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Research Article

Pneumococcal Conjugate Vaccines (Pcvs) Introduction in the Immunization Program and its Impact on Mortality Under 5 Years in Guyana, South America

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Objective

Assess the impact of routine childhood PCV vaccination on the mortality of children under 5 years of age due to all-causes, and also due to pneumonia infections as being the underlying cause of death.

Keywords: Correlation; Linear regression; Pneumococcal Conjugate Vaccines

Introduction

Pneumococcal infections are one of the most important causes of diseases in children under 5 years of age in countries throughout the world. Streptococcus pneumoniae (S.pneumoniae or pneumococcus) causes a variety of clinical syndromes, including pneumonia, meningitis, and bacteremia, as well as milder but more common illnesses such as otitis media and sinusitis [1].The World Health Organization (WHO) in 2012 recommended the introduction of pneumococcal conjugate vaccines (PCVs) in childhood immunization programs with high priority to countries with mortality rate >50 deaths/1000 births in children under 5 years of age [2]. Guyana has registered 517 deaths over the period 2000 to 2013 under the age of 5 years with the median

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age at death of 6 months due to respiratory system related illness, therefore in the light of the high number of respiratory illnesses and deaths the PCV vaccines were introduced.

Pneumococcal conjugate vaccines (PCVs) were first licensed in 2000. There are currently two commercially available vaccines. The first PCV to be developed, PCV7 Prevnar (7- valent, PCVs7), was licensed in 2000 in 2010, Synflorix (10-valent, PCV10) and Prevnar (13-valent, PCV13) were introduced to the market and replaced PCV7. PCV10 includes antigens for the seven S. pneumoniae serotypes in PCV7 and serotypes 1, 5,7F, while PCV13 includes antigens for the aforementioned 10 serotypes as well as 3, 6A, and 19A. All three vaccines have demonstrated excellent safety and efficacy profiles in clinical trials [2]. Guyana initiated the PCV 7 vaccines for children who were immunized suppressed and later in 2011-2012, did the nationwide introduction of PCV 13 to the under 1 years old. Three doses of these vaccines were given at 2 months, 4 months and 6 months. These vaccines were given from Regions 1-10 years throughout Guyana. Pneumococcal infections are one of the most important causes of diseases in children under 5 years of age in countries throughout the world. Streptococcus pneumoniae (S. pneumoniae or pneumococcus) causes a variety of clinical syndromes, including pneumonia, meningitis, and bacteremia, as well as milder but more common illnesses such as otitis media and sinusitis [1].

Several studies have reported on the effectiveness and impact of both PCV10 and PCV13 on the reduction of meningitis and pneumonia hospitalizations. However, there is scarce evidence on the impact of PCVs on mortality in children under 5 years of age. This is mainly due to challenges in accessing and analyzing nationwide mortality data. In Latin America countries, and Caribbean including Guyana data is routinely collected on morbidity and mortality data but no analysis has been done on the available data or the disease burden. There is a need to review the impact of this disease in view of the introduction of Pneumococcal Conjugate Vaccines (PCVs) in countries and Guyana [3].

Materials and Methods

This study used an ecologic study design by the reviewing of available secondary mortality data 2000 to 2013 from the Ministry of Public Health, Statistical Department. This included the period when no PCVs vaccination occurred prior to 2010, transition period, when vaccine was introduced in the country and coverages were still low 1 year after (in this case this was 50%) introduction and post-vaccine introduction period, when PCVs was routinely offered to all infants in all states in the country. Data was extracted without personal identifiers by the use of Excel software for the age at death below 5 years. The total sample size was 4931. As a specific cause of death that the authors interested in were deaths due to respiratory system. There were 517 cases registered under this category. Crude Mortality rates and cause specific mortality rates were calculated and compared. Frequency distributions with percentages, descriptive statistics such as mean, median and standard deviation, correlation and linear regression models were calculated for interpretation and prediction purposes.

Data analysis was done using SPSS 20.0 for the deaths due to pneumonia, as coded in the International Classification of Diseases 10th edition (ICD10) as J12-J18, and sub codes, deaths due to all-cases, including any cause as coded in the ICD10 under 5 years and deaths due to all respiratory causes, including all J00-J99 codes in the ICD10. G00-G99 In addition, diseases of the nervous system was also added to the group of RTIs due to the complications such as bacterial meningitis. Trends of observed monthly mortality rates during the post PCVs introduction period was compared with rates in the pre-vaccine period. The mortality rate for below the age of 5 was calculated as Mortality Rate= (Total Number of Deaths in the particular year) / (Total Number of live births in the same year)*100,000.

Results

Year	Total population	Population In children under-5	Infant Mortality*1000	PCV Vaccination Coverage (%)
2010	746,955	74,256	14.7	-
2011	746,955	72,326	14.8	50
2012	746,955	70,440	13.8	90
2013	746,955	68,510	13.6	96

Table 1: Guyana Bureau of Statistics Population and housing Census 2012, IMR and PCV coverage -Ministry of Public Health Data. Total population, under-5 population, infant mortality, PCV vaccination coverage for 3 doses, Guyana, 2010-2016 [4].

(Table 1) shows demographic information including total population, under-5 population, from 2010 to 2016; the infant mortality rate from 3.6 to 4.1 for 1000 births and the PCV vaccination rate was 50% in 2011 and increased to 95 % at the end of 2016 [5] .

Figure 1: Ministry of Public Health, Statistical Department 2017 Guyana under 5 mortality rate per 1,000 from 2000-2013, the study reviewed 4,931 mortality cases from 2000-2013 (refer Table 2) from the Ministry of Public Health data base

In [Figure 1] it was observed that the year 2004 has the highest mortality rate of 59.8 deaths in 1,000 births; this was due an outbreak of neonatal infections in the main referral hospital. Quality standards measures were put in place and this infection subsided. As the years progressed, there was a steady decline in the mortality rate to 35.3 per 1, 000 births at the end 2013. This trend line illustrates the downtrend in the mortality rate under 5 years in Guyana [6].

In [Figure 3 and Table 3] below, the mortality was highest in the under 1 age group; this is because that most causes of deaths under 5 years occurred in the perinatal period.

When this was compared with the introduction of the PCV vaccines, it was shown that the mortality rate was highest in the period prior to vaccination in 2011 and decreased to 263-254 cases (refer Figure 2).
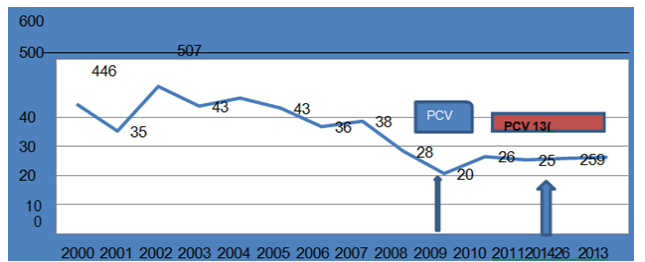

Figure 2: Mortality cases under 5 years prior to PCV vaccine Introduction and after in Guyana.
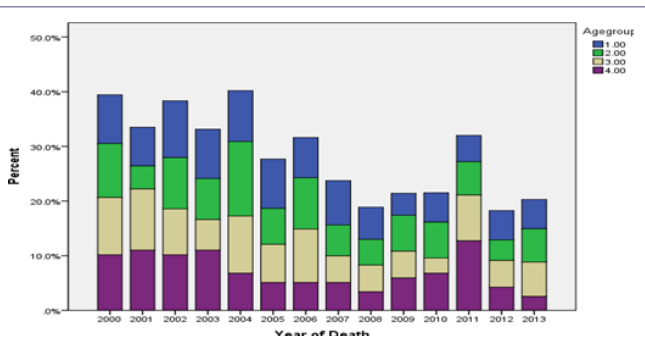

Figure 3: Mortality in children under the age specified groups from 2000-2013

With reference to [Table 2], P00-P96- certain conditions originating in the perinatal period had 2052, with a mortality rate of 41.6 per 1000. Respiratory tract infections accounted for ICD G00-G99 and J00-J99 with a total of 517 cases (refer Table 2).

Causes of Death	# U5 yrs deaths	Percent
A00-B99 Intestinal infectious diseases, tuberculosis, Certain Zoonotic bacterial diseases, Other bacterial diseases etc…	801	16.24
C00-D49- Malignant neoplasm	95	1.92
D50-D89- diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	70	1.41
E00-E89- Endocrine, nutritional and metabolic diseases including malnutrition, metabolic disorders	230	4.66
G00-G99- Diseases of the nervous system- including bacterial meningitis	118	2.39
H60-H95- Diseases of the ear and mastoid process	1	0.02
I00-I99- Diseases of the circulatory system	177	3.58
J00-J99- Respiratory tract infections	399	8.09
K00-K95- diseases of the digestive system	75	1.52
L00-L99- Diseases of the skin and subcutaneous tissue	4	0.08
M00-M99- Diseases of the musculoskeletal system and connective tissue	3	0.060
N00-N99- Diseases of the genitourinary system	27	0.547
O00-O99-diseases of the maxilla facial etc	1	0.020
P00-P96- certain conditions originating in the perinatal period	2054	41.65

Q00-Q99- Congenital malformations, deformations and chromosomal abnormalities	466	9.45
R00-R99- symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	56	1.13
V00-Y99- External causes of morbidity	355	7.199
Total	4931	100

Table 2: ICD Classification of diseases under 5 years.

	Age group				Total
Year	Below 1 Year	1-2 Years	2- 3 Years	3 – 4 Years	
2000	57(83.80%)	6(8.80%)	3(4.40%)	2 (2.90%)	68
2001	37(82.20%	2(4.40%)	4(8.90%)	2(4.40%)	45
2002	51(94.4%)	2(3.7%)	1(1.90%)	0(0%)	54
2003	30(78.90%)	6(15.80%)	1(2.60%)	1(2.60%)	38
2004	38(79.2%)	6(12.5%)	1(2.10%)	3(6.20%)	48
2005	36(81.80%)	5(11.40%)	2(4.50%)	1(2.35)	44
2006	31(96.9%)	1(3.15)	0(0%)	0(0%)	32
2007	20(74.1%)	6(22.2%)	1(3.7%)	0(0%)	27
2008	21(87.5%)	3(12.5%)	0(0%)	0	24
2009	21(80.8%)	3(11.5%)	0(0%)	2(7.75)	26
2010	17(70.80%)	4(16.70%)	1(4.2%)	2(8.3%)	24
2011	20(60.45%)	6(19.40%)	3(9.7%)	2(6.5%)	31
2012	18(75.0%)	3(12.5%)	1(4.2%)	2(8.3%)	24
2013	28(87.5%)	1(3.1%)	3(9.4%)	0(0%)	32
Total	425	54	21	17	517
	82.20%	10.40%	4.10%	3.30%	100%

Table 3: Age specific deaths for children below 5 years from 2000 to 2013 due to respiratory related illnesses and complications

In [Table 3], it is observed that 82% (425 cases) of the deaths due to respiratory related illness occurred below 1 year for the period 2000 to 2013. In [Figure 2], it is shown that the UM5R due to respiratory tract infections and complications decreased from 2000-2013 therefore, it is vital to continue to implement PCV vaccines into the national immunization programme [Figure 4].
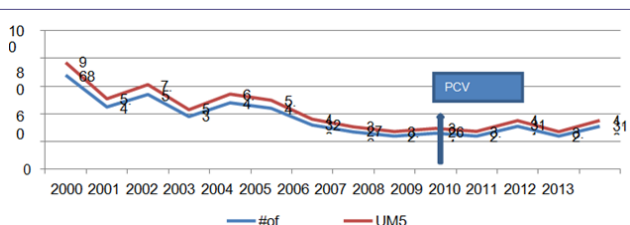

Figure 4: Under 5 mortality due to respiratory tract infections and complications.

There is a high negative correlation (-0.882) between Year and the number of deaths due to respiratory related illness for the children below 5 years of age and the correlation is highly significant since the p-value=0.000<0.05. This significant reduction in death in below 5 years was achieved by the successful implementation of PCV vaccination since 2010 [Tables 4 & 5].

	Correlations		
		Year	Number of deaths
Year	Pearson Correlation Sig. (2-tailed) N	1 17	-.882** .000 17
Number of deaths	Pearson Correlation Sig. (2-tailed) N	-.882** .000 17	1 17

Table 4: Pearson correlations according to the number of deaths Correlation is significant at the 0.01 level (2-tailed).

	Coefficientsa				
Model	Unstan- dardized Coefficients		Standardized coefficients	t	Sign.
	B	Std.Error	Beta	7.279	.000
1 (Con- stant)	5190.922	713.106		-7.233	.000
Year	-2.569	0.355	-0.882		

Table 5: A simple linear regression models to predict the number of deaths is shown in the above.

Linear regression model to predict the number of deaths.

a. Dependent variable: Number of deaths

As the year progresses, the number of deaths reduced by 2.569 times. The linear regression model is significant since the p-value = 0.000 < 0.05 and the coefficient of determination (R-square) is 77.7%. This shows that the implementation of PCV Vaccination contributes almost 78% in reduction of number of deaths due to respiratory related illness for children under 5 years of age.

Discussion

In the research, we can conclude that after the introduction of PCV vaccines the under 5 mortality rate has been decreased over the years including the respiratory tract infections. This is aligned to studies conducted to evaluate the impact of PCVs. According to South Africa following PCV introduction and the improvement in HIV interventions, 41,800 (95% CI 28,000-50,000) severe pneumococcal disease cases were estimated in 2012-2013 with a rate reduction of 1,277 cases per 100,000 child-years.

In addition Scotland revealed similar result. There was an 11 % reduction in deaths due to all-cause pneumonia, and 30 % reduction in pneumococcal hospitalizations across all age groups in the post-PCV13 period compared with pre-PCV period [4].

From this study, it was noted that the group most affected was under 1 year. The main cause of death was certain conditions originating in the perinatal period, 2052, with 41.65 %, followed by intestinal infectious diseases 801 with 16.24% and respiratory tract infections and complication 517 with 10.48%.

The linear regression model was significant with the p-value =0.000<0.05 and the coefficient of determination (R-square) is 77.7%. This shows that the implementation of PCV Vaccination contributes almost 78% in reduction of number of deaths due to respiratory related illness for children under 5 years of age.

Conclusion

This clearly shows that the national authorities should continue to invest in PCV vaccination to implement this vaccination and also look into other major causes of death and prepare a disease control chart for the administration to take necessary actions.

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