Paediatric Invasive Pneumococcal Disease : A 5-year Experience and Review of Hospital-Based Studies in Malaysia

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Abstract

Background: Invasive pneumococcal disease (IPD) is a serious preventable disease-causing significant mortality and morbidity among children below five years of age.

Methods: A five-year retrospective study involving hospitalised children aged below 14-years-old with IPD to two tertiary centres of two different states in Malaysia were conducted between year 2012- 2016. IPD was defined as isolates of *Streptococcus pneumoniae* from normally sterile body sites. This article reviewed previous hospital-based studies on paediatric IPD in Malaysia to provide an overview of the disease over the last three decades. A comparison was also made with the current study.

Results: A total of 54 children were identified with IPD in this study. Sixty per cent of the study population was below the age of two-years-old. A significantly higher number of IPD cases were found among the indigenous group. Both spectrums of malnourished children were also susceptible to the infection. This study found that the majority of children developed septicaemia (43/54, 80%), followed by pneumonia (34/54, 63%) and meningitis (13/54, 24%). Pneumonia ($p=0.001$) and meningitis ($p=0.03$) were more likely to occur in children less than one-year old. The study also showed that meningitis ($p=0.01$) was significantly associated with fatal cases. The second component of this article focussed on the review of the disease in Malaysia. There were 8 articles included, of which four each were clinical and microbiological studies. The review concurred that the young ones were vulnerable to the disease. The overall antibiotic resistance in Malaysia was low but on an increasing trend (10-30%). The mortality documented were only from the clinical studies, which showed a disparity of fatality rates in the different regions studied. The rate was low in Selangor (0-11%), in contradiction of a higher rate in Perak, the less developed area (26%).

Conclusions: The study highlighted that the younger age group, extremes of nutritional status and indigenous children were at risk of IPD. On the literature review of paediatric IPD in Malaysia, there was inadequate information on the disease. A concerted effort to better describe the disease is needed.

Background

The “Sustainable Millennium Goal” has given special emphasis to the eradication of infectious disease-causing death in children below five-years of age. Globally, one of five children live in extreme poverty putting them at risk of serious infections, including *Streptococcus pneumoniae*. Pneumococcal infection, which is a leading cause of mortality globally, becomes of paramount importance in this community. It has accounted for more deaths in children under 5, than all other causes combined in 2016(1). Most of these deaths occurred in countries in Africa and Asia. This vaccine preventable disease still imposes significant morbidity with serious and debilitating disability, particularly in the first two years of life (2).

However, data on invasive pneumococcal disease (IPD) in South-East Asia, more importantly Malaysia is still lacking. Due to scarce evidence, the pneumococcal vaccine has yet to be included in the national immunisation, even though it has been made available since 2006. To date, available clinical studies are confined to single centres and this prompted us to study the clinical manifestations and outcome of IPD in two major paediatric centres of different states in Malaysia. IPD was defined by the isolation of *S. pneumoniae* by culture from a normally sterile body fluid site. This study also reviewed previous hospital-based studies on paediatric IPD in Malaysia to provide an overview of the disease over the past three decades. A comparison was also made with our present study.

Materials And Methods

Study design and settings

A retrospective study of all positive *S. pneumoniae* isolates consistent with invasive disease from children below 14-years of age hospitalised in two tertiary hospitals in Malaysia between 2012 and 2016 was conducted. The two hospitals were Hospital Serdang (HS) and Hospital Raja Permaisuri Bainun (HRPB) located in two different states in West Malaysia. Both hospitals are government-funded multi-speciality tertiary hospitals with almost similar paediatric bed capacity. HS is located in Selangor, which is the most developed state in Malaysia, and the hospital serves an estimated population of 570,000 with a total number of 138 hospitals in its vicinity. On the other hand, HRPB is located in Perak, which is a less developed and bigger state, and the hospital serves an estimated population of 2.3 million, with 33 periphery hospitals. A comparison study of the disease between both hospitals was published recently(3).

A proforma sheet was used to record socio-demographic, nutritional status, clinical presentation, treatment, and outcome information. Concomitant mixed infection with *S. pneumoniae* and recurrent infection in the same patient were excluded. The assessment for nutritional status was in accordance with the WHO classifications(4).

Laboratory Methods

Blood cultures were performed using standard methodology. The antibiotic susceptibility pattern of the isolates was determined by the standard disc diffusion method. Minimum inhibitory concentration (MIC) level breakpoints in this study were based on CLSI 2008–2014 criteria(5). In Malaysia, serotyping was routinely performed in the Institute Medical Research, a national reference centre for all public hospitals in the country.

Literature review methodology

The MEDLINE (Ovid), Pubmed and Scopus database were used to identify relevant studies on hospital-based studies on paediatric IPD in Malaysia. Children were defined as those aged 15 years and younger. Search terms included: *Streptococcus pneumoniae*, invasive pneumococcal infection, pneumococcus, children, paediatric, invasive pneumococcal disease, Malaysia, and Malaysian, separated by binary operators “OR” and “AND”. Only articles published in

English were included. A review of pneumococcal epidemiology and infection in Malaysia has been published(6). The full reports of this manuscript were also screened for potentially relevant studies. In addition, manual searching of the reference list of identifications was also conducted.

The articles identified were downloaded and reviewed by the two investigators. Included studies were hospital-based with IPD in children. Studies that had involved both adults and children were only included if we could extract and segregate data on children. However, studies with purely adult involvement, data from non-invasive samples or non-hospital based, review and case reports were excluded.

Statistical analysis

All data obtained were analysed using IBM SPSS Statistics 21.0. Univariate analysis was used to analyse descriptive data for all variables. Chi-square test was used to determine the association between categorical variables, whereas Pearson's correlation test was used to determine correlations between continuous variables. Fisher's exact test was used with frequencies less than five. The acceptable level of statistical significance for all tests was set at $p < 0.05$. Ethical clearance for this study was obtained from both the Medical Research and Ethics Committee of the Ministry of Health, Malaysia and the University Ethics Committee for Research Involving Human Subjects.

Results

Socio-demography

Fifty-four episodes of invasive *S. pneumoniae* infection in children aged under 14 years were documented during the study period. The median age was one-year-seven months with the youngest infected in a five-day-old neonate. Sixty per cent of the study population was below the age of two-years-old. None were infected between the age of 12 to 14-years-old. There was no gender preponderance noted.

Figure 1 illustrates the distribution of invasive pneumococcal disease according to ethnicity in comparison to national ethnic breakdown. The indigenous group, which is a minority group representing 0.5% of the national population, became an outlier in this study population. All the indigenous children were from one single centre (HRPB).

Clinical

This study found that the majority of children developed septicaemia (43/54,80%), followed by pneumonia (34/54,63%) and meningitis (13/54,24%). The remaining five children were found to have abscesses; two each manifested as psoas and mastoid, and the remaining one with an appendicular abscess. Table 1 relates to the age of cases to clinical diagnosis. Meningitis ($p = 0.030$) and pneumonia ($p = 0.001$) were more likely to occur in children below one-year-old. On the other hand, septicaemia was conversely associated with older children of age below five-years-old ($p = 0.006$).

Table 1
Age distribution in relation to clinical diagnosis

Age Group (months)	Septicaemia		p value	Pneumonia		p value	Meningitis		p value
	Yes (n = 43)	No (n = 11)		Yes (n = 34)	No (n = 20)		Yes (n = 13)	No (n = 41)	
0 to 6	6 (14%)	0	0.327	1(2.9%)	5(25%)	0.022	4(30.8%)	2(4.9%)	0.025
0 to 12	13(30.2%)	2(18.2%)	0.708	4(11.8%)	11(55%)	0.001**	7(53.8%)	8(19.5%)	0.030**
0 to < 24	27(62.8%)	3(27.3%)	0.046	16(47.1%)	14(70%)	0.156	9(69.2%)	21(51.2%)	0.343
0 to < 60	40 (93%)	6(54.5%)	0.006	29(85.3%)	17(85%)	1.00	12(92.3%)	34(82.9%)	0.663

Eight children had laboratory confirmed meningitis, of which *S. pneumoniae* was isolated from the cerebrospinal fluid. Six others had clinical meningitis syndrome defined by the culture of the organism from blood alone. One child had brain abscess requiring craniotomy.

The median (IQR) length of hospitalisation for these children was seven days (1–65 days). Thirteen children either suffered neurological or respiratory sequelae upon discharge, resulting in a morbidity rate of 24%(13/54). The average fatality rate in our study was 20% of which sepsis was the cause of death in all eleven fatalities. The study also showed that meningitis was significantly associated with fatal cases as in Table 2 ($p = 0.001$). Apart from meningitis, shock and assisted ventilation were associated with adverse outcomes. Sixty-three percent (7/11) of fatalities were below two-years-old.

Table 2
The Clinical parameters associated with IPD mortalities

Characteristics	Death N = 11	Alive N = 43	p value
Female/Male	7(64%)	22(51%)	0.459
Ethnicity	7(64%)	22(51%)	0.459
Malay	2(18%)	3(7%)	0.266
Chinese	1(9%)	3(7%)	1.000
Indian	1(9%)	13(30%)	0.253
Indigenous	0(0%)	2(5%)	1.000
Others			
Age	5(45%)	1(2%)	0.667
0–6 Months	7(64%)	26(60%)	0.448
0–2 years Old	10(91%)	35(81%)	1.000
0–5 Years Old			
Pneumonia	5(45%)	29(54%)	0.294
Meningitis	8(72%)	5(12%)	0.001**
Septicaemia	11(100%)	32(74%)	0.095
Abscess	1(9%)	4(9%)	1.000
Malnourished	1(9%)	13(30%)	0.242
Undernourished	4(36%)	21(49%)	0.517
Obese	2(18%)	0(0%)	0.038*
Heart Disease	0(0%)	2(5%)	1.000
Prematurity	1(9%)	5(12%)	1.000
Syndrome	2(18%)	1(2%)	0.102
Assisted Ventilation	11(100%)	9(21%)	0.001*
Inotropes/Fluid Bolus	11(100%)	12(28%)	0.001*

Clinical characteristics in relation to the nutritional status of study population

Table 3 illustrates the clinical characteristics of IPD in association with the various nutritional status. Our study showed that severe pneumonia was more common among undernourished children ($p = 0.026$). On the other hand, obese children were associated with fatal outcome ($p = 0.043$), more so if they were syndromic ($p = 0.009$), as compared to undernourished children.

Table 3
Clinical characteristics of IPD in association to various nutritional status

Characteristics	Under nutrition N = 25	Normal N = 27	Obese N = 2	under nutrition versus normal p value	obese versus undernutrition p value	obese versus normal nutrition p value
Female/Male	13(52%)	15(55%)	1(50%)	0.797	1.000	1.000
Malay	15(60%)	13(48%)	1(50%)	0.419	1.000	1.000
Chinese	0(0)	5(19%)	0(0)	0.392	1.000	1.000
Indian	0(0)	3(11%)	1(50%)	0.052	-	1.000
Indigenous	8(32%)	6(22%)	0(0)	0.236	0.074	0.261
Others	2(8%)	0(0)	0(0)	0.427	1.000	1.000
0–5 years old	22(88%)	22(82%)	1(50%)	0.705	0.279	0.377
Premature	6(24%)	6(22%)	0(0)	0.284	1.000	1.000
Heart Disease	1(4%)	1(4%)	0(0)	1.000	1.000	1.000
Syndrome	1(4%)	0(0)	2(100%)	0.481	0.009**	0.002**
☒ Severe pneumonia	19(76%)	12(44%)	(100%)	0.026**	1.000	0.224
Meningitis	6(24%)	7(26%)	0(0)	0.873	1.000	1.000
Septicaemia	21(84%)	21(78%)	2(100%)	0.845	1.000	1.000
Abscess	4(16%)	1(4%)	0(0)	0.186	1.000	1.000
Respiratory sequele	3(12%)	2(7%)	0(0)	0.662	1.000	1.000
Neurological sequele	3(12%)	5(19%)	0(0)	0.705	1.000	1.000
Death	4(16%)	5(19%)	2(100%)	1.000	0.043**	0.052

☒ :Severe pneumonia defined as WHO 2013 :the presence of cough or difficulty in breathing and tachypnoea, plus one or more of the general danger signs, but not lower chest indrawing

Microbiological Results

Figure 2 describes the antibiotic resistant patterns for *S. pneumoniae* isolates. The non-susceptibility rate to penicillin was 17% (8/47). Serotyping was only available for five samples. Three isolates were of 6B, one each of 6A and 11A in serotyping. The other samples could not be processed as they were not viable.

Review Of Hospital-based Studies On Paediatric IPD In Malaysia

From the online literature search, we retrieved 141 articles from PubMed, 40 from Scopus and 60 from Medline. A total of 22 articles involving children, between 1987 till 2020 were identified for initial inclusion. Of these, eight studies with adequate information relating to IPD were finally included in the review. Fourteen articles were excluded-two were non-hospitalised studies, seven were single-site infection with inadequate data, four data could not be differentiated in terms of adults versus children, and finally, one study was excluded as data was still in the file.

With an exception of our study, the clinical studies (n = 4), identified were single-centred which were based in the densely populated urban areas in Kuala Lumpur (the capital city of Malaysia) and Selangor(3, 7–9).The clinical studies were retrospective in nature with small sample size. The remaining four articles in this review were microbiological studies, in which three were country-wide surveillance studies from several public hospitals in different states in Malaysia, as shown in Table 4(10–13).

In general, children aged less than 2 years were most susceptible to the infection. All studies involved multi-ethnic groups of the country, of which the main ethnic group comprising Malay, Chinese and Indian were included. However our study, apart from the main ethnic group, had highlighted the indigenous group as a vulnerable population to the infection. The association of nutritional status on the disease was also evaluated in our study, which was not described in any previous studies.

The clinical studies reported pneumonia followed by bacteraemia as the main common presentation. However, this information could not be obtained from the microbiological studies. Mortality was only stated in the clinical studies, while information was lacking in the microbiological studies. The mortality rate in our study was higher (20%) compared to previous rates reported (0–11%). A comparison between the two centres, a disparity was found between the two centres. HRPB documented a higher fatality rate of 26% versus 11% in HS(3). The mortality rate in HS was comparable to the other studies (7–9), and these centres are based in the most developed part of Malaysia.

In terms of antibiotic non-susceptibility, the pneumococcal penicillin rate was low in the national surveillance reports (11–13). However, on the contrary, data from several single centre studies documented an increased penicillin non-susceptibility rate as high as 60% (7). In terms of serotyping, overall there were inadequate publications with only a few reports being published in the last decade in children and confined to surveillance studies. In the most recent study of paediatric invasive pneumococcal on Malaysian children aged < 5 years, serotype 14, 6B, 19A, 6A, and 19F were the most common serotypes detected (11).

Table 4.
Summary of studies of hospitalised paediatric invasive pneumococcal disease in Malaysia, 1999–2020

∞ All age groups including: adults and children

1. ∞∞∞ :Four most common serotypes

∞ resistant pattern for all age groups

Discussion

This study reports the overall socio-demography, clinical presentation, and outcome of IPD in two public hospitals in Malaysia. We also reviewed IPD in Malaysian children in the literature. It confirms IPD primarily affects young children. The highest rate was found in children below two-years-old; it then decreased rapidly towards the age of five-years and beyond. This age-dependent pattern concurs with global findings in all other pneumococcal studies in children (2, 14, 15).

In our study, the study population was not representative of the breakdown in the national ethnic demographic data (16). This study highlighted that the indigenous children were susceptible to contracting IPD as compared to the other races. All these children were from one centre, which is based in the state of Perak. This is expected as the state houses almost one third of the total indigenous population in the country (17). In addition, the hospital is also a referral centre for indigenous children from the other neighbouring states. This study corroborates the findings of Cortese MM et al, that specific risk populations such as Alaskan and Australian natives are 10 to 50 times at higher risk of IPD (18). The elevated risk in these marginalised children has been attributed to the various underprivileged socioeconomic factors (19). Low income may represent limited access to health care, increased household crowding with poorer quality housing and hygiene, increased exposure to cigarettes and undernutrition, which are all potential mechanisms by which this poverty driven community may contribute further to the increased risk of IPD.

Effects of the extreme spectrum of nutrition were also studied, specifically the consequence of under-nutrition and obesity on IPD. Our study showed that undernourished children were more likely to present with severe pneumonia. Our findings were supported by other published reports that malnutrition resulted in various nutritional deficiencies leading to severe infections including pneumonia (20–22). The increased predisposition of the nutrient-deficient host to infection is presumed to be largely due to impairment in the immune system (21, 23). On the contrary, we found that obesity, especially among syndromic children, was associated with a fatal outcome in the disease. Obesity in general, is more likely to develop various infections than children of normal weight, including to develop serious complications of common infections. Impaired intracellular bacterial killing by polymorphonuclear leukocytes with resultant poor immunologic response in obesity coupled with challenging ventilation could lead to significant adverse fatal association in this group of patients (24).

In general the types of invasive infections caused by *S. pneumoniae* varied with age. We found that children below one-year-old, particularly in those less than six-months were found at risk of pneumonia and meningitis. On the other hand, septicaemia was seen in children less than five-years-old. The age predominance of these clinical syndromes is in keeping with other studies (1, 2, 14), further reinforcing that IPD is predominantly a serious disease of young children. Our study also showed that meningitis was poorly associated with fatal cases, an established association with other IPD studies (25–27).

On the review of IPD in Malaysian children, a generalised and comprehensive conclusion could not be inferred as the studies were mostly confined to single centres, laboratory-based surveillance studies and were retrospective. The clinical studies were considerably small in terms of sample size, lack multi-centre/state involvement with obvious absent data from many states in Malaysia and serotyping results were not available. On the other hand, the surveillance studies, although were nationwide participation from multi-state centres, lack essential detailed clinical data such as severity of the disease and outcome, as surveillance data relied on information collected via case report forms rather than complete medical records.

Comparing our data from previous hospital-based studies in Malaysia, there were differences in terms of the outcome of the disease. Even though, in general, Malaysia had low penicillin resistance (10–30%), it was increasingly prevalent over the past decades (11, 13, 28). A disparity was however observed in certain parts of the country, with obvious high non-susceptibility rates documented in the more urban developed states as shown in the several single-centre studies within Kuala Lumpur and Selangor (7, 9). The differences could reflect the overzealous inappropriate antibiotic prescribing and usage in children receiving primary care treatment in these areas (29).

The increased mortality rate documented in this study as opposed to the other local studies is also disconcerting. In comparison with the global pneumococcal fatality of 11% in children, the fatality rate of 20% in our study was still higher. There was also a marked difference in the death rates between the two centres in our studies. The variation in mortality in IPD by sites is not surprising and in agreement with other studies (22, 30). In our case, the polarity observed between the two hospitals in both states were of varied socioeconomic status and health care accessibility. This resulted in different disease severity and burden of cases seen, with consequent higher mortality in HRPB, as highlighted by Sithra et al in comparing the disease in the two centres (3).

Our 5-year study has a few limitations. First, this study is confined to two hospitals in urban Malaysia, a sample which may reflect selection bias and involvement of a relatively small number of isolates; hence unlikely to reflect the true incidence of IPD among Malaysian children. Secondly, the retrospective nature of the study has disadvantages including missing data and recall bias leading to an underestimation of the incidence of pneumococcal diseases. Furthermore, isolate serotype data were not available for the majority of the samples. On the other hand, the limitations on the review include retrospective

Study	Study period	Subject population	Age Range (yrs)	Total pneumococcal isolated	Site of isolation	Antibiogram	Non susceptible (%)		Resistant (%)		Serotypes fff	M
1)1999 M. Y. Rohani et al Prospective Microbiological study	1995-1996	6 state-hospitals	All ∞	Total 273 <2-years 55/273(20%) (26 /55 invasive)	CSF Blood Body fluids	Penicillin Cefuroxime Chloramphenicol Cotrimoxazole Erythromycin Tetracycline	β 7% 0.4% 4.9% 13.6% 2.6% 21.8%	β 7.0% 0.4% 3.4% 9.7% 1.1% 21%	Total 28 serotypes 1=6 19B=3 14=3 23F=2		NA	
2)2007 Lim LH et al Retrospective clinical study	1999-2004	UMMC, Kuala Lumpur	Below 14 years old	Total 50 < 2years old 38/50 (76%) 10% less than 6 months	Blood Pleural fluid Bronchoalveolar lavage Nasopharyngeal aspirate Tracheal aspirate Aspiration from site of infection (arthritis) CSF	Penicillin	(60%)30/49		8/49 16%		NA	Nil
3)2011 Le et al Retrospective microbiological study	1999-2007 (except 2001 & 2004)	UMMC, Kuala Lumpur	All∞	151 <5 years old 47/151(31.1%) (12 invasive)	Sputum Blood CSF other	Penicillin	β 49.7% (75/151)	β 21.2% (32/151)	1, 19F, 23F, 6A/6B		NA	
4)2011 Yasin et al Retrospective microbiological study	2008-2009	State hospitals	All∞	156/ 510 < 2years old 120/156 (23.5%) (50 invasive)	Blood CSF Sputum Pus of eye, ear,and others	Penicillin oral Ceftriaxone(non meningitis) Cefotaxime(non meningitis) Cotrimoxazole Erythromycin Tetracycline	β 28.45% - - 62.41% 35.81% 43.61%	β 5.44% 0.00% 0.0% 43.97% 33.33% 38.65%	19F =6(8.12%) 6B=12(16.22%) 14=7 (9.46%) 6A=7 (9.46%) 19A=7 (9.46%)		NA	
5) 2016 Nor Azizah et al Retrospective clinical study	2001-2011	Hospital Selayang	Below 13 years old	28/222	Blood	Penicillin	NA		17.9%		NA	CF (1,
6) 2017 Aisha Abdullah et al Retrospective clinical study	2002-2005	Hospital Kuala Lumpur	Below 12 years old	24 <2 year year old 17/24 (71%)	Blood CSF Peritoneal fluid	Penicillin Ceftriaxone Erythromycin Trimethoprim Tetracycline Cefuroxime Cotrimoxazole	40% 10% 20% 0% 0% 0% 10%	25% (6/24) 8.3% 20.8%		NA		2/; (8.
7)2019 Arusothy et al Retrospective microbiological study	2014-2017	All Hospitals in Malaysia	below 5 years old	245 invasive < 2years old 163/245 (66%)	CSF (9/245) blood (236/245)	Penicillin (meningitis) Ceftriaxone Cefotaxime Co -trimoxazole Erythromycin Tetracycline	22.2% 5.9% 5.5% 43.6% 1.8% 1.8%	22.2% 2.2% 1.9% 35.9% 42.9% 42.9%	14 (66/245; 26.9%) 6B (48/245; 19.6%) 19A (29/245; 11.8%) 6A (26/245; 10.6%) 6B majority in CSF samples		NA	
8)2020 Current study Sithra et al Retrospective Clinical study	2012-2016	Hospital Serdang, Selangor, Hospital Raja Permaisuri Bainun Ipoh(HRPB)	below 14 years	54 < 2 years old 30/54, 55%)	Blood CSF Tissue Pus	Penicillin Vancomycin Tetracycline Trimethoprim Erythromycin	HRPB 9.4% - - - -	HS 33% - - -	HRPB 3% 0% 11.5% 53% 8.6%	HS 0% 0% 11% 20% 74%		HF HS

sample size population studies, non-standardised sampling method, and it is not representative of the nationwide incidence data as many are confined to one region of the country. Incidence of paediatric IPD throughout Malaysia may vary according to geographic areas, healthcare accessibility, and population characteristics.

Conclusion

As a conclusion, albeit this small study may not reflect the true impact of the disease in the Malaysian children, it has highlighted that the younger age group, extremes of nutritional status and indigenous children were found to be at greater risk of contracting IPD. The review also provides an insight on the inadequate information of IPD among the Malaysian children, with a mismatch of available information between the clinical and microbiological surveillance data. This calls for a coordinated and concerted effort to better describe the burden and epidemiology of the disease in the country. The information obtained may help guide national vaccine policy prior to the inclusion of pneumococcal vaccine in the national immunisation programme. Despite Malaysia is an upper middle income country, pockets of poverty remain in the population with regional disparities(31). In the midst of the current global pandemic crisis, prioritisation in the vaccine delivery targeting at the high risk population is a sensible strategy, to kickstart the immunisation programme in Malaysia.

List Of Abbreviations

IPD	: Invasive pneumococcal disease
HS	: Hospital Serdang
HRPB	: Hospital Raja Permaisuri Bainun
WHO	: World Health Organisation
MIC	: Mean inhibitory concentration
CLSI	: Clinical and Laboratory Standards Institute

Declarations

Ethical clearance

Ethical clearance was obtained from both the Medical Research and Ethics Committee of the Ministry of Health, Malaysia (NMRR 17 971 35952 MREC (5)KKM/NIHSEC/P17-908) on 5th June 2017 and the University Ethics Committee for Research Involving Human Subjects. No consent to participate was required as there was no direct contact of any form with patients.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Competing interests

As declared in the cover letter, there is no conflicts of interest associated with this publication

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Authors contributions

Norlijah Othman (NO) conceived and designated the analysis. Sithra Rengasamy (Sithra et al) collected the data and analysed the data. The data was interpreted by NO. The article was drafted by Sithra and final critical revision was by NO. The final approval for the version to be published was agreed by both authors (NO and Sithra).

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Figures

Figure 1

National ethnic breakdown based on Malaysia Dos. Press Release Population Projection (Revised), Malaysia, 2010-2040. 2016. Figure 1 illustrates the distribution of invasive pneumococcal disease according to ethnicity in comparison to the national ethnic breakdown. Out of the 54 children hospitalised with IPD during the study period of 2012-2016, majority of cases were among the Malay ethnicity. This majority is foreseeable as it parallels with the ethnic distribution of the Malaysian population. The indigenous community on the contrary only accounted for 0.5% of the national population ranked the second most ethnic hospitalised with IPD in this study population.

Figure 2

Figure 2 describes the antibiotic resistant patterns for *S. pneumoniae* isolates. Penicillin sensitivity was still high at 46% in both centres.