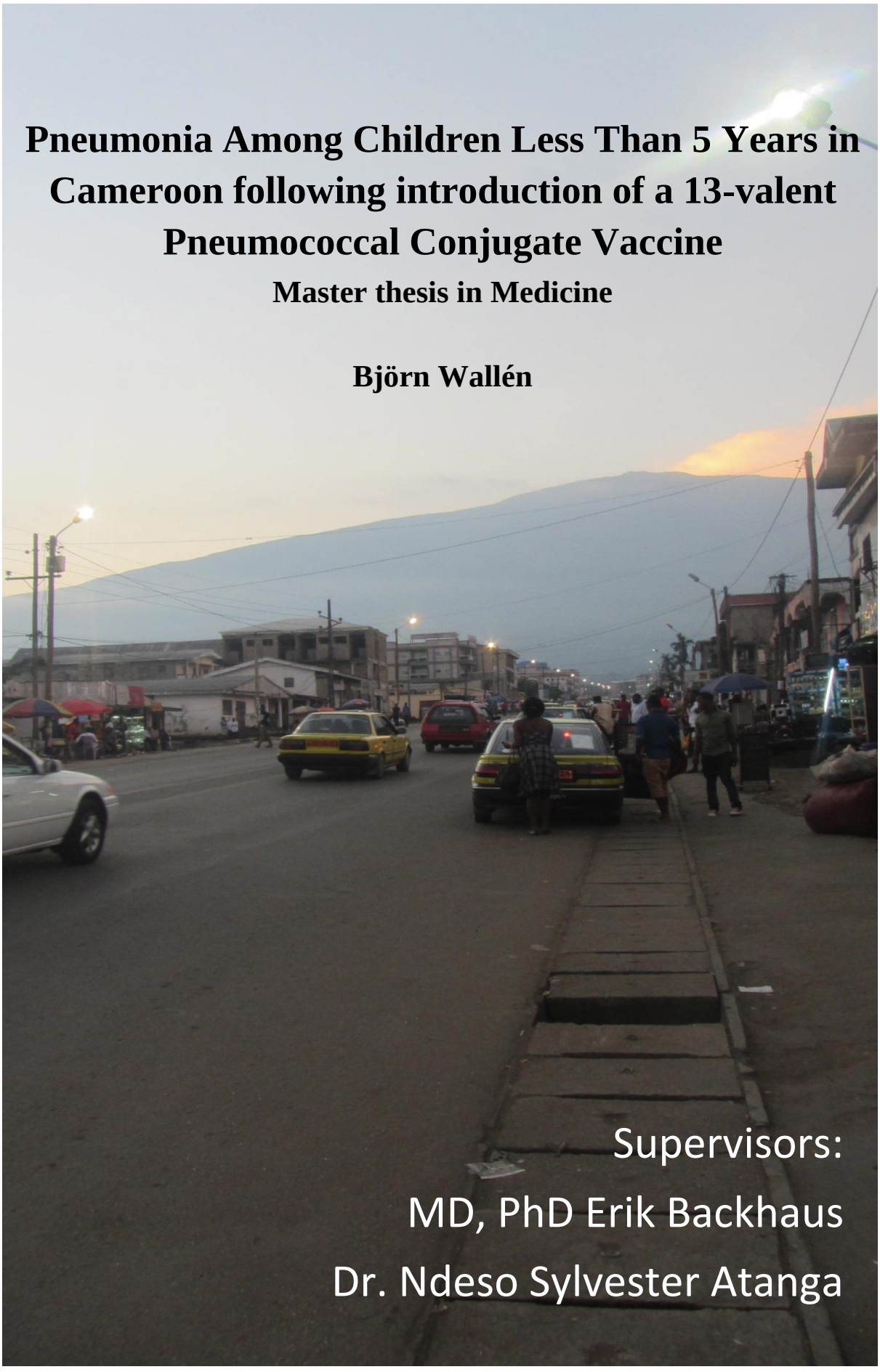
Pneumonia Among Children Less Than 5 Years in Cameroon following introduction of a 13-valent Pneumococcal Conjugate Vaccine

Master thesis in Medicine

Björn Wallén



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Gothenburg, Sweden 2014

Abstract

Master thesis, Sahlgrenska academy, pneumonia among children less <5 Years in Cameroon following introduction of a 13-valent pneumococcal conjugate vaccine, Björn Wallén, 2014, Gothenburg, Sweden.

Introduction Pneumonia is the largest killer in children under 5 years worldwide. In Cameroon it accounts for 18% of deaths in children < 5. Immunization is the most effective way to prevent pneumonia. Several studies show good effect with Pneumococcal Conjugate Vaccines (PCV). In Cameroon the PCV-13 vaccine was launched 2013-07. No evaluation has been done in Cameroon about all-cause pneumonia incidence after introduction of the vaccine.

Aim The aim of the study was to see if the number of pneumonia cases decreased after launching the PCV13-programme? Are there changes in severity and mortality after immunization? Have the rates of invasive pneumococcal disease (IPD) declined?

Method It was a retrospective study conducted at Buea and Limbe Regional Hospital during two months in autumn 2013. Cases were collected from 2009-06 to 2013-10. Inclusion criteria were having a pneumonia diagnosis and being 1 month - 5 years old. The study time was divided into one period before introduction of the PCV-13 vaccine program, and one period after the introduction.

Results No change in number of cases, no positive effect on proportion of severe cases, and no decline in mortality were observed after vaccine introduction. More boys than girls were affected by pneumonia. There was a seasonal variation with negative correlation between rainfall and number of pneumonia cases.

Discussion Reasons for the negative results remain unclear. Herd effects also take time to develop. Supposedly, Cameroon has a high percentage of non-vaccine serotypes? Do other factors, such as rainfall contribute to the result?

Conclusions It is too early to conclude no vaccine effect for children in the region. More studies are needed. Finally, knowledge about serotype distribution among disease-causing pneumococci in the area is needed.

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Introduction

Global situation of pneumonia

There are approximately 120 million episodes of pneumonia in children younger than 5 years every year(1), and pneumonia is the leading cause of death for children <5 worldwide(1-3), with an estimated 1.3 million deaths every year - more than AIDS, malaria and tuberculosis together(2). The majority of deaths due to pneumonia occur in low-income countries in Africa and Southeast Asia(1). Pneumonia can be caused by virus, bacteria as well as fungi. *Streptococcus pneumoniae* is the most common cause of pneumonia in children worldwide. Case fatality rates for children under 5 years of age and especially those under two years of age may be as high as 20% for pneumonia in developing countries(4).

In year 2000 following the millennium summits of the United Nations, eight international millennium development goals were established (MDG). The fourth millennium goal is about reducing child mortality by 2/3 from 1990 till 2015. As pneumonia alone stands for more deaths in young children than any other illnesses, controlling pneumonia is of crucial importance in achieving millennium goal nr 4(5). There are several factors contributing to pneumonia. In order to greatly reduce the number of episodes, a battery of interventions is needed. The Global Alliance for Vaccines and Immunization (GAVI) lists five interventions that have the most impact in reducing the burden of the disease that causes around one fifth of deaths worldwide(6).

These are:

- Immunization against whooping cough (pertussis), measles, Haemophilus influenza type b (HiB) and pneumococci;
- Exclusive breastfeeding for 6 months and continued breastfeeding complemented by nutritious solid food up to age 2;
- Safe drinking water, sanitation and hand washing facilities;

- Improved cooking stoves to reduce indoor air pollution;
- Treatment, including amoxicillin dispersible tablets and access to oxygen.

Of these five interventions, the WHO states that immunization is the most important and effective way to prevent pneumonia(2).

Several studies from South Africa (7), United States (8-10), Italy(11, 12) and from the Gambia (13) have shown that pneumococcal conjugate vaccines (PCV) are quite effective against childhood invasive pneumococcal disease (IPD) and clinical (or radiologically confirmed) pneumonia. In the randomized, placebo-controlled, double-blind Gambia study, the efficacy of the vaccine was 77% against IPD caused by vaccine serotypes and 50 % against IPD caused by all serotypes. In the same study, efficacy was 16% against mortality (13). In the WHO bulletin, volume 86, the authors estimate that the 13-valent vaccine may prevent 30-50% of radiologically and lethal pneumonia(14).

In the two studies from Italy, the number of children hospitalized with all-cause pneumonia in the age group 0-2 years, decreased with 19% respectively 15% the year after introduction of the PCV-7 vaccine(11, 12).

In a vast multidisciplinary group with support from GAVI Alliance and the Bill & Melinda Gates Foundation, the impact of immunization was estimated in 73 countries. Immunization with pneumococcal conjugate vaccine was estimated to avert 26 percent of the estimated, under-five pneumonia and meningitis deaths(15).

Etiology and pathophysiology

Pneumonia is defined pathologically as acute inflammatory consolidation of alveoli or infiltration of the interstitial tissue with inflammatory cells or a combination of both(16).

Often, the smaller bronchi and bronchioles are also affected as the infection usually originates from the upper respiratory tract.

Pneumonia can be classified in different ways:

- According to localization as in *segmental pneumonia, lobar pneumonia* or *interstitial pneumonia*
- As cause of disease, for example *aspiration pneumonia*,
- Due to causing agents such as *Streptococcus pneumoniae, Haemophilus influenzae, Chlamydophila pneumoniae*

The most common bacterial agent of pneumonia in children is *Streptococcus pneumoniae*(17). More than 90 different serotypes of the *Streptococcus pneumoniae* are known(4).

Carriage of *Streptococcus pneumoniae* in the nasopharynx is common. In pre-school children, carriage rates may be as high as 30-70 %(18). This does not necessarily lead to pneumococcal disease or pneumonia. However, people with immunodeficiency, people of old age and particularly infants are at greater risk(18, 19). In infants, pneumococcal pneumonia most commonly derives from the upper respiratory tract, with inflammatory secretion from the airways which later causes bronchial obstruction(16). When the bronchi are affected the infection spreads to include the alveoli that become packed with inflammatory exudate and involved parts of the lung become consolidated. Without treatment, infection may spread to involve lung lobes(19).

Pneumococcal conjugate vaccines

In the 1980s, polysaccharide vaccines were released on the market. These vaccines have capsular polysaccharides from 23 different pneumococcal serotypes. Polysaccharides induce a

B-cell dependent immune response (20). However, polysaccharide vaccines are not suitable for children under 2 years of age because of children's immature immune system(21). Young children simply don´t have the same ability to produce antibodies against polysaccharides (20). The last decade's pneumococcal conjugate vaccines have been developed and 7, 9 and 10-valent pneumococcal vaccines have reached the market and have been implemented in immunization programs over the world (20). The advantage is that they are suitable and immunogenic for children below two years of age, unlike the pneumococcal polysaccharide vaccine (4, 18, 20, 21). Pneumococcal conjugate vaccines are made of polysaccharides from the capsule which are conjugated to a carrier protein, thereby making it possible for a T-cell dependent immune response to take place: a B-cell binds the vaccine, type 2 helper T-cells interact with the B-cell-complex; then, antibody isotype switching, affinity maturation and production of memory B-cells follows (20). The newest of the PCV-vaccines is the 13-valent vaccine that is now being used also in Cameroon. It may protect against severe disease caused by the 13 different serotypes which are represented in the vaccine(15, 22). Unfortunately the PCV-13 vaccine does not have effect on non-vaccine serotypes or other pathogens(15).

Diagnostics

Pneumonia can present a variety of different symptoms such as difficult breathing, cough, fever, abdominal pain, headache, chills, grunting, convulsion and vomiting(3). Not only the symptoms vary, there are also different diagnostic criteria for pneumonia internationally (23). Diagnostic guidelines are also much dependent on site and medical facilities (23, 24). Microbiological methods and especially, chest x-ray has in many guidelines been "golden standard" for diagnosing pneumonia (3, 24). Though, for example in UK and US x-ray is not recommended in "non-hospital-settings"(24). To facilitate for health personnel, and particularly in low-income countries, in 1991 the WHO set up a model with guidelines to diagnose pneumonia and categorize it according to severity, based only on clinical symptoms

(see Table 1). This model is now integrated in the IMCI (Integrated Management of Childhood Illness)(3).

Table 1. *Pneumonia –WHO-definition with level of severity.*

Non-Severe	*Severe*	*Very Severe*
Cough or difficult breathing and tachypnea None of the signs of severe or very Severe pneumonia. Other signs of pneumonia may be present: crackles, reduced breath sounds, or an area of bronchial breathing.	Cough or difficult breathing plus at least one of the following signs: Lower chest wall indrawing Nasal flaring Grunting (in young infants). No signs of very severe pneumonia	Cough or difficult breathing plus at least one of the following: Central cyanosis, Inability to breastfeed Or drink, or vomiting everything Convulsions, lethargy or unconsciousness Severe respiratory distress

To our knowledge, there are no diagnostic guidelines for pneumonia in Cameroon.

Cameroon

Public spending in the health sector in Cameroon is low. With only 1.5 % of GDP few countries in Africa allocate less money for health care than Cameroon. The average public spending as percentage of the GDP for the other sub-Saharan countries is almost twice as high(25).

There has been only small progress in the general health situation in Cameroon since 1990. Life expectancy has even fallen with two years. Maternal mortality is higher than the average for Sub-Saharan Africa, with 0.7 % case fatality rate for each pregnancy(25). Cameroon is far from achieving millennium goal 4; 12.2 % of all children die before reaching the age of 5 years. From 1990 to 2010 child mortality reduced with only 12%, to be compared with 38% in average for the other sub-Saharan countries(25).

In Cameroon, malaria, pneumonia and diarrhea are the major causes of death in children. 18% of deaths among children < 5 are due to pneumonia(25, 26).

Study Area

Buea is the administrative centre of the South West region in Cameroon with a population of 138 801(27). It is situated on the foot of Mount Cameroon close to 1000 meter above sea level, some 70 km west of economic capital of Douala, and only 20 km from the Atlantic Ocean. Buea is extremely humid with an yearly average rainfall of 3500 mm(28), and situated in the very proximity to the rainforest. There are two seasons: the rain season that stretches from May till September and the dry season that continues from late November to March. In-between the seasons are the transition periods. With numerous eruptions from the still active volcano of Mount Cameroon, the soil is highly fertile. The country´s second largest employer, CDC (Cameroon development cooperation), have large plantations of banana, rubber, and palm oil in the region. The Tole Tea estate is another big employer. The city also comprises one of only two Anglophone Universities in the Country. The Buea area is best described as a semi-urban area, moderately rich for Cameroon standards with a population of farmers, students and administrative personnel working for the government.

Study Setting

The study was performed at the pediatric clinic in Buea Regional Hospital (BRH) and later also extended to include the pediatric clinic in Limbe Regional Hospital. Both of them are public hospitals.

Buea Regional Hospital comprises thirteen different services, administration, pediatrics, surgery, maternity, operating theatre, x-ray, laboratory, dental, diabetes unit, tuberculosis unit, eye unit, family planning, outpatient, HIV / AIDS unit and the male and female medical units. Limbe Regional Hospital comprises services for radiology, surgery, dental surgery, gynecology and obstetrics, ophthalmology, pediatrics, maternity and general medicine.

Pediatric wards in Buea and Limbe.

The ward is divided into two rooms with 8 beds in each room and the nursing unit situated in between the two. In-patients are children aged 0-14 years. Only one pediatrician is working in the Buea ward. Outside of office hours, a doctor is on call at the hospital. Every day there are also three nurses and one head nurse working the day shift and two nurses working the long evening/night shift. The pediatric department in Limbe comprises 10 beds.

The maternity ward and the pediatrics are equipped with two incubators. There is oxygen treatment available. Blood pressure arm cuffs for children under 12 years of age were not present. There was no pulsoxymeter.

Health system and fees

Patients pay themselves for healthcare. For example, if attending medical care patients pay a consultation fee upon arrival at the hospital. To consult a general practioner in Buea, the fee is 600-1500 CFA (8-20 SEK) depending on daytime/nighttime/week-end. To consult a specialist, the fee is from 2500 (35 SEK) CFA and upwards. In-patients then pay bed fee 500 CFA (7 SEK) per night at the hospital, but has to bring their own sheets and food. Additionally, all medications, laboratory investigations, x-rays (chest x-ray 4-5000 CFA), surgery etc. the patients pay themselves. For a child with a pneumonia diagnosis, staying 2-3 days at the hospital with standard investigations, the total cost for the parents is around 10000 CFA (130 SEK). These fees should be put in comparison with a normal monthly income (hospital nurse in Buea) of around 100.000 CFA (1300 SEK).

Immunization

Cameroon has an on-going vaccination program which includes immunization with BCG, DTP, Hep B, HiB, PCV-13, poliomyelitis, measles and yellow fever. Additionally vitamin A

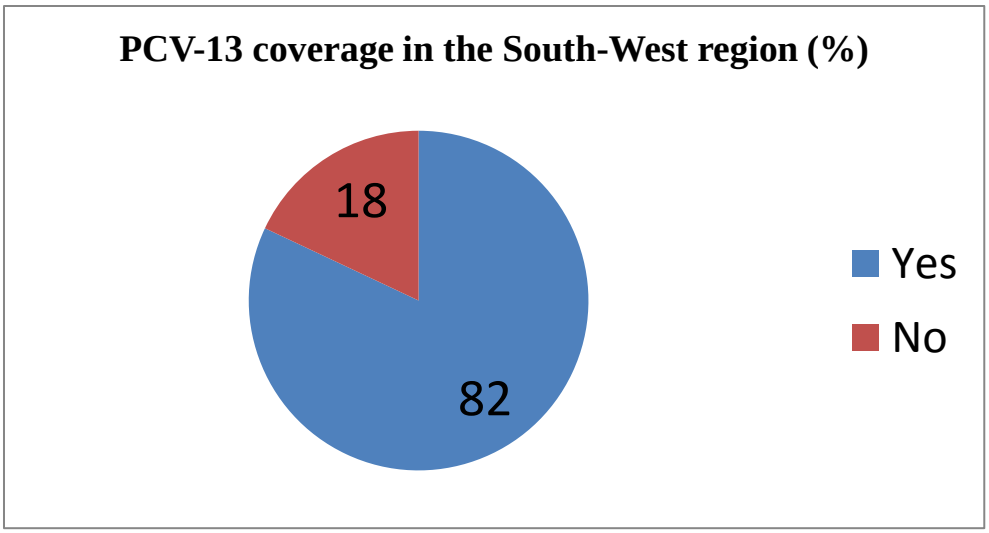
is administered together with the vaccines. Vaccination is free; in some health centers parents pay only a small administrative fee for their children (100 CFA = 1.4 SEK).

In July 2011 the PCV-13 vaccine was launched on a national basis. It is administered in three doses; at 6, 10 and 14 weeks of age.

Little is known about the epidemiology of causative agents for pneumonia in Cameroon before introduction of the PCV-13 vaccine. However, among the invasive infections causing acute bacterial meningitis, two studies from Cameroon shows that 56.2 respectively 57.1 % of all cases were due to *Streptococcus pneumoniae*(29, 30).

There are major regional differences in vaccine coverage in Cameroon. In the South-West, where Buea and Limbe are situated, 75.2 % of the population had a full immunization in 2011, compared to only 30.9 % in the Extreme North(25). In the South West in 2013, two years after the introduction of the PCV-13 vaccine, an estimated 82 % of children up to two year old had received all three doses of the vaccine. In 2012 and the later part of 2011, coverage was 77% and 14% respectively(27).

Figure 1. *PCV-13 coverage in children <2 in the South-West region(27).*



Treatment Guidelines Pneumonia

There were standardized guidelines for treating pneumonia posted in the wall of the pediatric clinic in Buea. These were:

1. Oxygen
2. Antibiotic therapy

   In child 2 months – 3 years.

   - Amoxicillin – clavulanic acid 80-100 mg/kg/24 h.

     (in 3 doses iv).

   In child 3 years and above

   - Ceftriaxone 50-75 mg/kg/24 h

     (in 1 dose iv or im)

     OR

   - Ampicillin or amoxicillin 150mg/kg/24 h.

     (in 3-4 doses iv or im).
3. Antipyretics
   - Aspirin (in 3-4 doses iv, im or per os)
   - Paracetamol (in 3-4 doses iv or per os)
4. Cough syrups
   - Mucolytics - acetylcystein
   - Expectorants - carboncystein

Aim

To our knowledge, no investigation about the epidemiology of childhood pneumonia in Cameroon has been performed after introduction of the PCV-13 vaccine. The aim of this study is to investigate the epidemiology of childhood pneumonia and to examine early effects of the PCV13-vaccine in Buea, Cameroon:

- Has the number of confirmed pneumonia cases decreased after launching the PCV13-programme?
- Are there any early changes in mortality and severity when comparing the periods before and after immunization?
- Have the rates of invasive pneumococcal infections among children under five declined after immunization?

Method

Study population and data collection

The design was a retrospective hospital-based study at The Buea Regional Hospital (BRH). Limbe Regional Hospital was later also to become included in the study. At both hospitals all cases of pneumonia under 5 years of age, from June 2009 to October 2013, were identified through the admission book in the pediatric unit. Inclusion criteria was being between 1 month and 5 years of age and having a pneumonia diagnosis in the admission book. Altogether 333 cases were included.

The study period was divided into two periods of 26.5 months each; a "before period" June 2009 to August 15 2011 and an "after period" August 15 2011 to October 2013. The vaccine was introduced July 2011 and the reason for setting the break point six weeks later, at 15th of August 2011 is that children receive their first dose at the age of 6 weeks.

In Buea, the admission book held brief information about *age, weight, gender, symptoms, investigations, concomitant diseases, treatment, no of days stayed at the hospital and case fatality*. After identifying pneumonia cases that met the inclusion criteria, information was then obtained from the patients' medical files stored in the archive. After going through four entire months of medical records, we learned that the medical files contained very little, or no additional information, compared to the admission book. All medical records were therefore not further investigated and focus was instead put on collecting a larger number of cases, why the study was extended to also include Limbe Regional Hospital.

In Limbe Regional Hospital, the admission book comprised the same information as in Buea except that information about *symptoms, investigations and treatment* were missing.

Classification

All 205 cases in Buea Hospital were classified according to level of severity. As tachypnea is one of the clinical markers for non-severe pneumonia and as there was no information about respiratory rate, all cases that did not have any of the symptoms indicating severe or very severe pneumonia were automatically diagnosed as non-severe pneumonia. As there was only brief information about symptoms in the admission book, all cases that had any of the WHO-symptoms severe- or very severe pneumonia were merged into one and classified as severe pneumonia. No classification according to level of severity was made for the Limbe Hospital cases due to the lack of information of symptoms.

Statistical methods

The raw data was analyzed using IBM SPSS Statistics version 21. The correlation between gender and other variables were assessed using the crosstabs. P-values were obtained using Fisher's exact test. Descriptive statistics and frequencies were used to construct the tables presenting the results. To make the graphs Microsoft Excel 2010 was used. The significance cut off was set to p-value < 0.05.

Ethical considerations

Ethical clearance was obtained from the Ministry of Public Health, in the Regional Delegation of the South West Region, Cameroon. Copies of the authorization to collect research data were given to the General Supervisor of the Buea Regional Hospital and to the Director of the Limbe Regional Hospital, and thereafter also stamped and approved. The study did not interfere with the care or treatment of the children in the pediatric unit during the time of the study. All cases and all medical information have been treated anonymously.

Results

Of all the cases 4 were excluded due to lack of information about gender, and 11 were excluded because they were younger than 1 month. Remaining were 205 cases that met the inclusion criteria in Buea and another 128 cases in Limbe. Altogether 333 cases were included in the study. Mean age was 22,0 months. There was no information about vaccination status for each individual case; ; nevertheless vaccine coverage was reported to be 82 % in South-West region in June 2013. Distribution of cases according to gender and fatality before and after vaccination is shown in table 2.

Table 2. *Distribution of cases before and after vaccine introduction.*

	No of cases	Boys	Girls	Fatal cases
Before	167	92	75	2
After	166	98	68	6
Total	333	190	143	8

When comparing the periods before and after the beginning of PCV13-vaccination, no decrease in the no of cases was seen. In both the before and the after period, there were more

boys than girls diagnosed with pneumonia. The distribution of concomitant diseases is shown in table 3

Table 3. *Concomitant diseases*

Concomitant diseases (N =333)	%
Malaria	29.8
Gastroenteritis	6.0
Malnutrition	2.1
Rhinopharyngitis	1.8
HIV	0.6
Tuberculosis	0.6

One third of all the pneumonia cases also suffered from malaria. The proportion of severe cases did not change after vaccination, p = 0,551 NS, (see figure 2). Girls had severe pneumonia to a higher extent than boys; 38,9% compared to 27,0 %, p = 0,073 NS, (see figure 3).

Figure 2. *Classification according to severity before and after introduction of the vaccine.*

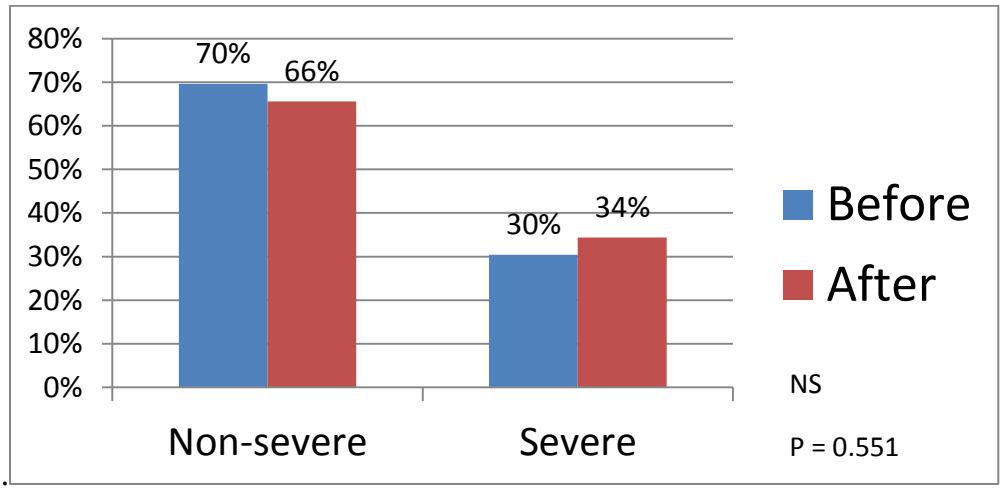
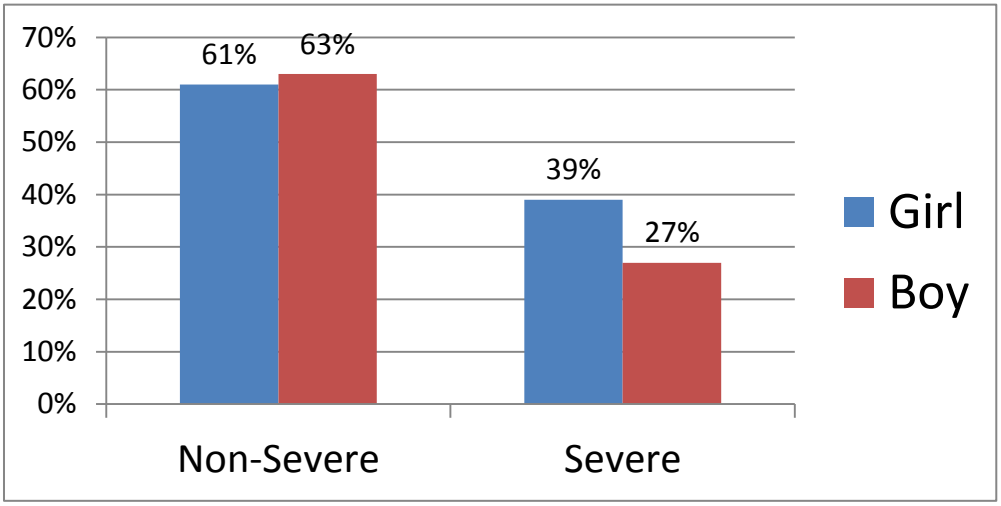


Figure 3. *Severity related to gender*



We separated the children aged 1-24 months from the bigger < 5 age group and analyzed it separately. In this age group the number of pneumonia cases in Buea and Limbe rose from 101 to 114 in the 1-24 months age group after vaccine introduction.

Fatal cases

The case fatality rose from 2 cases to 6 cases after vaccine introduction, p = 0.174 NS.

Case fatality related to gender

Of the 8 fatal cases that occurred during the study period, four were boys and four were girls.

Invasive pneumococcal disease

It was not possible to answer the third aim about rate of invasive pneumococcal disease. There was simply no information about IPD as blood cultures were not performed in Buea or Limbe regional hospital.

Seasonal variation

There was a seasonal variation over the 53 months that the study was conducted (see Figure 4). We then calculated the monthly average of pneumonia cases over the study period (see Figure 4) and found out that from November to February was the highest number of pneumonia cases and from June to September we found the lowest monthly average of

pneumonia cases (see Figure 5). These months correlates very well with the dry season and the wet season respectively. A comparison was thus made between the average monthly precipitation and the monthly average of pneumonia cases (see figure 6). It appeared to be a negative correlation between rainfall and number of pneumonia cases. In the four driest months of the year put together, November - February, the average rainfall was 269 mm and the monthly average of pneumonia cases 36, 75. In the four wettest months, June - September put together, the average rainfall was 2505 mm and the monthly average of pneumonia cases only 17. That makes a 20-fold increase in rainfall and half the incidence in number of pneumonia cases during the wet season compared to the dry season.

Figure 4. *Seasonal variation on number of cases.*

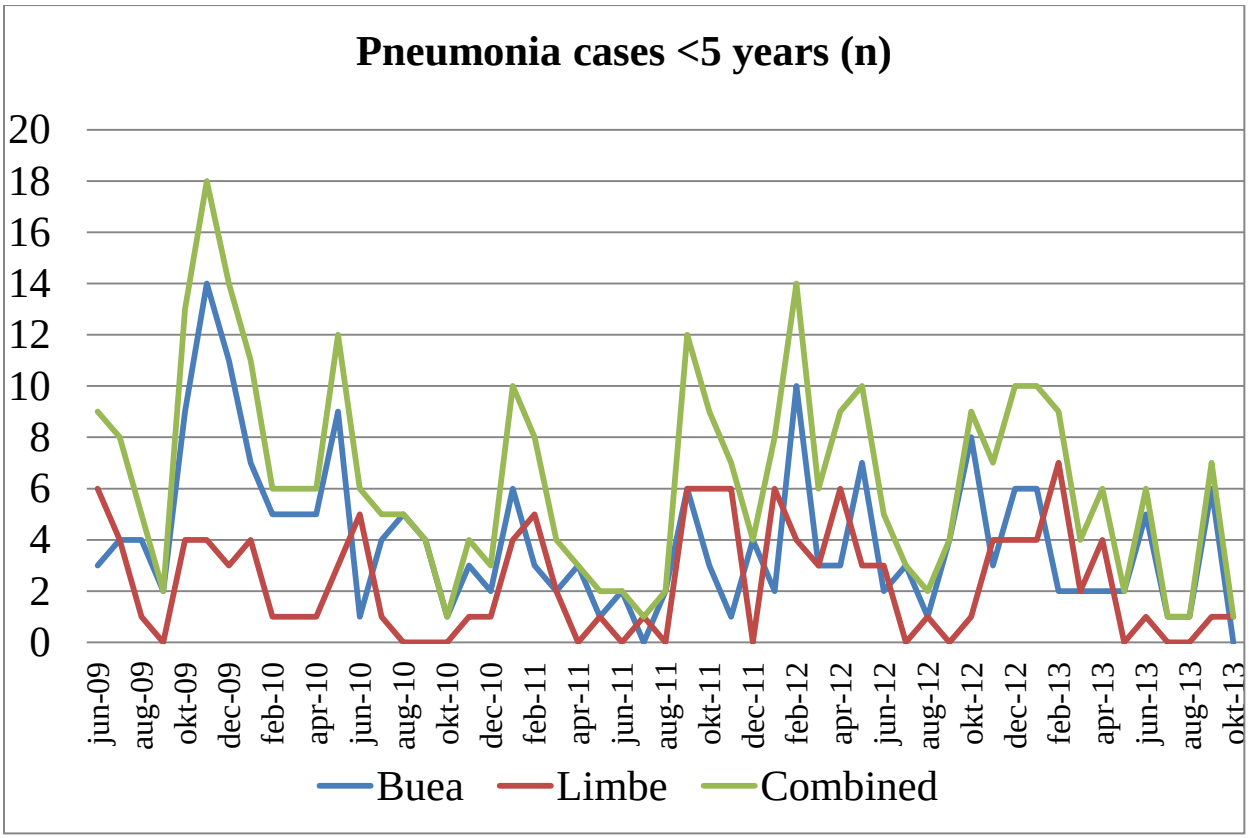


Figure 5. *Monthly distribution of pneumonia cases over "peak months" and "bottom months".*

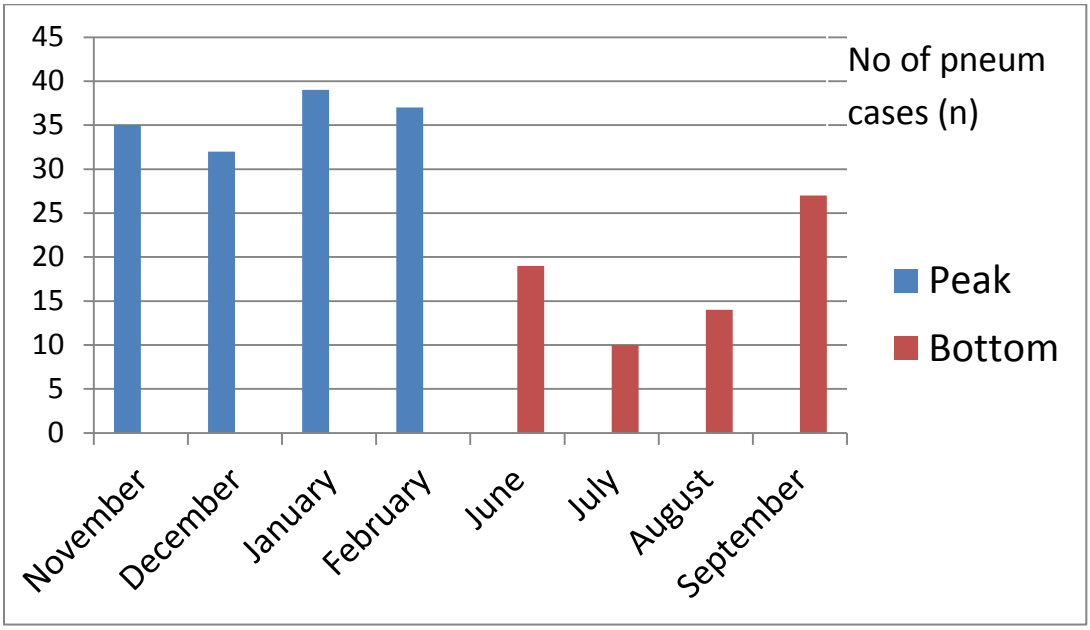
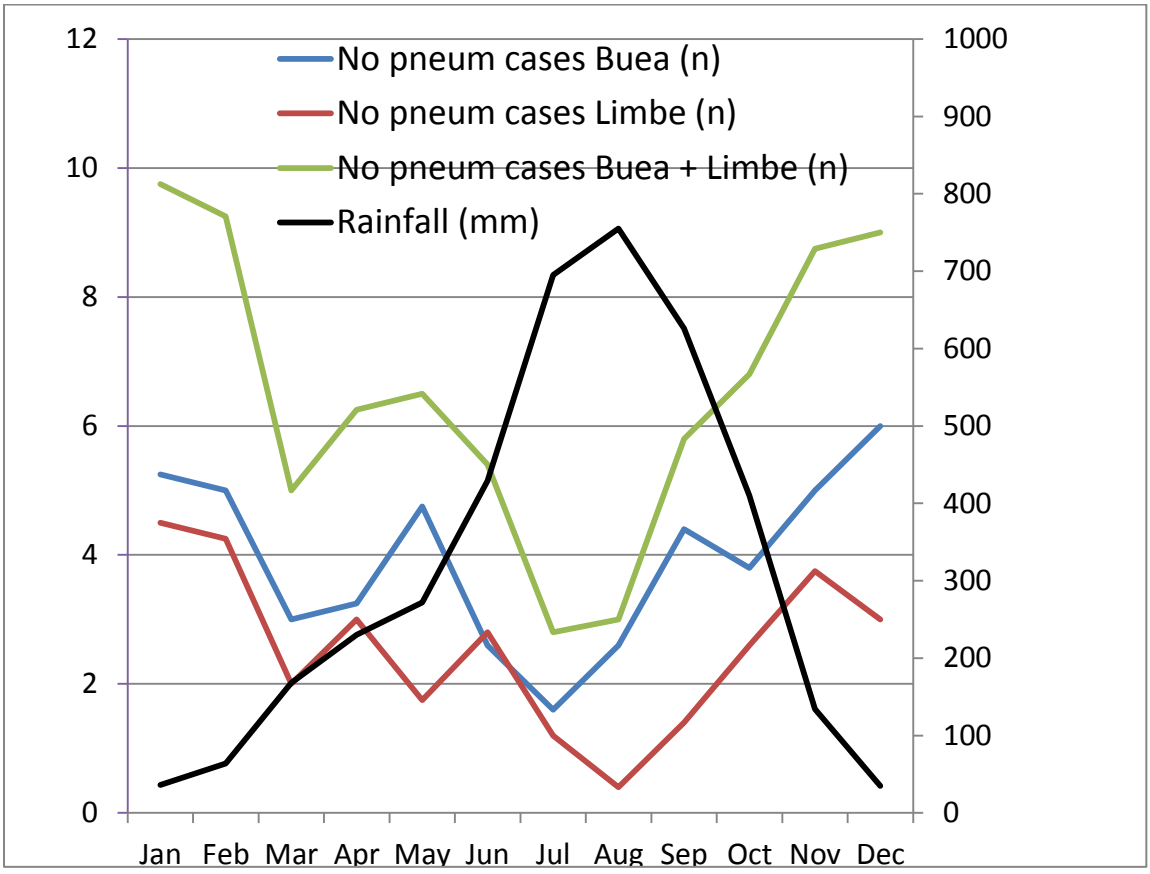


Figure 6. *Seasonal variation and correlation between average rainfall and average number of pneumonia cases*



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Oxygen treatment was used in 18 of the 205 (8,8 %) cases in Buea. The most common antibiotic treatment was the third generation cephalosporin *Ceftriaxone* (or equivalent generics) in combination with G*entamycin*, followed by *Ceftriaxone* as single treatment. In 45, 4 % of the cases, gentamycin were used despite the fact that it was not included in the treatment guidelines (See Table 4 and Treatment Guidelines).

Table 4. *Antibiotic treatments given*.

Antiobiotic treatment	N (%)
Third generation cephalosporin + Gentamycin	69 (33,5)
Third generation cephalosporin	63 (30,6)
Ampicillin + Gentamycin	16 (7,8)
No antibiotics	13 (6,3)
Ampicillin or Amoxicillin	12 (5,8)
Ampicillin + clavulanic acid	8 (3,9)
Ampicillin + third generation cephalosporin	8 (3,9)
Ampicillin + third generation cephalosporin + Gentamycin	8 (3,9)
Other	8 (3,9)
Total	205 (100%)

Discussion

Contrary to results from studies from England, Italy, US, South Africa and the Gambia, there was no change in the number of cases, level of severity or mortality in our study after introduction of the PCV-13 vaccine (7-13). What this stands for is not evident. Perhaps, we set the breakpoint too early after vaccine introduction. Herd effects are expected but take time to develop. In an evaluation of the PCV-vaccine from British Columbia, Canada, 7 years after vaccine start IPD decreased with 78 % among children < 5 (31). Interestingly, among the population aged 16 years and above, there were also clear evidence of herd immunity (31).

Over all, to make a more precise prognosis of vaccine effect, knowledge about serotype distribution among disease-causing pneumococci in the area is needed. The pneumococcal bacteria exist in more than 90 different serotypes and serotype coverage for the PCV-13 vaccine differs between countries as the pneumococcal serotype distribution varies. In the *Pneumococcal global serotype project*, Johnson et.al analyzed a large number of studies from 13 of Africa's countries. In Africa as a whole, the data analysis declared mean average serotype coverage for the PCV-13 vaccine with 77% (22). However, it appears as if West Africa has a higher prevalence of non-vaccine serotype pneumococci. In a study from the West-African countries Burkina Faso and Togo, Traore Y. et al. found that serotype coverage was just 62%(32). Possibly, Cameroon has a high prevalence of non-vaccine serotypes?

As a result of vaccine routines, we predicted a higher vaccine rate for children aged 1-24 month and a declince in number of cases after vaccine introduction. However, the number of pneumonia cases in Buea and Limbe rose from 101 to 114 in the 1-24 months age group after vaccine introduction. These results are the direct opposite to what we had expected and the findings are difficult to explain.

Unfortunately, there was no information about IPD as blood cultures were not performed in Buea or Limbe regional hospital. As a consequence, we don´t know the proportion of invasive disease that is caused by pneumococci.

Several diseases as severe malaria, sepsis, meningitis etc. had defined diagnostic criteria posted on the walls of the pediatric unit and/or in the emergency ward or in the outpatient unit. However, there were no written diagnostic criteria for pneumonia in Buea or Limbe. The doctors in Buea and Limbe defined pneumonia as how they had learned in medical school. The definition differed somewhat between doctors, with different focus on auscultation, rate of chest x-rays etc. Although a mutual finding was that respiratory rate was not measured and calculated on a regular basis.

There were more boys than girls affected with pneumonia, both before and after vaccine introduction. It is known from other diploma studies from the Sahlgrenska Academy and Denmark among others that boys are treated for pneumonia more frequently than girls (33-35). It remains unclear if this is due to physiological disadvantages or if girls are being taken to hospital to a lesser extent. However, when in hospital, girls were diagnosed with severe pneumonia to a higher extent than boys. What this stands for remains unclear. One hypothesis is that girls are being taken to the hospital in a later stage of the disease and as a consequence develop more severe forms of pneumonia before initiating treatment.

The low HIV-figures are probably an underestimation. Supposedly some of the patients may have had HIV that wasn´t being noted in the ledger. Possibly, it could be that parents of HIV-infected children did not inform the medical staff about the underlying illness, or that the children might have been treated elsewhere, for example at the HIV-/AIDS-unit.

Previous studies have shown that a drop in temperature to a certain level may increase the number of pneumonia cases (36). In a large population-based study from Taiwan with a study

sample of more than 477.000 pneumonia cases, there was a clear correlation between *temperature* and number of pneumonia cases(36). A drop in temperature implied an increase in number of pneumonia cases. Interestingly, there was also a correlation with *rainfall.* Similar to our findings, with higher precipitation, there was a decline in number of pneumonia cases. In Buea and Limbe, the climate is temperate and varies only a few degrees Celsius over the year in contrast with the average rainfall that varies substantially. Hence, the small drop in temperature during the wet season in Buea and Limbe is probably not the reason for the absence of pneumonia cases. The negative correlation between rainfall and pneumonia incidence in this study remains as an interesting finding. Could rainfall or humidity play a role in pneumonia incidence? More studies are needed to test this hypothesis.

A problem with today's vaccines is that they are not thermo stable. For example the PCV-13 vaccine has to be stored between 2-8 degrees Celsius. This demands a stable cold chain system and appropriate equipment. Health care centers and hospitals thus need refrigerators/freezers, educated personal and alternative sources of power to avoid power interruption. Infrastructure such as good roads is also essential in order to deliver vaccines to health centers throughout the country. Low vaccine coverage in some regions of Cameroon is partly explained by bad roads, poor cold chain equipment and power interruption(4, 37). There was an underuse of oxygen therapy compared to treatment guidelines. There was an overuse of broad spectrum antibiotics compared to the written guidelines. Almost half of the cases were treated with Gentamycin as combination therapy, despite the fact that Gentamycin is not mentioned in the treatment guidelines. It would of course be ideal to do blood cultures and streamline the prescription of antibiotics. Though, it is understandable that physicians sometimes need to prescribe broad spectrum antibiotics as no blood cultures were being made on a regular basis at the hospitals; and as blood cultures are expensive and might not be the first matter to prioritize when money is scarce.

Limitations

For the time of this study, the one pediatrician at the Buea Regional Hospital, where the bigger part of the study was conducted, was unfortunately on leave. The department was then run by two general practioners taking turns every second week. Useful information from an experienced specialist might have gone missing that way.

There was no way to find out if the individual cases included in the study had been vaccinated. No information about vaccination status was kept in the medical records. In general, the medical records did not comprise summaries or profound information about the patients.

To be able to investigate gender differences, knowing gender was highly important to us. Hence, we had to exclude four of the cases with no information about gender.

The study period stretched over 53 months with a breakpoint in the middle. It was divided into two periods 26.5 months long. This was the easiest way to compare the two periods with each other. Though, the periods have different start and end months. That means that the "before" period in total have one more month of wet season compared to the dry season. This could play a marginal role when comparing the "before" and "after" periods.

The medical files stored in the Limbe Regional Hospital archive seemed to comprise slightly more detailed information compared to the medical records in Buea Regional Hospital. It would have been of interest going through all of the medical files in Limbe for additional information regarding symptoms and treatment of the in-patients in Limbe. However, within the time frame of this master thesis and the limited amount of time left after collecting data in Buea Regional Hospital, this was not possible.

Some of the strengths of the study were that the admission book in both hospitals, but especially in Buea, comprised brief but seemingly accurate information. The total number of cases collected was also high regarding the short period of time that the study was conducted.

Conclusions

- Despite the negative results, it is too early to conclude that the PCV-13-vaccine will not have any effect on pneumonia incidence among children in the region. A longer follow up time, and more studies and larger numbers are necessary.
- To make a more precise prognosis of vaccine effect, knowledge about serotype distribution both among disease-causing and carriage isolates of pneumococci in the area is needed.

Implications

- Use oxygen treatment more frequently. If possible, streamline the use of antibiotics.
- Implement common written diagnostic guidelines for pneumonia in the emergency ward, pediatrics, out-patient department etc for optimizing treatment. Measure respiratory rate on a regular basis.
- If vaccination status of individual children would have been known and registered in the medical records it would have been much easier to evaluate vaccine effect.

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Populärvetenskaplig sammanfattning

Lunginflammation orsakar varje år 1.3 miljoner dödsfall bland barn under 5 år världen över. Det är fler än AIDS, tuberkulos och malaria sammantaget. Majoriteten av dessa inträffar i Afrika söder om Sahara och i södra Asien. I Kamerun är lunginflammation den näst vanligaste dödsorsaken (efter malaria) bland barn under 5 år och orsakar 18 % av alla dödsfall. Lunginflammation botas relativt enkelt med antibiotika, och kan effektivt förebyggas med förbättrad levnadsstandard och bättre luftförhållanden samt genom vaccinering. Enligt WHO är vaccinering det mest effektiva sättet att förebygga insjuknande i lunginflammation.

Lunginflammation kan orsakas av bakterier, virus såväl som svampar. Den vanligaste orsaken är infektion med bakterien *Streptococcus pneumoniae*. I juli 2011 infördes ett 13-valent konjugatvaccin (PCV-13) mot pneumokocker i Kamerun. Inga utvärderande studier av vaccinets effekt har hittills gjorts i Kamerun.

Vi gick igenom alla fall av lunginflammation för barn i åldern 1 månad till 5 år som vårdats på Buea- samt Limbe Regional Hospital någon gång sedan juni 2009. Antalet fall i lunginflammation, allvarlighetsgrad- samt dödlighet i sjukdomen studerades före och efter vaccinstart. Även val av behandling undersöktes.

Det gick inte att se några tidiga effekter av vaccinet. Varken på antal fall av lunginflammation, allvarlighetsgrad eller dödlighet. En minskning från 137 fall till 136 fall perioden efter vaccinets införande noterades. Andelen allvarliga lunginflammationer ökade något efter vaccinstart. Antalet dödsfall till följd av sjukdomen var 2 före vaccinets införande respektive 6 perioden efter vaccinstart. Vi studerade även den yngsta delen av populationen (1-24 månader) där andel vaccinerade rimligvis borde vara som högst, men inte heller där syntes några positiva effekter av vaccinet. Tvärtom ökade antalet fall från 101 till 114 i yngsta gruppen. Dock är inga av ovanstående resultat statistiskt säkerställda.

Det fanns en tydlig säsongsvariation med färre fall av lunginflammation under regnperioden och fler fall under torrperioden. Detta samband har även setts i andra studier men orsakerna till detta är fortsatt ej klarlagda.

Flera studier har visat på god effekt av PCV-vacciner. Varför ingen effekt påvisats i denna studie är öppet för diskussion. Det tar tid att uppnå allmänna mätbara effekter av vaccinering och möjligen var den studerade tidsperioden efter vaccinstart för kort? Eventuellt finns det i Kamerun, en hög andel varianter av bakterien *Streptococcus pneumoniae* som inte täcks av PCV-13 vaccinet? Kanske har andra faktorer såsom nederbörd eller luftfuktighet inverkan på förekomst av lunginflammation?

Det är dock för tidigt att säga att PCV-13-vaccinet inte har några effekter för barn under 5 års ålder i Kamerun. Fler, större och fördjupade studier på området behövs för att vidare undersöka vaccinets effektivitet. Framtida studier behövs även för att undersöka ett eventuellt samband mellan pneumoni och nederbörd.

Acknowledgments

Supervisor Erik Backhaus, MD, PhD, Chief Physician, Department of Infectious Diseases, Skaraborg Hospital, Skövde, Sweden.
For helping me form the study plan and for supervising me during the whole period of the project.

Supervisor Dr Ndeso Atanga Sylvester, MPH, PhD, Director of Higher Institute of Applied Medical Sciences, Buea, Cameroon.

For accepting me to do my master thesis in Buea, arranging everything from ethical clearances to interesting study visits and for showing me around in Cameroon.

Director Dr George Enow Orock and General Supervisor of Buea Regional Hospital
For allowing me to perform my study at Buea Regional Hospital

Director Dr. Thompson Kinge and General Supervisor of Limbe Regional Hospital
For allowing me to perform my study at Limbe Regional Hospital

Head Nurse and all of the other Staff at the Pediatric Department of Buea Regional Hospital.
For all the help, good patience and laughter during my work in the pediatric department.

Head Nurse and all of the other Staff at the Pediatric Department of Limbe Regional Hospital.
For good help and nice time during the short time I spent in the Limbe Regional Hospital.

Coc and all the health staff Buea Road Integrated Health Center
For valuable information and letting me take part of vaccine routines.

Pediatrician Dr. Martin Neba Ngwa in Bafoussam.
For all the hospitality, letting us visit his clinic in Bafoussam and for providing valuable information.

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