asthma. The American Journal of Medicine. 1982 March; 72(3).
- Flynn MGL. Hospital admission rates for asthma and pneumonia in Fijian and Indian children. Journal of Paediatrics and Child Health. 1994 February; 30(1).
- Poulos L, Cooper S, Ampon R, Reddel H, Marks G. Mortality from Asthma and COPD in Australia. Annual Report. Canberra: Australian Insitute of Health and Welfare, Australian Insitute of Health and Welfare; 2014. Report No.: ISBN 978-1-74249-600-9.