Epidemiological and clinical characteristics of *Streptococcus pneumoniae* infections in a tertiary care centre in Bahrain (2010-2014)

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Abstract

Objective: To describe the epidemiology of invasive and non-invasive pneumococcal disease during a 5-year period in a major hospital in Bahrain.

Design and Setting: This retrospective study investigates cases of pneumococcal diseases among patient ≥ 14 years old during a five-year period (2010-2014), who attended Salmaniya Medical Complex, Bahrain.

Patients and Methods: Laboratory data were obtained from inpatient and outpatient with cultures positive for *Streptococcus pneumoniae*. Demographics and clinical records from medical files of patients were then reviewed.

Results: A total of 144 culture positive *S. pneumoniae* representing 139 patients met the inclusion criteria. Ninety-five patients had non-invasive pneumococcal disease and 44 patients had invasive pneumococcal disease. Pneumococcal disease was more common among male patients (58.99%) with mean age of 56-year (15-95). The most common comorbidities were hypertension, Diabetes Mellitus followed by cardiovascular disease. Twenty-seven patients received mechanical ventilation during their admission, and 13 patients were admitted to the intensive care unit. The overall mortality rate recorded in our centre was 14.4%.

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Conclusion: This study supports the current literature where pneumococcal infection is more prevalent in elderly and those with comorbidities. The overall mortality was low and related to age, certain chronic medical illness, admission to intensive care unit and need for mechanical ventilation.

Keywords

Streptococcus pneumoniae; Pneumococcal Diseases; Epidemiological; Bahrain.

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Introduction

Streptococcus pneumoniae, is a Gram-positive diplococcus, causes a spectrum of diseases; ranging from invasive to non-invasive pneumococcal disease (NIPD) [1]. Invasive pneumococcal disease (IPD) refers to isolation of *S. pneumoniae* from a normally sterile body sites like blood, cerebrospinal fluid (CSF) or pleural fluid [2]. IPD can manifest as serious diseases such as bacteremia, meningitis and bacteremic pneumonia. NIPD includes the commonly occurring diseases like sinusitis, acute otitis media and non-bacteremic pneumonia. *S. pneumoniae* is considered the most common cause of community acquired pneumonia (CAP) [1].

Risk factors for developing pneumococcal disease include age, coexisting medical illness such as chronic obstructive pulmonary disease (COPD), chronic heart disease and Diabetes Mellitus [3]. The risk of IPD and sepsis has been reported to be increased among patients older than 65 years old with chronic underlying conditions. *S. pneumoniae* has been shown to occur more frequently in immunocompromised individuals, and possibly with more frequent relapses [4].

Gram stains and culture are routinely used as the first step to identify *S. pneumoniae*, while new laboratory methods have been introduced such as antigen and nucleic acid detection assays [5-6]. In the United States alone, 4 million pneumococcal disease

episodes occur annually with 22,000 deaths among adults [7]. In addition, over 600,000 cases are admitted each year to the hospitals with pneumococcal pneumonia [8]. *S. pneumoniae* is responsible for considerable mortality reaching as high as 60% in elderly patients with pneumococcal bacteremia and 22% in adults with pneumococcal meningitis [1].

This study aims to provide an overview of the burden of culture-proven pneumococcal disease in patients 14 years of age and older who were admitted to Salmaniya medical complex during 2010-2014 period. To the best of our knowledge, this is the first report describing the epidemiology of *Streptococcus pneumoniae* infection in adults of Bahrain. A secondary aim of the present study is to compare our findings to that in other parts of the world.

Methods

Study design and setting

The study was conducted as a retrospective, descriptive study of patients 14 years and older with cultures positive for *Streptococcus pneumoniae* between January 2010 and December 2014. This age cut-point was included as it covers patients treated in adult wards in our unit. The study had been conducted in Salmaniya Medical Complex, which

is the main tertiary care hospital in the Kingdom of Bahrain with around 1200 beds and covering around 80% of the population in the Kingdom of Bahrain (1.4 million as of 2017).

Data collection and participants

Data were obtained from Microbiology laboratory electronic database for all patients with positive culture specimens for *Streptococcus pneumoniae*. Specimens included blood, CSF, pleural fluid, sputum, deep tracheal aspirate (DTA), bronchial wash, eye discharge, middle ear fluid, skin, abscess, wound, vaginal swab, vitreous fluid, and synovial fluid. In our labs, standard microbiological methods are used to identify *S. pneumoniae*.

Demographics and clinical characteristics were then retrieved from medical files and entered in Excel sheets. Data collected included patient demographics (age, sex), specimen collection site, data of positive culture, admission diagnosis, coexisting medical conditions (Diabetes Mellitus, hypertension, chronic lung disease, chronic liver disease, chronic kidney disease, sickle cell disease, hypothyroidism, stroke, cardiovascular disease), immunocompromising conditions, hematological malignancies, solid tumors, chemotherapy, organ transplant receiver, smoking, length of stay for hospitalized patients, need for mechanical ventilation, admission to intensive care unit (ICU), and mortality. In-hospital mortality was defined as death from any cause during the pneumococcal-related admission [10]. The length of stay (LOS) was calculated as the number of days in the hospital. Case fatality rate (CFR) was calculated by dividing the proportion of persons who die from a specified disease among all individuals diagnosed with the disease over a certain period of time.

Exclusion criteria

Hospital-acquired infections; defined as infections occurring 48 hours after admission [11].

Definitions

Invasive pneumococcal disease (IPD) was considered as the isolation of *S. pneumoniae* from sterile body site such as blood, cerebrospinal fluid (CSF), and/or pleural fluid. Non-invasive pneumococcal disease (NIPD) included non-bacteremic pneumonia cases and those with isolates from non-sterile sites such as middle ear fluid and eye discharge.

Statistical Analysis

The data was processed and analyzed using Microsoft Excel 2016 and the Statistical Package for the Social Sciences (SPSS), version 25 (IBM Corp., Chicago, Illinois, USA).

Ethical considerations

All data were dealt with in complete privacy. The study was approved by the research committee of the Ministry of Health in Bahrain.

Results

Age and gender

Eighty-two cases (58.99%) occurred in male patients, while 57 (41.01%) in female patients. Mean age was 56 years (SD 18.048), ranged from 15 to 95 years of age, with 47 (33.81%) cases occurring among patients ≥ 65 years old. **Figure 1** illustrates the frequency of IPD and NIPD in relation to age

Figure 1: Frequency of invasive and non-invasive pneumococcal disease in Bahrain by age group (2010-2014).

groups. In addition, characteristics of the study cohort are summarized in **Table 1**.

Table 1. Characteristics and outcomes of the study cohort (n=139).

Characteristics	All patients	
	%	n= 139
Age, year		
Mean± SD	56 ± 18.048	
Patients ≥ 65y	47	33.81
Gender		
Males	82	58.99
Females	57	41.01
Out-patients	43	30.94
In-patients	96	69.06
Mechanical ventilation	27	19.42
ICU	13	9.35
Overall Mortality	17/118	14.41
Treated successfully	101/118	85.59

Clinical Manifestations

During the study period 144 positive specimens of *S. Pneumonia* were recorded in our study. Cases meeting study criteria constituted of 139 patients;

95 (68.35%) with the non-invasive pneumococcal disease and 44 (31.65%) with invasive pneumococcal disease. *S. pneumococci* were isolated from the following sites: DTA or sputum in 62, blood 43, CSF in 3, and 36 from other body sites.

Comorbidity

The most common comorbidities were hypertension, Diabetes Mellitus followed by cardiovascular disease. Moreover, 17 (12.2%) patients were smokers, 14 (10.1%) had chronic lung disease, 10 (7.2%) had solid tumors, and 7 (5%) were receiving chemotherapy therapy for their comorbidities as shown in **Table 2**.

Complications/Outcomes

Out the total study population, 13 patients were admitted to the intensive care unit (ICU); of those 4 had IPD and 9 had NIPD. Twenty-seven patients needed treatment with mechanical ventilation during their admission; 13 with IPD and 14 with NIPD. **Figure 2** illustrates the frequency of complications in both IPD and NIPD groups. The length of stay (LOS) for hospitalized patients, varied between one and 151 days (mean 26.4 days, median 9 days).

Table 2. Co-morbidities in 126 patients with pneumococcal disease; frequency, proportion, Case Fatality Rate(CFR) and relative risk(RR) to die.

Co-morbidity	N	%	No. died	CFR	RR of death	95% CI	P value
Hypertension	42	30.3	6	15	1.0636	0.4244 to 2.6658	0.895
Diabetes Mellitus	42	30.3	5	13.2	0.8772	0.3328 to 2.3121	0.790
Cardiovascular diseases	28	20.1	7	26.9	2.4769	1.0458 to 5.8665	0.040
Chronic lung disease	14	10.1	1	9	0.6080	0.0889 to 4.1578	0.598
Chronic kidney disease	12	8.6	2	16.7	1.1778	0.3056 to 4.5399	0.814
Chronic liver disease	4	2.9	2	50	5.1111	2.0187 to 12.9407	0.009
Stroke	4	2.9	2	66.7	5.1111	2.0187 to 12.9407	0.009
Sickle cell disease	6	4.3	0	-	-	-	-
Hematological malignancy	3	2.2	1	33.33	2.3958	0.4539 to 12.6466	0.302
Solid tumors	10	7.2	4	40	3.3231	1.3317 to 8.2922	0.016
Chemotherapy	7	5	1	14.3	0.9911	0.1527 to 6.4328	0.922
Smoker	17	12.2	2	11.8	0.7922	0.1987 to 3.1584	0.737
HIV	0	-	-	-	-	-	-

Table 3. Complications of pneumococcal disease in 139 patients: frequencies, case fatality rate, relative risk of death.

Complication	Frequency	Discharged successfully	No. died	CFR	RR	95% CI	P value
Mechanical ventilation	27	14	13	48.1%	10.95	3.89 – 30.84	0.0001
Admitted to ICU	13	8	5	38.5%	3.37	1.41 – 8.03	0.0111

Figure 2: Frequency of complications and mortality in patients with IPD and NIPD.

Mortality profile was missing for 21 patients. Out of the remaining 118 patients; 101 (85.59%) patients were treated successfully and discharged. There were 17 deaths, giving an inpatient mortality rate of 18.28% in both IPD and NIPD cases, and an overall mortality rate of 14.4%. Twelve of those died had IPD, and had 5 NIPD. **Table 3** illustrates the case fatality rate among patients who developed complications.

Discussion

A previous study has reported the incidence of pneumococcal infections in Bahrain, but it focused exclusively on the paediatric population [9].

Overall, this study has shown that non-invasive pneumococcal disease was the most common presentation among our population. Other investigators in United States [10] and Lebanon [12] have reported similar results.

It is well established in the literature that *S. pneumoniae* have higher incidence in the elderly and among male patients [3]). Older age has not been

associated with higher incidence only, but also with more severe disease [13] and higher mortality rates [13-15]. The pattern of age-related incidence and mortality which was noted in our population as well as in terms of gender predominance, males predominated was similar to what has been reported in other countries, such as United States [10], Lebanon [12], and Taiwan [16-17].

The most commonly observed comorbidities in our study were hypertension, Diabetes Mellitus, and chronic cardiovascular disease, however, the mortality rate was not significantly higher in diabetic and hypertensive patients. When compared to findings from other countries. We have noticed a geographical variation in relation to reported comorbidities among patients with pneumococcal disease. In the Gulf Corporation Countries (GCC) diabetes ranked among the top comorbidities [18-20], where as much lower rates were reported in Italy [13], Denmark, and the United Kingdom [21]. This may reflect the underlying geographical variations in Diabetes prevalence. GCC countries have the highest prevalence of diabetes in the Middle East and North Africa region with 21%, 19.6% and 19.3% in Saudi Arabia, Bahrain and United Arab Emirates, respectively [22-24]. This is in contrast to Europe where it doesn't exceed 5.1% in Italy as example [25].

On the other hand, chronic cardiac conditions have been reported in most countries to have high risk of mortality [17, 21, 26]. In the literature, congestive heart failure has been recognized as having significant risk for mortality, while ischemic heart disease has not [3]. In our study, however, all heart diseases were included under one title, so it was

not possible to make this distinction. Furthermore, in countries like the United States where Human Immunodeficiency Virus (HIV) is prevalent, a study reported HIV as the most common underlying conditions among patients with pneumococcal disease and second most common among those who died of pneumococcal disease [27], while no HIV infected case was diagnosed in our study.

Despite that chronic lung diseases are reported to be associated with significant risk for pneumococcal infection [3] and prevalent among investigated cohorts in many studies [19, 19, 28]. This study shows that the proportion of patients with lung disease didn't exceed 10.1% (14/139) with one death occurring among them, while other medical conditions related to high mortality were solid tumors, which is consistent with the reports of literature [1, 28].

The mortality rates we observed agreed with other studies, which range from 6% to greater than 50% depending on a number of factors, including age, disease severity and comorbid conditions [10]. The overall in-hospital mortality rate in our study was 18.28% for both IPD and NIPD cases and the overall mortality rate was 14.4%, which is comparable to rates in US (13.6%) [10].

Mortality was associated with age, certain comorbidities (cardiovascular disease, chronic liver disease, solid tumors), admission to ICU and the need for mechanical ventilation. Mechanical ventilation was reported as one of the factors associated with a fatal outcome among adult patients with bacteremic pneumococcal in Finland by which a need for mechanical ventilation was the most common complication (16%) [29]. Whereas, in our study, a higher rate (19.4%,) of patients receiving mechanical ventilation. *Ricketson et al.* [28] have reported that ICU admission, mechanical ventilation and advanced age were found to have a significant contribution in mortality among patients with IPD. Although the presence of comorbidities contributes to high mortality, it is difficult to ascer-

tain the attributable risk of pneumococcal disease to mortality in patients admitted to ICU as overall mortality is high in ICU patients [30].

Finally, a number of potential limitations need to be considered. First, this study has a few limitations. As it required cases that were diagnosed primarily by cultures. Prior antibiotic use or failure to collect cultures by treating physicians may underestimate the real burden of the disease. The small sample size may be a limiting factor as well. The relatively small number of positive cultures compared to the number of samples processed per case may be explained by the usual care of these patients, as most of the patients have received several courses of antibiotics in out-patient or in-patient settings prior to admission to this hospital. Moreover, a proper selection of antimicrobial treatment is also important factor for successful control of pneumococcal infection.

Conclusion

This study provided baseline epidemiological data on invasive and non-invasive pneumococcal disease in a major hospital in Bahrain. It showed the high burden of disease among males and elderly people and those with hypertension, diabetes and cardiovascular diseases. Non-invasive pneumococcal disease was the most frequent diagnosis among our study population. These findings are similar to reports from other GCC countries. The mortality reported in this study would further necessitate the need or improvement of national preventive measure.

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