EVALUATION OFCOMMUNITY ACQUIRED PNEUMONIA TREATMENT OUTCOMES AND COST OF ILLNESS
AND
DEVELOPMENT OF MORTALITY MODEL

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by

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DEDICATION

This work is dedicat to the people in my life that I appreciate and love more than words can say:

My mother, Anisah Shoieb, who died in accident 2003, but I will never forget her; my father who suffered a lot to educate me; my uncle Professor Ahmed Al-haddad who help and love me always; my wife, my kids, my brothers and sisters for their unconditional love, sacrifices, encouragements and supports.

I ask Almighty Allah the most Gracious and the most compassionate to forgive us and let us meet again in paradise, at the highest "Firdawse" Amen

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LIST OF ABBREVIATIONS

ARF	Acute renal failure
ATS	American Thoracic Society
AUC	Area under the curve
B	Regression coefficient value
BTS	British Thoracic Society
CAP	Community acquired pneumonia
CI	Confident interval
COPD	Chronic obstructive pulmonary disease
CRB-65	Confusion, respiratory rate, blood pressure and age more than or equal 65 years old.
CURB-65	Confusion, urea, respiratory rate, blood pressure and age more than or equal 65 years old.
DBP	Diastolic blood pressure
DM	Diabetes Mellitus
e.g.	example
FCT	Fever clearance time
HAP	Hospital acquired pneumonia
Hgb	hemoglobin
HPP	Hospital Pulau Pinang
HUSM	Hospital Universiti Sains Malaysia
ICU	Intensive care unit
IDSA	Infectious Disease Society of America
Lab	Laboratory
LOS	Length of hospital stay
Ml	Milliliter
mmol	Millimole
mo.	Month
Na	Sodium
no.	Number

NP	Nosocomial pneumonia
NPV	Negative predictive value
OR	Odds ratio
PPV	Positive predictive value
PSI	Pneumonia Severity Index
RBG	Random blood glucose
RR	Respiratory rate
SBP	Systolic blood pressure
SD	Standard Deviation
SPSS	Statistical Package For Social Sciences Software
UK	United Kingdom
USA	United State of America
WBC	White blood cells
WHO	World Health Organization
yr.	Year

PENILAIAN RAWATAN HASILAN PNEUMONIA ARUHAN KOMUNITI DAN KOS PENYAKIT
DAN
PEMBANGUNAN MODEL MORTALITI

ABSTRAK

Pneumonia aruhan komuniti (CAP) adalah punca mortaliti dan kematian utama di seluruh dunia termasuk Malaysia. Pengenalan perbezaaan dalam keputusan perubatan dan kos di antara hospital universiti dengan hospital umum (GH) boleh membantu perkembangan dalam rawatan pneumonia dan membantu pasukan kesihatan melakukan perkhidmatan perubatan dengan tepat and berkesan. Perkembangan dan pengesahan model mortaliti pneumonia yang mana berdasarkan faktor risiko yang boleh didapati pada masa kemasukan hospital boleh membantu mengenalpasti pesakit yang berisiko tinggi dan merawat mereka dengan tepat. Perawatan CAP adalah mahal dan kos adalah berhubungan dengan kepanjangan tinggal di hospital (LOS). Oleh kerana itu, pengesahan factor risiko dari peningkatan LOS boleh menyebabkan penurunan kos perawatan CAP. Maka, penyelidikan ini bertujuan pertamanya membandingkan keputusan perawatan dan kos di antara hospital universiti dengan GH; Hospital umum dan keduanya mengembang kan model mortaliti pneumonia di Hospital Pulau Pinang dan Hospital Universiti Sains Malaysia; ketiganya, mengenalpasti faktor risiko bagi peningkatan LOS. Satu penyelidikan restrospektif secara pemerhatian telah dijalankan di antara pesakit dewasa CAP yang dimasukkan ke Hospital Pulau Pinang dengan Hospital Universiti Sains Malaysia dari 1hb Januari 2007 sampai 31hb Disember 2008. Secara umumnya tidak tardapat sebarang perbezaan hasitan rawatan diantara Hospital Universiti Sains Malaysia dan Hospital Pulau Pinang terdapat perbezaaan jelas di antara kos di HUSM dan HPP. Penemuan nenunjukkan bahawa HPP memberi keputusan

perubatan yang serupa dengan kos perubatan pneumonia yang lebih rendah berbanding dengan HUSM. Model mortaliti pneumonia mengandungi pembolehubah bebas termasuk: kekeliruan, kadar pernafasan lebih daripada 30 pernafasan per minit, tekanan darah sistolik kurang daripda 90 mmHg, glukosa darah rawak lebih daripada 13 mmol/l, ventilasi mekanik, kemasukan ICU, penyakit seiring lebih daripada atau sama dengan tiga, Hgb < 8 g/dl, urea > 11 mmol/l, dan albumin < 30 g/dl. Kepekaan model adalah 69.6 %, kekhususan (*specificity*) adalah 98.0%, *Positive Predictive Value* (PPV) adalah 83.6 %, *Negative Predictive Value* (NPV) adalah 95.8 % dan keluasan dibawah keluk (AUC) adalah 0.839. Terdapatnya bebas faktor berikut termasuk peningkatan LOS, komplikasi, umur, penyakit seiring dengan pneumonia, kelambatan penggunaan antibiotik lebih daripada lapan jam, dan memulakan perawatan dengan satu antibiotik.

EVALUATION OF COMMUNITY ACQUIRED PNEUMONIA TREATMENT OUTCOMES AND COST OF ILLNESS AND DEVELOPMENT OF MORTALITY MODEL

ABSTRACT

Community acquired pneumonia (CAP) is a major cause of morbidity and mortality worldwide including Malaysia. Identification of the differences in the outcome and cost between a university hospital and a general hospital (GH) could lead to the development of pneumonia interventions and guide the health team to accurately perform and administrate health care services effectively. The development and validation of the pneumonia mortality model, which is easily accessible at the time of admission can, identify patients who are at risks, and treat them appropriately. Treatment of CAP is costly and the cost is related to the length of hospital stay (LOS).Therefore, identification of the risk factors of increase the LOS is lead to decrease the cost of CAP treatment. Therefore, this study aims firstly to compare the treatment outcome and cost between a university hospital and a general hospital; secondly, to develop pneumonia mortality model in Hospital Pulau Pinang (HPP) and validation the model in Hospital Universiti Sains Malaysia(HUSM); thirdly, to identify the risk factors of increase the LOS. A retrospective observational study was conducted among the adult patients with CAP who admitted to the Penang General HPP and to the HUSM from 1st January 2007 to 31st December 2008. Generally, there is no significant difference between the outcome between the HUSM and HPP. However, there is a significant difference between the cost between the HUSM and HPP. The findings show that the HPP provided a similar treatment outcome at lower CAP treatment cost in comparison to HUSM. The pneumonia mortality model composed of the following independent variables: confusion, respiratory rate > 30

breaths/min, systolic blood pressure < 90 mmHg, random blood glucose > 13 mmol/l, mechanical ventilation, ICU admission, concomitant disease more than or equal 3, Hgb < 8 g/dl, urea > 11 mmol/l, albumin < 30 g/dl. The model sensitivity is 69.6 %, specificity is 98.0 %, Positive Predictive Value (PPV) is 83.6 %, Negative Predictive Value (NPV) is 95.8 % and area under the curve (AUC) is 0.839. There were the following independent risk factors that significantly increase the length of hospital stay; presences of the complications, elderly, presence of the concomitant diseases associated with pneumonia, delay administration of antibiotics more than 8 hours and start the treatment with single antibiotic. It was concluded that the HPP provided a similar treatment outcome at lower CAP treatment cost in comparison to HUSM. The validated model composed of easily accessible variables at the time of admission can, identify patients who are at risks, and treat them appropriately.

CHAPTER 1

INTRODUCTION

1.1. Problem statement and rational of study

Pneumonia is the inflammation and consolidation of lung tissue due to an infectious agent (Marrie TJ, 1994). Depending on the onset of signs and symptoms of pneumonia, it is divided to two types; community acquired pneumonia and nosocomial acquired pneumonia or hospital acquired pneumonia. If the signs and symptoms of pneumonia occurred outside the hospital or within 48 hours of the admission to the hospital it is called community acquired pneumonia. If the signs and symptoms of the pneumonia occurred inside the hospital or 48 hours after the admission to the hospital it is called nosocomial acquired pneumonia or hospital acquired pneumonia (Bartlett JG *et al*., 1995; Bergogne-Berezin *et al* .,1995 ; Craven, D *et al* ., 1995 ; Craven, D *et al* ., 1998 ; Garner, J *et al*., 1988; Coalson, J. 1995 ; Bauer, T *et al*., 2000 ; Chastre, J *et al* ., 2002 ; Kollef, M. 1999b). Mandel LA 2004 stated that the community acquired pneumonia is the common type of pneumonia. Community acquired pneumonia is characterized by cough, cough with sputum, fever, chills, chest pain, anorexia, headache, vomiting, nausea, myalgia, sore throat, arthralgia, abdominal pain, diarrhea, hemoptysis, dyspnea and fatigue (Fine *et al*., 1999; Marrie *et al*.,1989 and Metlay *et al*., 1997b)

Community acquired pneumonia (CAP) is a major cause of morbidity and mortality worldwide, CAP among the main ten causes of admission to the hospital and mortality worldwide. CAP is associated with significant utilization of health care resources.

It is costly and lead to restricted daily activity (Adams PF and Marano MA, 1995; Graves, E. J. & Gillum, B. S. 1996; Lacroix *et al*., 1989; Marston *et al*., 1997; Woodhead *et al*., 1987; Guest JF and Morris 1997; Almiral *et al*., 1993; Marrie 1990, Fine *et al*., 1996; BTS, 2001; BTS, 2009"Lim *et al*., 2009"; Niderman MS *et al*., 2001; Makela *et al*., 1993; Tsirgiotis E *et al*., 2000; Jin Y *et al*., 2003; Whittle J *et al*., 1998; Metlay *et al*., 1997b; Birnbaum HG 2001; Almirall *et al*., 2000; Bartlet JG *et al*., 1998; Lutifiyya MN *et al*., 2006; Bauer TT *et al*., 2005)

Pneumonia represented one of the 10th leading causes of hospitalization and deaths in Malaysia during 1996-2007 (Ministry of Health, Malaysia, 1996, 1997, 1998, 1999, 2000, 2001, 2002b, 2003, 2004, 2005b, 2006b and 2007)

Table 1.1 Ranking of the pneumonia as one of the top causes of hospitalization and death in Malaysia

Year	Cause of hospitalization	Cause of death due to pneumonia
1996	5th (6.47%)	8th (4.17%)
1997	5th (6.58%)	8th (4.33)
1998	5th (6.51%)	7th (4.76%)
1999	4th (6.76%)	7th (4.83%)
2000	4th (6.69%)	8th (4.69%)
2001	5th (6.61%)	7th (4.98%)
2002	5th (6.35%)	6th (5.11%)
2003	5th (6.73%)	6th (5.32%)
2004	5th (6.83%)	6th (5.58%)
2005	5th (6.98%)	6th (5.30%)
2006	4th (7.30%)	5th (5.81%)
2007	4th (7.38%)	5th (7.43%)

Pneumonia like other infectious diseases that the people seeking the treatment either in university or general hospitals. A general hospital deals with most of the services that people need for their medical care and/or their surgical care. Many general hospitals do a lot of complicated surgery such as cardiac surgery. Most of the general hospitals are considered as a secondary care. University hospitals provide more specialized services such as transplant services. A university hospital contains more advanced technology. University hospitals focused also in medical education, training of the medical students and research. Seeking treatment at a university hospital is costly than a general hospital (lezzoni *et al*., 1990; Zimmerman *et al*., 1993; Blumenthal *et al*., 1997; Ayanian and weissman 2002; Polanczyk *et al*., 2002; Taylor *et al*., 1999). A comparison of outcome between different types of hospitals is very necessary to the policy makers (Hofer T *et al*., 1996; Hartz AJ, 1989). There are few published studies world wide that compared the university hospitals versus others types of hospitals but most of these studies focused on the comparison the quality of care. Few studied compared the outcome like length of hospitalization and mortality (Lave JR *et al*., 1996; Siegel RE. *et al*., 2000; Polanczyk *et al*., 2002; Rosenthal *et al*., 1997). There is a gap in the literature regarding to investigate that the general hospitals can provide a comparable outcome of treating pneumonia with lower costs. Treatment of community acquired pneumonia is costly (Fine *et al*., 2000; Nathan *et al*., 2006; Barlow et al 2003; Whittle *et al*., 1998; Lave *et al*., 1996; Guest *et al*., 1997; Halm *et al*., 2001; Glibert *et al*., 1998) .

Increase the length of hospital stay is increase the total cost of treating community acquired pneumonia. It was reported that the following factors cause increase the length of hospital stay such as the concomitant diseases associated with community acquired pneumonia, complications of treating community acquired pneumonia, severity of community acquired pneumonia, anemia, hypoxemia, level of albumin, delay of administration of antibiotics more than eight hours from the time of admission to the hospital, in appropriate selection of the antibiotics in the treatment of community acquired pneumonia, performance of the culture (Niderman *et al*., 1998; Lave *et al*., 1996; Fine *et al*., 1997; Fine *et al*., 1996; Fine *et al*., 1999; Fine *et al*., 1993; Hartz *et al*., 1996; Wingarten *et al*., 1994; Fine *et al*., 2000; Runciman *et al*., 2002; Halm *et al*., 2001; Nathan *et al*., 2006; Gleason *et al*., 1999; Meehan *et al*., 1997; Frei *et al*., 2006; Battleman *et al*., 2002; Houck *et al*., 2004; Rubin *et al*., 2001; Graff *et al*., 2002; Farr *et al*., 1991; Bauer *et al*., 2005; Menéndez *et al*., 2003; Weingarten *et al*., 1996).

The recent community acquired pneumonia management guidelines recommended that the previous models used in severity-of-illness scores, such as the CURB-65 and Pneumonia Severity Index model (PSI); can be used to decide whether the community acquired pneumonia patient treated as inpatient or as outpatient (American Thoracic society 2007 " Mandell *et al*., 2007" ; Infectious Diseases Society of America 2007 " Mandell *et al*., 2007"; British Thoracic Society 2009 "Lim *et al*., 2009").

1.2. Significance of the study

- Since the application of the pharmacoeconomic studies in 1978, few publications were reported regarding pneumonia, to date there is no published study had been performed in Malaysia to evaluate the cost of CAP treatment.
- There is a gap in the literatures, there is a worldwide lack in studies evaluation and compared the outcome and cost of treating pneumonia between a university hospitals and a general hospitals to investigate whether the general hospitals can provide a comparable outcome of treating pneumonia with lower costs. Therefore, this study compares the outcome and cost of treating pneumonia between a university hospital and a general hospital in Malaysia.
- Identification of the differences in the outcome and cost between a university hospital and a general hospital (GH) could lead to the development of pneumonia interventions and guide the health team to accurately perform and manage health care services effectively.
- Identification of the risk factors that cause increase the length of hospital stay can help to decrease the total cost of treating of community acquired pneumonia.
- The development and validation of the pneumonia mortality model which are easily accessible at the time of admission can identify patients who are at risks, and treat them appropriately.

1.3. Hypothesis of the Study

- **H1:** There are significant differences of the characteristics, treatment outcome and direct cost between a Hospital Universiti Sains Malaysia (HUSM) and a Pulau Penang Hospital (HPP).
- **H2:** There are risk factors associated with a significant increase in the risk of pneumonia related death in Malaysian inpatients.
- **H3:** There is a risk factors are associated with a significant increase in the length of hospital stay in HUSM and HPP

1.4. Objectives of the study

1.4.1 General objectives

1. Evaluation of pneumonia treatment outcomes and cost of illness in HUSM versus HPP.
2. Development of pneumonia mortality model.

1.4.2 Specific objectives

1. To compare the sociodemographic characteristics, concomitant diseases with pneumonia, signs and symptoms of pneumonia, chest radiograph findings and laboratory findings, distribution of microorganisms in blood and sputum, pneumonia severity index (PSI), CURB-65 and distribution of antibiotics prescribed in HUSM versus HPP.

2. To compare the outcome parameters measures included length of hospital stay (LOS), fever clearance time, resolution of signs and symptoms, duration of antibiotics therapy in the ward, readmission within one month, complications and 30-day mortality in HUSM versus HPP.

3. To compare the cost of illness, cost parameters included cost of LOS, laboratory and clinical investigations, antibiotics, drug administration, non antibiotics and total costs of treating CAP in HUSM versus HPP.

4. Identification of the risk factors that increase the length of hospital stay in both hospitals HUSm and HPP.

5. Development of pneumonia mortality model in HPP.

6. Write the model equation.

7. Validation of the model in HUSM.

8. Compare the validated pneumonia mortality model with other models such as; PSI, CURB-65 and CRB-65 models in terms of calculate the sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and area under the curve (AUC)

1.5. Research questions

1. What is the difference of the sociodemographic characteristics, concomitant diseases with pneumonia, signs and symptoms of pneumonia, chest radiograph findings and laboratory findings, distribution of microorganisms in blood and sputum, pneumonia severity index (PSI), CURB-65 and distribution of antibiotics prescribed in HUSM versus HPP?

2. What is the difference of the outcome parameters measures included length of hospital stay (LOS), fever clearance time, resolution of signs and symptoms, duration of antibiotics therapy in the ward, readmission within one month, complications and 30-day mortality in HUSM versus HPP?

3. What is the difference of the cost of illness; cost parameters included cost of LOS, laboratory and clinical investigations, antibiotics, drug administration, non antibiotics and total costs of treating CAP in HUSM versus HPP?

4. What are the risk factors that increase the length of hospital stay in both hospitals HUSM and HPP?

5. What is the pneumonia mortality model equation?

6. What is the difference between the validated pneumonia mortality model with other models such as; PSI, CURB-65 and CRB-65 models in terms of calculate the sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and area under the curve (AUC)?

CHAPTER 2

LITERATURE REVIEW

2.1. Definition of community acquired pneumonia

Community-acquired pneumonia (CAP) is defined as that type of pneumonia when the signs and symptoms occurred before the admission to the hospital or within the two days of admission to the hospital (American Thoracic society 2007 " Mandell *et al*., 2007" ; Infectious Diseases Society of America 2007 " Mandell *et al*., 2007"; British Thoracic Society 2009 "Lim *et al*., 2009"; Bartlett JG *et al*., 1995; Bartlett JG *et al.*, 1998; Metlay JP *et al.*, 1997; Smith PR, 2001)

2.2. Epidemiology & Incidence of community acquired pneumonia

Community acquired pneumonia is a major cause of morbidity and mortality worldwide. CAP within the top ten causes of admission to the hospital worldwide. (Adams PF and Marano MA, 1995; Graves, E. J. & Gillum, B. S. 1996; LaCroix *et al*., 1989; Marston *et al*., 1997; Woodhead *et al*., 1987; Guest JF and Morris 1997; Almiral *et al*., 1993; Marrie 1990, Fine *et al*., 1996; BTS, 2001; BTS, 2009"Lim *et al*., 2009"; Niderman MS *et al*., 2001; Makela *et al*., 1993; Tsirgiotis E *et al*., 2000; Jin Y *et al*., 2003; Whittle J *et al*., 1998; Metlay *et al*., 1997b; Birnbaum HG 2001; Almirall *et al*., 2000; Bartlet JG *et al*., 1998; Lutifiyya MN *et al*., 2006; Bauer TT *et al*., 2005)

British Thoracic society, 2009 reported that the incidence of Community acquired pneumonia was 0.5 to 1.1 % (Lim *et al*., 2009).

Adult community-acquired pneumonia is a serious, life-threatening illness that affects more than 3 million people each year and accountable for more than half a million annual hospital admissions in the United States alone (Lynch JP, 1992) .

In US, each year there are more than 900 000 cases of community acquired pneumonia occur in the United States, accounting for nearly 3% of all hospital admissions (National Center for Health Statistics: *Washington*, 1992).

Pneumonia is a major cause of morbidity and mortality in UK. It is cause over 10% of all deaths (66,581 deaths in 2001), the majority of which occur in the elderly (BTS, 2001).

In Japan, according to the Japanese Respiratory Society (2000), community acquired pneumonia is one of the major cause of morbidity and mortality in Japan. It is the fourth leading cause of death, and from 57 to 70 persons per 100,000 populations died per year of this disease in the last decade (The Japanese Respiratory Society, 2000).

In Hong Kong, according to the Department of Health, Government of the Hong Kong Community acquired pneumonia (CAP) is one of the major causes of morbidity and mortality (Annual Report, Department of Health, and Government of the Hong Kong 2003).

In Thailand, according to the Thailand Ministry of Public Health (1998) Pneumonia is one of the most infectious disease and one of the top causes of the admission to the hospital and the ministry reported that the incidence is approximately 1.5 per 1000 population (Ministry of Public Health. Thailand, 1998)

In Malaysia, according to the Ministry of Health Malaysia (MOH), Pneumonia represented one of the 10th leading causes of hospitalization and deaths in Malaysia through 1995-2009 (Ministry of Health, Malaysia, 1995- 2007)

2.3. Signs, symptoms and laboratory findings of community acquired pneumonia

A prospective observational study by Song *et al*., 2008 of 955 cases of adult CAP in 14 tertiary care hospitals in eight Asian countries (South Korea, China, Taiwan, Hong Kong, India, Singapore, Vietnam and The Philippines), it was reviewed all the cases admitted to the medical centers between January 2002 and December 2004, it was found that 92.8 % of the CAP patients were had cough at the time of admission to the hospitals; 88.1 % were had purulent sputum, 62.5 % were had chest pain and 10.7 % were mentally altered. It was found also that 9.3 % of CAP patients were admitted to the hospitals with respiratory rate more than 30 breaths per minute; 6.9 % were admitted with pulse rate more than or equal to 125 beat per minute, 5.4 % were admitted with temperature more than or equal to 40 ^{0}C or less than 35^{0}C and 3 % of the patients were admitted with systolic blood pressure less than 90 mmHg. It was found that 66.7 % of the patients were admitted with elevated white blood cells; 19.4 % of the patients were admitted with abnormal blood urea nitrogen; 9.2 % were admitted with abnormal serum sodium, 8.9 5 were admitted with glucose level more than or equal to 250 mg per deciliter and 6.9 % of the cases were admitted with arterial pH less than 7.35 %.

A prospective observational study by Ngeow *et al*., 2005 of 926 adult cases of adult CAP in 12 medical centers in Asia (Beijing, Shanghai, Hong Kong, Seoul, Taipei, Bangkok, Manila, Kuala Lumpur, Petaling Jaya, Singapore, Jakarta, Surabaya), it was reviewed all the cases admitted to the medical centers between October 2001 and December 2002, it was found that 100 % of the CAP patients were had cough at the time of admission to the hospitals; 96.9 % were had fever, 83.9 % were had crepitations; 59.6 % were had malaise; 55.1 % were had dyspnea; 43.5 % were had rhonchi; 19 % were had chills; 8.5 % were had chest pain; 23.9 % were had wheezing and other symptoms were found in many cases i.e. diarrhea.

Bartlet JG *et al*., 1995; Fine *et al*., 1999; Marrie *et al*.,1989 and Metaly *et al*., 1997b, Kothe *et al*.,2008 reported that the signs and symptoms such as cough, sputum production either with blood or without blood, fatigue , fever, chills, chest pain, sweating, tachycardia, tachypnea and other signs and symptoms is different from one patient to another, and it depends on the age of the patient, immunity status of the patient and the severity of the community acquired pneumonia whether severe or no.

A multicenter prospective study conducted by Kothe *et al*., 2008 among 2,647 adult's patients in 10 clinical centre's in Germany between March 2003 and October 2005. It was found that the majority of the patients were admitted with cough, fever, purulent sputum, dyspnea and pleuritic pain. While few patients were admitted with confusion (5.2 % of the 1298 adults patients age less than 65 years old and 16.4 % among 1349 elderly patients).

2.4 Concomitant diseases with pneumonia

A prospective observational study by Ngeow *et al*., 2005 of 926 adult cases of adult CAP in 12 medical centers in Asia (Beijing, Shanghai, Hong Kong, Seoul, Taipei, Bangkok, Manila, Kuala Lumpur, Petaling Jaya, Singapore, Jakarta, Surabaya), it was reviewed all the cases admitted to the medical centers between October 2001 and December 2002, it was found that the diabetes mellitus (DM) was the most common concomitant diseases and represented 14.4 % of the total cases, followed by chronic obstructive pulmonary disease (COPD) 13.6 %, congestive heart failure 7.8 % , asthma 7.2 %, renal diseases 4.9 %, liver diseases 2.9 %, and others concomitant diseases 21.9 %.

A prospective observational study by Song *et al*., 2008 of 955 cases of adult CAP in 14 tertiary care hospitals in eight Asian countries (South Korea, China, Taiwan, Hong Kong, India, Singapore, Vietnam and The Philippines), all the cases admitted to the medical centers between January 2002 and December 2004 were reviewed, it was found that the percentage of the patients were admitted with concomitant diseases was 69.9 %, bronchopulmonary diseases was the most common concomitant diseases and represented 29.9% of the total cases, followed by cardiovascular diseases 19.9 %, neoplastic disorder 11.7 %, liver diseases 4.4 %, renal diseases 4.1 % and hyposplenia 0.7 %.

A prospective study conducted by LOH *et al*., 2004 of 108 cases of adult CAP in urban-based university teaching hospital in Malaysia. It was found that the percentage of the patients admitted with concomitant diseases was 59.3 %. It was found that the percentage of the patients admitted with one concomitant disease was 45.4 %; the percentage of the patients admitted with two concomitant diseases was 50.9 % and the percentage of the patients admitted with three concomitant diseases was 3.7 %.

A prospective study by Liam CK *et al*., 2001 of 127 cases of community acquired pneumonia 12 years old or older admitted to the University Malaya Medical Centre between August 1997 and May 1999. It was found that the percentage of the patients were admitted with concomitant diseases was 59.9 %. It was found that the diabetes mellitus (DM) was the most common concomitant diseases and represented 19.7 % of the total cases, followed by chronic obstructive pulmonary disease (COPD) 18.9 %, cardiac diseases 7.9 %, renal diseases 3.1 % and others.

A 12 months prospective follow up study conducted by Menendez R *et al*., 2003 on four public hospitals one of them is a university referral teaching hospital and three is general hospitals in Valencia, Spain. Among 425 community acquired pneumonia patients admitted to the four hospitals, 229 CAP patients were admitted to the teaching hospital (hospital A), 73 CAP patients were admitted to the first general hospital (hospital B), 58 CAP patients were admitted were admitted to the second general hospital (hospital C) and 65 CAP patients were admitted to the third general hospital (hospital D). It was found that 32, 41, 31, 34 chronic obstructive pulmonary disease (COPD) were associated with the CAP cases in the four hospitals prospectively. Followed by cardiac diseases (33, 18, 26 and 23 cases); liver disease (5, 4, 7 and 8 cases); central nervous disease (15, 11, 15 and 19 cases) and renal disease (5, 3, 9 and 6 cases) were associated with the CAP patients in the four hospitals prospectively.

A prospective study conducted by Reechaipichitkul W *et al*., 2005 among the patients 15 years or older was admitted to a university hospital in Khon Kaen Thailand between January 2001 and December 2002. It was found that the percentage of the patients were admitted with concomitant diseases was 87 %. It was found that the cardiovascular diseases was the most common concomitant diseases and represented 23.6 % of the total cases, followed by diabetes mellitus 17.7 %, autoimmune disease 13.4 %, renal disease 11.4 %, neurological disease 9.4 %, hematological disease 8.3 %, chronic obstructive lung disease 5.5 %, asthma 3.1 % and cirrhosis 2.4 %.

A cross sectional study was conducted by Reechaipichitkul W and Pisprasert V. 2004 between January 1999 and December 2001 among 383 patients diagnosed with community acquired pneumonia. Among 105 cases; it was found that the diabetes mellitus was the most common concomitant diseases and represented 25.5 % of the total cases, followed by cardiovascular disease 15.2 %, hematologic disease 14.3 %, chronic renal failure 13.3 % and other concomitant diseases.

Kornum *et al*., 2007 on the population cohort study on 29,000 adult's patients with pneumonia admitted to the northern Denmark. It was found that 2,931 patients admitted with DM type 2. It was found that the percentage of the patients admitted without any co morbidities was 28% among diabetes patients and 43 % among non diabetes patients. It was found that the percentage of the patients admitted with one or two co morbidities was 46 % among diabetes patients and 40 % among non diabetes patients. It was found that the percentage of the patients admitted with three or more co morbidities was 18% among diabetes patients and 16 % among non diabetes patients.

A retrospective study conducted by Kuraishi NY *et al*., 1992 between July 1987 and December 1990 on the patient's age 12 years or older diagnosed with community acquired pneumonia to the King Fahd Specialist Hospital in Al-Qassim Saudi Arabia. It was found that among 567 of the cases that diagnosed with community acquired pneumonia cases, 53.7 % of the patients were admitted with concomitant diseases i.e. 24.9 % DM; 10.7 % asthma; 11.4 % cardiovascular diseases; 12.7 % COPD; 10.1 neurological disorders, 7.8 % liver diseases; 5.5 renal failure and others.

An observational study conducted by Irfan M *et al*., 2009 on the Aga Khan University Hospital in Pakistan among 329 adult patients admitted with community acquired pneumonia between January 2002 and August 2003. It was found that the percentage of the patients were admitted to the hospital with asthma was 8.2%; 45.60 % with cardiovascular diseases; 30.16 % with DM; 9.40 % with neurological diseases; 5.2 % with chronic renal failure; 3.6 % with chronic liver disease.

2.5. Diagnosis of community acquired pneumonia and radiological findings

There microorganisms can enter to the lung by three routes: inhalation, via blood stream, and aspiration or from an extrapulmonary site of infection (DeLong PA,Kotloff RM, 2000; Ward PA, 1996; Brandtzaeg P, 1995; Standiford TJ, 1997 and Cunha BA, 2001)

Diagnosis of community acquired pneumonia is based on the laboratory investigations, signs and symptoms, blood culture, sputum culture and radiographic findings, chest x-ray is very important to make the accurate diagnosis of community acquired pneumonia (American Thoracic society 2007 " Mandell *et al*., 2007" ; Infectious Diseases Society of America 2007 " Mandell *et al*., 2007"; British Thoracic Society 2009 "Lim *et al*., 2009"; American Thoracic Society, 2001" Niderman *et al*., 2001"). Canadian Community-Acquired Pneumonia Working Group 2000 stated that the chest X-ray, laboratory investigation and physical examination are reliable to confirm the diagnosis of community acquired pneumonia (Mandel LA 2000).

A prospective study conducted by LOH *et al*., 2004 of 108 cases of adult CAP in urban-based university teaching hospital in Malaysia. It was found that the percentage of the patients with one lobe infiltrate was 41.7 %; 30.6 %.were found with two lobes infiltrate; 27.8 %.were found with three lobes infiltrate; 20 %.with pleural effusion.

A prospective observational study by Song *et al*., 2008 of 955 cases of adult CAP in 14 tertiary care hospitals in eight Asian countries (South Korea, China, Taiwan, Hong Kong, India, Singapore, Vietnam and The Philippines), all the cases admitted to the medical centers between January 2002 and December 2004 were reviewed, it was found that the percentage of the patients admitted with pleural effusion was 15 %.

A multicenter prospective study conducted by Kothe *et al*., 2008 among 2,647 adult's patients in 10 clinical centre's in Germany between March 2003 and October 2005. It was found that the percentage of the patients admitted with pleural effusion was 12.6%. among 1298 adults patients age less than 65 years old and 18.3 % among 1349 elderly patients.

A population based study conducted by Bartolome *et al*., 2004 of community acquired pneumonia in Barceolana, Spain among 14 years patients or older. Off 134community acquired pneumonia patients treated as inpatients between December 1993 and November 1995. It was found that the percentage of the patients admitted with pleural effusion was 13.4 %. It was that the percentages of the patients admitted with multilobar was 9.7%.

2.6. Etiology of community acquired pneumonia

Marston *et al*., 1997 on their study stated that they are many etiology causes of pneumonia such as bacteria, fungi and viruses. Bartlett JG et al 1998 reported that one of the causes of community acquired pneumonia in hospitalized patients was viruses and it causes around 15% of the total causes. Bartlett JG *et al*., 2000 found that Influenza virus is the most common cause of pneumonia in the civilian population.

File *et al*., 2004; Reimer LG 2000 and Marrie 2001 found that the *Streptococcus pneumoniae* causes around 75 % of the total causes of community acquired pneumonia cases, also they found that the pneumonia cause was known only of few cases about 30 % cases .Infectious Disease Society of America (2000) stated that Streptococcus pneumonia is the cause of 66% of the bacteremic pneumonia cases (Infectious Disease Society of America 2000 " Bartlett *et al*., 2000"

A multicenter prospective study conducted by Kothe *et al*., 2008 among 2,647 adults patients in 10 clinical centre's in Germany between March 2003 and October 2005. It was found that the pathogens causes of community acquired pneumonia was detected in 271/1298 adults patients age less than 65 years old and in 268 /1349 elderly patients. It was found that *Streptococcus pneumoniae* was the most frequently isolated pathogen and represented 42.1% of the cases in the adults patients age less than 65 years old and 43.3 % of the cases in the elderly patients; followed by *Legionella spp*. (16.6 % in adults and 17.5 % in elderly); *Gram-negative bacilli* (3.7 % in adults and 7.1 % in the elderly); *Staphylococcus aureus* (1.5 % in adults and 2.2 % in the elderly); *Haemophilus influenza* (4.8 % in adults and 3.4 % in elderly); *Chlamydia pneumonia* (1.1 % in adults);

Mycoplasma pneumonia (14 % in adults and 0.7 % in elderly); *Influenza virus A* (5.9 % % in adults and 14.9% in elderly)

A prospective study by Liam CK *et al*., 2001 of 127 cases of community acquired pneumonia 12 years old or older admitted to the University Malaya Medical Center between August 1997 and May 1999. It was found that the etiological diagnosis done in 41.7% of the cases. It was found that the *Klebsiella pneumoniae* was the most frequently isolated pathogen and caused 10.2% of all the cases, followed by *Streptococcus pneumoniae* (5.5%), *Haemophilus influenzae* (5.5%), *Mycoplasma pneumoniae* (3.9%) and *Pseudomonas aeruginosa* (3.9%). It was concluded that the microorganisms of the hospitalized CAP patient's in Malaysia different from that reported in the western countries, in western countries it was reported that the *Streptococcus pneumonia* was the most common cause of CAP (Marrie *et al.,* 1989; File *et al*., 2004; Reimer LG 2000 and Marrie 2001). It was found that the gram-negative bacilli were more frequently isolated in older patients and in those with co morbidity.

A prospective study conducted by Loh *et al*., 2004 of 108 cases of adult CAP in urban-based university teaching hospital in Malaysia. It was found that 40% had positive sputum cultures; 20% had positive blood cultures.. It was found that the percentage of *Klebsiella pneumonia* 17.8%; *Mycobacterium tuberculosis* 15.1%; *Acinetobacter* species; 4.1%; *Pseudomonas* species. 2.7% and *Enterobacter* species (2.7%).