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Prevalence of Respiratory Syncytial Virus in infants in Khartoum State, Sudan

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ABSTRACT

Respiratory syncytial virus (RSV) is the most important cause of acute lower respiratory tract infections (ALRI) in early childhood. The main purpose of this study was to investigate the prevalence rate of the respiratory infection in infants 0-2 years, with special reference to RSV through detecting its antibodies (IgG) in infants in Khartoum state. Data about the incidence of respiratory infection in infants in Sudan during 2004-2008 was collected and analyzed. A total of 92 serum samples were collected during June – September in 2009 from infants with respiratory disease in Gaafer Ibn Ouf and Almaygoma hospitals in Khartoum State. Sera were tested for the detection of RSV IgG using ELISA. It was noticed that the main disease that cause hospitalization and leading to death in infants was pneumonia and it had higher prevalence rate in Khartoum state. A total of 24 (26%) sera were found to be positive for RSV IgG. The sero-prevalence rate of RSV was found higher in 1-2 year age group, no significant difference (P = 0.635) between males and females was found. The data showed that there was a significant difference between clinical signs and RSV infection in pneumonia, acute bronchitis and asthma (p = 0.05, 0.035, 0.035). RSV antibodies were detected more in re-infected infants with respiratory infections than first time infected infants (28.8%). There was a significant difference between the RSV infection in infants and the past history of respiratory infections in their mothers (p = 0.015). The study showed that RSV infection was found to be highly prevalent in Khartoum state and it has major role in causing respiratory tract infection. Greater efforts are needed to prevent pneumonia among children.

INTRODUCTION

RSV belongs to the genus pnemovirus, sub family paramyxovirinae of the family paramyxoviridae; it is an enveloped non-segmented negative-sense RNA virus (peiris and modeley, 2007). Respiratory syncytial virus (RSV) is the most common cause of bronchiolitis and pneumonia among infants and children under 1 year of age. Illness begins most frequently with fever, runny nose, cough, and sometimes wheezing. During the first RSV infection, between 25% and 40% of infants and young children have signs or symptoms of bronchiolitis or pneumonia, and 0.5% to 2% require hospitalization. Most children recover from illness in 8 to 15 days (peiris and modeley, 2007).

Other health problems can also develop as a complication of RSV infection these include, ear infections (otitis media), dehydration, collapsed lung (atelectasis), and sudden heart failure. This complication is most common in older adults who have heart problems or other lung problems (Levin and Weinberg, 2007).

Recent studies has estimated that for a given year (2005), 33.8 million new episodes of RSV-associated acute lower respiratory tract infections (ALRI) occurred worldwide in children younger than 5 years of age, with at least 3.4 million episodes representing severe ALRI necessitating hospital admission, and an estimated 66,000–199,000 fatal cases, 99% of which occurred in developing countries (Nair *et al.*, 2010). Several diagnostic methods for RSV have been developed (Arens *et al*., 1986, Waner *et al*., 1990, Hierholzer et *al*., (1989), McGivney *et al*., 2011). In Sudan, no literature was so far available about the existence of RSV infections in infants.

Here, the epidemiology of respiratory infection in infants during 2004-2008 is investigated and the results of the prevalence of the respiratory syncytial virus infection in infants were presented through detecting its antibodies (IgG) in infants in Khartoum state.

MATERIALS AND METHODS

Study Area:

The current study was conducted in Gaafer Ibn Ouf hospital and Almaygoma health center, Khartoum State, Sudan. Infants up to 2 years of age showing respiratory signs were included in the study.

Data Collection:

Records concerning respiratory infection in Sudan during 2004-2008 was collected. Data were statistically analyzed using SPSS software programme.

Sample collection and storage:

A total of 92 blood samples were collected from infants with respiratory disease during (June –September) 2009. Serum was separated from blood sample and stored at -20°C till used.

Detection of respiratory syncytial virus antibodies:

ELISA kits for detection of RSV antibodies (IgG) (Serion Virion, Fried Rich Bergius, Germany) were used in all collected sera samples. The Kits were used according to the instructions of the manufacturer.

RESULTS

Epidemiology of respiratory infection

Different respiratory signs in infants reported in different states of Sudan

It was noticed from the data collected over five years (2004-2008) that the main different respiratory sings reported in Sudan were, middle ear infection (158), pneumonia (34984.2) and Asthma (24496.8) in Khartoum state, The acute bronchitis was 1600.2 in eastern states and allergy was 321.2 in central state. The data showed significant differences between clinical signs and states of Sudan ($p = 0.006$, 0,000, 0.000, 0.000, 0.007) (Table 1 and Figure 1).

Table 1: Respiratory infections in infants in different states of Sudan 2004-2008

Clinical sings	State	Mean	P-value
Middle ear	Northern states	10.8	
	Khartoum	158	
	east states	55.2	
	central states	45	***0.006***
	Kordfan	7.2	
	Darfur	4	
	Total	46.7	
Pneumonia	Northern states	9453.4	
	Khartoum	34984.2	
	East states	11964.2	
	Central states	27763.2	***0.000***
	Kordfan	5232.6	
	Darfur	2435.4	
	Total	15305.5	
Acute bronchitis	Northern states	91.2	
	Khartoum	1382.4	
	East states	1600.2	
	Central states	530.6	***0.000***
	Kordfan	65.4	
	Darfur	35.4	
	Total	617.5333	
Asthma	Northern states	1129.4	
	Khartoum	24496.8	
	East states	1599.6	
	Central states	3162.6	***0.000***
	Kordfan	1430.4	
	Darfur	184.4	
	Total	5333.867	
Allergy	Northern states	153.4	
	Khartoum	215.2	
	East states	71.2	
	central states	321.2	***0.007***
	Kordfan	89	
	Darfur	124.6	
	Total	162.4333	

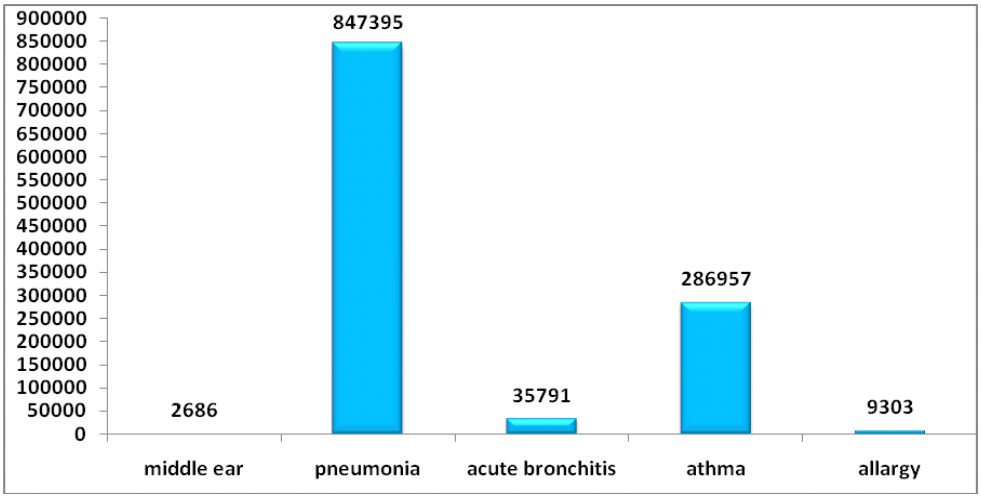

Figure 1: Signs of respiratory infection in infants in Sudan (2004-2008)

Different respiratory signs reported in infants hospitalized in Sudan

The study showed that pneumonia had the highest number of reported respiratory signs at 0-1 years of age during 2004, 2007, 2008 the reported cases were, 29731, 3798, 26275 and it's deaths were 840,641,496. In 2005 and 2006 also pneumonia showed the higher number of hospitalized infants at 1-4 years of age (30255, 33453), and its deaths were 245, 263. A significant difference was found in discharged patients between age group and different clinical signs in middle ear, pneumonia and asthma (p =0.012, 0.012, 0.002) while there was no significant difference in acute bronchitis and allergy (Table 2).

Table 2: Respiratory infection that needed hospitalization in infants in Sudan (2004-2008)

Year	age	Total	middle ear	deaths	pneumonia	deaths	acute bronchitis	deaths	asthma	deaths	allergy	deaths
2004	**< 1 year**	30813	1(0%)	0	29731(96%)	840	501(2%)	2	510(2%)	2	70(0%)	0
2004	**1- 4 year**	28193	12(0%)	0	24792(88%)	286	400(1%)	6	2887(10%)	3	102(0%)	2
2005	**< 1 year**	32047	8(0%)	0	29772(93%)	637	1087(3%)	16	1109(3%)	8	71(0%)	1
2005	**1- 4 year**	34304	18(0%)	1	30255(88%)	245	683(2%)	1	3009(9%)	7	339(1%)	0
2006	**< 1 year**	34452	17(0%)	0	32017(93%)	551	1184(3%)	15	1143(3%)	2	91(0%)	0
2006	**1- 4 year**	37916	28(0%)	0	33453(88%)	263	1039(3%)	6	3236(9%)	3	160(0%)	1
2007	**< 1 year**	41642	38(0%)	0	37598(90%)	641	2114(5%)	10	1675(4%)	6	217(1%)	1
2007	**1- 4 year**	43149	52(0%)	0	36671(85%)	274	1643(4%)	4	4503(10%)	5	280(1%)	0
2008	**< 1 year**	29376	93(0%)	0	26275(89%)	496	2363(8%)	12	545(2%)	9	100(0%)	2
2008	**1- 4 year**	29582	163(1%)	0	25375(86%)	158	1689(6%)	2	2196(7%)	7	159(1%)	1

Different respiratory signs reported in infants visited the clinics in Sudan.

The data showed that Acute bronchitis was the highest infection in patients that needed clinical visits in 2004 at 1-4 years of age (201907, 55%), and pneumonia was the highest infection in 2005-2008 at 1-4 years of age (167029, 50.7%), (187970 87.8%), (136225, 71.5%), (274515, 73.1%), respectively. The study showed that a significant difference in outpatient was found between age group and different clinical signs in asthma and allergy (p =0.00, 0.00). And no significant difference in middle ear, pneumonia and acute bronchitis (Table 3).

Table 3: Respiratory infections that needed clinical visits (out patients) in Sudan (2004-2008)

Year	Age	Total	Middle ear		pneumonia		Acute bronchitis		Asthma		Allergy	
			No.	%	No.	%	No.	%	No.	%	No.	%
2004	< 1 year	253221	478	0.2%	117945	46.6%	128509	50.7%	1087	0.4%	5202	2.1%
2004	1- 4 year	367358	2023	0.6%	150178	40.9%	201907	55.0%	4676	1.3%	8574	2.3%
2005	< 1 year	171838	2274	1.3%	116495	67.8%	47393	27.6%	1570	0.9%	4106	2.4%
2005	1- 4 year	329123	7391	2.2%	167029	50.7%	92937	28.2%	6247	1.9%	55519	16.9%
2006	< 1 year	136460	2023	1.5%	124117	91.0%	4586	3.4%	1847	1.4%	3887	2.8%
2006	1- 4 year	214158	3448	1.6%	187970	87.8%	8002	3.7%	6664	3.1%	8074	3.8%
2007	< 1 year	123027	4472	3.6%	98042	79.7%	6360	5.2%	3573	2.9%	10580	8.6%
2007	1- 4 year	190578	10804	5.7%	136225	71.5%	10143	5.3%	12571	6.6%	20835	10.9%
2008	< 1 year	236575	5144	2.2%	186237	78.7%	32954	13.9%	5191	2.2%	7049	3.0%
2008	1- 4 year	375714	12354	3.3%	274515	73.1%	57926	15.4%	17292	4.6%	13627	3.6%

Role of respiratory infections in causing hospitalization in infants

The data showed that within the ten top listed diseases causing hospitalization in infants, Pneumonia accounted for 28.3-30% during 2004-2008. Asthma accounted for 1.8 -2.5% during 2004-2007 while acute bronchitis was accounted for 2% in 2008 (Table 4 and Figure 2).

Table 4: Incidence of respiratory infection out of the 10 leading causes of hospitalization in infants in Sudan (2004-2008)

Year	Diseases	Number	%
2004	Pneumonia Asthma	54523 3397	28.3 1.8
2005	Pneumonia	60027	29.1
	Asthma	4118	2
2006	Pneumonia	65470	29.4
	Asthma	4379	2
2007	Pneumonia	74269	29.9
	Asthma	6178	2.5
2008	Pneumonia	51650	25.9
	Acute bronchitis	4052	2

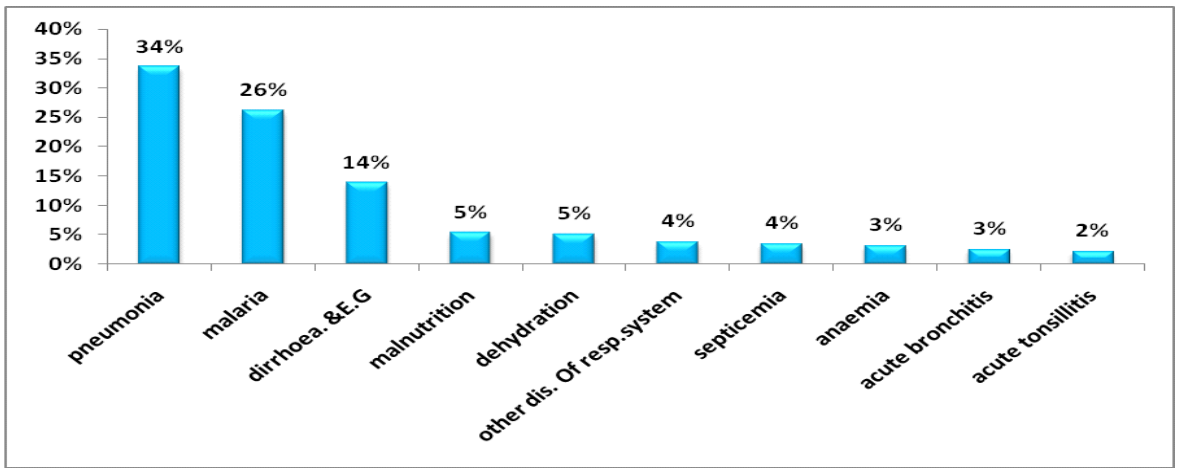

Figure 2: Prevalence of respiratory infection within the 10 leading causes of hospitalization in infants in Sudan (2008)

Diseases causing death in infants

The reports showed that pneumonia was the first disease leading to death during 2004, 2005 and 2006 (1126, 918, 814). In 2007 and 2008 the first disease causing death was septicemia (1010 and 715), Then pneumonia was the second (915 and 654) (Table 5).

Table 5: Significant diseases leading to death in infants in Sudan (2004-2008)

Year	Diseases	Number	%
	Pneumonia	1126	17
2004	Malnutrition	756	11
	Malaria	749	11
	Pneumonia	918	15
2005	Malnutrition	780	13
	Septicemia	648	11
	Pneumonia	814	13
2006	Septicemia	805	12
	Malaria	565	9
	Septicemia	1010	15
2007	Pneumonia	915	13
	Malnutrition	650	10
	Septicemia	715	13
2008	Pneumonia	654	12
	Malnutrition	401	8

Detection of respiratory syncytial virus antibodies in infants in Khartoum

The overall detected RSV antibodies in sera of infants were 24 (26%). It was noticed that the sero-prevalence of RSV was higher in 1-2 year age group (38.8%). There was a significant statistical difference between the age groups ($p = 0.003$) (Table 6).

Table 6: Detection of RSV antibodies using ELISA in infants in Khartoum State

Age group	Total tested	Total positive	Total negative	% positive	P-value
< 1 year	43	5	38	11.6%	*0.003*
< 2 year	49	19	30	38.8%	

Sex distribution of RSV patients

Table (7) showed that RSV antibodies were detected in 24 of tested sera. Eleven of positive sera were form males and 13 were females. No significant difference between them was observed (p =0.635) (Table 7).

Table 7: RSV antibodies in male and female infants detected using ELISA in Khartoum (2009)

Gender	Total tested	Total positive	Total negative	%positive	P-value
Male	46	11	35	23.9%	0.635
Female	46	13	33	28.3%	

RSV antibodies in infants with different respiratory signs

The results had showed that positive percentage of pneumonia was 19.3%, acute bronchitis was 40%, asthma was 40%, middle ear was 0% and allergy was 40%. The data showed significant difference between clinical signs and RSV infection in pneumonia, acute bronchitis and asthma (p = 0.05, 0.035, 0.035). And no significant difference was found in allergy and middle ear (Table 8).

Table 8: Sero prevalence of RSV in infants with different clinical signs in Khartoum state (June – September 2009)

Clinical signs		Total tested	Total positive	Total negative	%positive	P-value
Pneumonia	Yes	57	11	46	19.3%	0.05
	No	35	13	22	37.1%	
Bronchitis	Yes	30	12	18	40%	0.035
	No	62	12	50	19.4%	
Asthma	Yes	30	12	18	40%	0.035
	No	62	12	50	19.4%	
Middle ear	Yes	1	0	1	0	0.550
	No	91	24	67	26.4%	
Allergy	Yes	5	2	3	40%	0.446
	No	87	22	65	25.3%	

The relation between prevalence of RSV in infants and previous exposure of their mothers to respiratory infection

RSV percentage for infants who their mothers had past history of respiratory infections was 42.9%. There was a significant difference between the mothers who had past history of respiratory infections and their infants who have RSV infection (p = 0.015) (Table 9)

Table 9: RSV antibodies in infants and its association with the previous exposure of their mothers to respiratory infection

Past history	Total tested	Total positive	Total negative	%positive	P-value
No	64	12	52	18.75%	0.015
Yes	28	12	16	42.9%	

RSV antibodies in infants with recent and previous respiratory infection

RSV antibodies were detected more (28.8%) in infants re infected with respiratory infections than in first time infected infants (Table 10).

Table 10: Sero prevalence of RSV in infants showing current and past respiratory infection

Infection	Total tested	Total positive	Total negative	% positive	P-value
Re infection	80	23	57	28.8%	0.133
First infection	12	1	11	8.3%	

Discussion

In the present study, the data obtained from annual reports of Ministry of Health, Sudan showed that, in hospitalized infants, pneumonia had higher numbers of reported cases at 0-4 years of age, during 2004-2008, then asthma. Acute bronchitis was the highest infection in patients that needed clinical visits at 1-4 years of age in 2004 (201907 ,55%), these results are in agreement with Døllner et al (2004) who reported that out of 236 Norwegian children admitted because of respiratory tract infection 24 (48%) had bronchitis and 17(34%) had pneumonia.

Our data showed that pneumonia was the highest reported infections in patients that needed clinical visits at 0-4 years of age in Sudan in 2005- 2008. There was a similarity with the results described by Nokes *et al.,* (2009) in children aged less than 5 years admitted to Kilifi district hospital in coastal Kenya where 7359 patients (29%) had severe or very severe pneumonia.

Our results noted that highest level of reported cases of middle ear, pneumonia and asthma was in Khartoum state, this could be attributed to difference in medical care in Khartoum.

Acute bronchitis was reported in eastern states and allergy was in central states, this could be due to the mass use of pesticides in this area.

The data showed that pneumonia was one of the diseases requiring hospitalization in infants in 2004-2008 (28.3-30%), then asthma (1.8, 2.5%) during 2004-2007. Pneumonia was the first disease leading to death in infants during 2004-2006, and the second one in 2007, 2008.

In this study RSV is detected in 26% of 92 infants sera collected during June – September 2009 in Khartoum state. This

indicated the wide spread of RSV infections in Sudan; however the obtained results are lower than that described by Sastre *et al.* (2012). They reported that RSV antibodies was 36.3% of 80 infants sera collected from archives of the Institute of Virology of the University Hospital Bonn. Although the prevalence rate of RSV obtained in our study is lower than the previous reports, negative antibodies patients may have IgM antibodies which are found during the first infection of the disease (Meurman *et al*., 1984).

The prevalence of RSV antibodies (IgG) obtained in this study using indirect ELISA in infants 0-1 year of age was 11.6%, 1- 2 years was 38.8%, a significant statistical difference between the age groups (p = 0.003) was found. This indicates that at 1-2 years of age, infants may be exposed to repeated infections with RSV. Our results slightly differ from the results reported by Meurman et al. (1984) in which all 26 children 1-2 years of age with acute primary RSV infections showed IgG antibodies, this may indicate the higher prevalence rate of RSV in infants in that study. Summer is known to show lower prevalence rate of RSV infections in which the outbreaks occur annually during the winter months (Roca *et al*., 2001). The results revealed that there was no significant difference between males and females.

ELISA for antibodies in infants with different clinical sings showed a significant difference in association with pneumonia, acute bronchitis and asthma with RSV (p = 0.05, 0.035, 0.035), it is in agreement with the results reported by Albargish and Hasony (1999) which showed that RSV was detected in 188 (37.6%) children with acute respiratory infection. The infection was highest in those with severe acute respiratory infection, particularly severe bronchiolitis and pneumonia.

The present study found that there is a significant difference between infants infected with RSV and their mothers who previously exposed to respiratory infection (p = 0.015). RSV antibodies (IgG) were detected in re infected infants than those infected for the first time (28.8%), this is coincident with the results reported by Roca et al (2002) in which higher levels of RSV IgG were highly prevalent in the control group when compared to the infected case group, Which is mainly due to repeated infections.

Our findings highlight the significant role of RSV in causing lower respiratory tract infection in infants in Sudan. The respiratory tract infection is one of the most diseases leading to death in infants; further work is needed to investigate the existence of RSV antigen and antibodies in different areas of Sudan as well as the molecular characterization of the virus.

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