

Studies on congenital infections in infants in Sudan: Seroprevalence of cytomegalovirus

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ABSTRACT: The occurrence of congenital infections in Khartoum State and the presence of human cytomegalovirus (HCMV) antibodies among pregnant women (IgG) and neonates (IgM) were studied. During 2002-2007 the total of births reported at Omdurman was 122503 with 2.4% deaths. In Khartoum province during 2004-2007 out of 6138 deliveries, 178 had died. The main reported congenital infections were jaundice, anomalies, hydrocephalus, and respiratory infections. In Omdurman the total infected neonates were 3189 with 873 deaths, retardation of growth had the higher percentage in infected cases and deaths. In Sudan during 2005-2007, respiratory infections had the higher number of reported clinical signs and Khartoum had the higher number of infections. Using ELISA 59 out of sixty (98.3%) pregnant women at last stage of pregnancy were positive for CMV IgG. Fifty out of 53 neonates plasma were positive for CMV IgM (94.3%). CMV was found to be highly prevalent in Khartoum State and it has a major role in causing congenital infections.

KEYWORDS: CMV, congenital infections, IgM, IgG, Sudan.

INERODUCTION

Human cytomegalovirus (HCMV) is existing throughout all geographic locations and socioeconomic groups, and infects between 50% and 80% of adults in the United States (Ryan et al., 2004). HCMV is the virus most frequently transmitted to a developing child before birth. HCMV infection is more widespread in developing countries and in communities with lower socioeconomic status and represents the most significant viral cause of birth defects in industrialized countries (Stars et al., 2006).

CMV is the most common cause of congenital infection and its incidence has been estimated to be between 0.2- 2.2% of all live births in different parts of the world (Wong et al., 2000). Most congenital infections are asymptomatic; only 10% of infected fetuses will develop clinical signs of CMV infection.

Transmission of CMV infection to the fetus has been identified in all trimesters of pregnancy. Abortion can result from ascending CMV endometritis and the virus has been isolated from post-abortion uterine discharge (Dehner et al., 1975). In a study conducted in Malaysia, 1688 infants with congenital abnormalities were screened for evidence of congenital Cytomegalovirus infection and it was detected in 11.4% of the infants (Balasubramanium et al., 1994). As described by Rubina et al (2004) cytomegalovirus specific IgM antibodies was detected by ELISA in 15.9% of the 1918 studied pregnant women.

In Sudan very sparse work was conducted on cytomegalovirus, The first study of HCMV in Sudan was done in 2004 in blood donors and antenatal women (Eldoma, 2004). The second study was done in 2006, in candidate recipients,

kidney candidate donors and blood donors (Bushera, 2006). The most recent study was done in 2007 in Renal transplant patients and Haemodialysis patients (Awad, 2007). However no study has been conducted to investigate the role of cytomegalovirus in causation of congenital infections in Sudan. This study is intended to elucidate the prevalence of congenital infections caused by cytomegalovirus in Sudan.

MATERIALS and METHODS

Data Collection

Data about cases of congenital infections in Khartoum state during 2004-2007 was collected from annual records of Ministry of Health and statistically analyzed using SPSS soft ware programme.

Study Area

Two hospitals in Khartoum state have been selected for this study (Soba, Omdurman).

Targeted groups

New borns admitted to hospital and complained from jaundice, mental retardation and neurological signs beside pregnant women at the last stage of pregnancy (8 or 9 months).

Sample collection and storage

A total of 113 blood samples were collected from congenitally infected neonates (n = 53) and pregnant women in late month (n = 60), plasma was separated from blood samples and stored at -20°C till used.

Detection of cytomegalovirus Antibodies

CMV antibodies (IgG in pregnant and IgM in neonates) were examined in all collected plasma samples using ELISA technique.

SERION ELISA classic Cytomegalovirus IgG/IgM

Serion ELISA IgG/IgM are quantitative and qualitative tests for detection of human antibodies in serum, plasma or cerebrospinal fluid against Cytomegalovirus. The IgM-ELISA is used for the detection of acute infections. The IgG-ELISA is used for determination of the

serological status as well as for the detection of recent infection. The Kits were obtained from Virion\Serion GmbH, Würzburg, Germany. The test was performed according to the manufacturer instructions.

RESULTS

Epidemiology of congenital infection Reported births and deaths in Omdurman and Khartoum

It was noticed from the data collected that over the last years (2002-2007) the total of births reported at Omdurman were 122503 while the number of deaths were 2898 (2.4%). The percentage of deaths was increased during 2004-2006 with some decrease in 2007; the details are presented in Table 1.

The data of births and deaths in Khartoum province (Soba hospital) during 2004-2007 showed that out of 6138 deliveries, 178 had died. There was marked increase in number of deliveries and deaths during 2005 and 2006 and decrease in 2007 (Table 2). It was noticed that there were significant difference between the reported birth and death during the period of the study ($P = 0.000$).

Reported congenital infections

The study showed that the main reported congenital infections are jaundice, anomalies, hydrocephalus, and respiratory infections. In Khartoum (Soba hospital) the totals of congenitally infected neonates during (2004-2007) were 276; respiratory infections had the higher number (168) and its deaths were 13, the details are shown in Table 3. During (2004 - 2007) there was statistically significant difference between symptoms in Soba Hospital ($P = 0.000$).

It was noticed from the data collected about congenital infection in Omdurman that the total reported congenital infection was 3189 and the deaths were 873, the percentage of deaths during 2004-2007 was 4.7, 3.9, 17.5, 34.8, respectively, the retardation of growth showed the higher

percentage in infected and deaths. The details are presented in Figures 1 and 2.

The data collected about congenital infection in Sudan during 2005-2007 showed that respiratory infections had the higher number in the clinical signs and Khartoum had the higher number of infected cases, the details are presented in Table 4. The results showed that there was a significant difference between symptoms and area for all years ($P = 0.000$).

Sero-epidemiology of congenital infections: Detection of cytomegalovirus anti-bodies (IgM) in neonates plasma using enzyme linked immunosorbent assay (ELISA)

A total of 53 plasma samples were collected from neonates complained from jaundice, mental retardation or neurological signs. The samples were tested for cytomegalovirus using ELISA, as shown in Figure 3, a total of 50 samples were found to be positive (94.3%).

Detection of cytomegalovirus anti-bodies (IgG) in plasma of pregnant women at the last stage of pregnancy using ELISA.

A total of 60 samples were tested for cytomegalovirus IgG, 59 samples were found positive (98.3%), the details are presented in Figure 4.

DISCUSSION

Cytomegalovirus (CMV) was first described in 1881 when large cytoplasmic inclusions (protozoan-like cells) were seen in the kidney of a still-born infant. The term cytomegalia was introduced in 1921, but the viral aetiology of the disease was confirmed in 1926. CMV is the leading cause of congenital viral infection in developed countries, occurring with a stable incidence of 0.4 to 2.2% of all live births (Awosere et al., 1999). Cytomegalovirus (CMV) is known to have an intrauterine route of transmission with significant mortality and morbidity (Surpam et al., 2006). Primary CMV infection in pregnancy causes a

higher incidence of congenital malformations and fetal loss (Tubndkar et al., 2003).

The prevalence of CMV antibodies among women varies with geographical location, socio – economic status and occupation (Awosere et al., 1999). One of the most important aspects of the epidemiology of the virus is its extreme high prevalence in both developed (Turbadkar et al., 2003) and developing countries (Mustakangas et al., 2000).

In the present study the epidemiological features of congenital infections were investigated. The reported percentage of deaths of neonates in Omdurman was 2.4% and was increased during 2004-2006 with some decrease in 2007. In Khartoum (Soba hospital) the percentage of deaths was 2.9% which is slightly higher than in Omdurman. According to the clinical signs of congenital infections, the retardation of growth had higher percentage of cases and deaths in Omdurman than Khartoum (Soba hospital).

Human cytomegalovirus (HCMV) is a major public health problem throughout the world. Serological surveys have shown HCMV infection in almost every population that has been tested. HCMV is a known cause of congenital defects in babies of infected mothers. The prevalence of HCMV infections among 253 pregnant women attending ante-natal clinic at the Federal Medical Centre in Bida, Nigeria between the months of November 2004 and January 2005 was studied. Serological screening for HCMV antibodies (IgG) was done, two hundred and thirteen (84.2%) were positive (Okwori et al., 2008).

In Sudan studies on cytomegalovirus are scares. The first study of HCMV in Sudan was done in 2004, in blood donors and antenatal women, IgG antibodies among blood donors and pregnant women in Sudan were 77% and 95%, respectively (Eldoma, 2004). Bushra (2006)

detected 96% seropositivity for IgG in pre-transplant kidney recipients, 17% in healthy candidate donors, and 84% in blood donors. Awad (2007) detected 98% and 95% in renal transplant and haemodialysis patients. In a recent study Enan (2008) reported the detection of CMV antibodies in kidney transplant recipients (100% IgG and 6.1% IgM).

In this study cytomegalovirus IgG was detected in 98.3% of 60 pregnant women studied in Khartoum State. This indicates the wide spread of CMV infection in Sudan; the obtained results are in agreement with the previous reports. CMV IgM was detected in 94% of tested neonates, which is a very high prevalence in contrast to the previous report (Enan, 2008), this is expected as samples tested in the previous reports were from adult kidney Transplant recipient, in whom the IgM is most probably has disappeared with a rise in IgG, this finding is a new conclusive finding, and alarming for the significant role of CMV in causing congenital infections.

Detailed molecular biology based study to characterize the HCMV circulating in Sudan is highly recommended.

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Table 1: Births and deaths in Omdurman Maternal hospital (2002-2007)

Year	Total	Births		Deaths		Percentage of deaths		Deaths (%)
		Male	Female	Male	Female	Male	Female	
2002	15663	7968	7695	136	97	0.9%	0.6%	1.5%
2003	17414	9035	8378	159	152	0.9%	1.8%	0.9%
2004	18045	9411	8634	280	245	1.6%	1.4%	2.9%
2005	21562	11015	10547	360	285	1.7%	1.3%	3.0%
2006	22635	11437	11198	346	312	1.5%	2.8%	2.9%
2007	24287	12406	11881	287	239	1.2%	1.0%	2.2%
Total	119605	61272	58333	1576	1330	1.3%	1.1%	2.4%

Table 2: Reported births and deaths in Khartoum (Soba hospital) during (2004-2007)

Year	Total of births	births		Deaths		Percentage of deaths		Total deaths (%)
		Male	Female	Male	Female	Male	Female	
2004	2453	1224	1229	54	46	2.2%	1.9%	4.1%
2005	71	35	26	5	5	14.3%	19.2%	14.1%
2006	47	17	30	7	6	15.0%	12.8%	27.7%
2007	3399	1682	1717	39	16	1.1%	0.5%	1.6%
Total	5960	2958	3002	105	73	1.8%	1.2%	3.0%

Table 3: Reported congenital infections causes and deaths in Khartoum (Soba hospital) during (2004-2007)

Year	Total	Gender	Clinical signs observed							
			Jaundice		Anomalies		Hydrocephalus		Respiratory infection	
			Infected	Deaths	Infected	Deaths	Infected	Deaths	Infected	Deaths
2004	42	Male	10(23.8%)	0	0	0	0	0	32 (76.2%)	2
	35	Female	12 (34.3%)	0	0	0	0	0	23 (65.7%)	4
2005	68	Male	13 (19.1%)	0	10 (14.7%)	0	0	0	45 (66.1%)	0
	23	Female	4 (17.4%)	0	0	0	0	0	19 (82.6%)	6
2006	43	Male	0	0	0	0	10 (23.3%)	2	33 (76.7%)	0
	25	Female	0	0	0	0	9 (36%)	1	16 (64%)	1
2007	15	Male	0	0	0	0	15 (100%)	2	0	0
	25	Female	0	0	0	0	25 (100%)	1	0	0
Total	276		39	0	10	0	59	6	168	13

Table 4: Reported congenital infections in Sudan during (2005-2007)

Year	Area	Clinical sign observed									
		Respiratory infection		Anomalies		Jaundice		Hydrocephalus		Pneumonia	
		Infected	%	Infected	%	Infected	%	Infected	%	Infected	%
2005	Eastern	295940	35.9	0	0	1658	13.6	0	0	0	0
	Central	38429	4.7	26	2	1945	15.9	0	0	0	0
	Khartoum	400913	48.7	1269	95.6	7138	58.4	0	0	0	0
	Northern	49898	6.1	1	0.1	754	6.2	0	0	0	0
	Kordofan	320578	38.9	10	0.8	373	3.1	0	0	0	0
	Darfur	38470	4.7	22	1.7	360	2.9	0	0	0	0
2006	Eastern	1084	12	10	0.7	0	0	9	2.9	10423	2.1
	Central	3019	33.5	21	1.5	0	0	0	0	25511	5.1
	Khartoum	3583	39.9	1398	97	0	0	298	97.1	451661	89.6
	Northern	673	7.5	0	0	0	0	0	0	10305	2
	Kordfan	353	3.9	0	0	0	0	0	0	3879	0.8
	Darfur	292	3.2	12	0.8	0	0	0	0	2281	0.5
2007	Eastern	505	4.4	22	1	391	9.1	5	1.3	13359	11.8
	Central	4092	35.4	15	0.7	1080	25.3	0	0	33318	29.4
	Khartoum	5244	45.3	2088	97.2	2094	49	380	98.7	45548	40.1
	Northern	811	7	2	0.1	281	6.6	0	0	11213	9.9
	Kordofan	471	4.1	0	0	49	1.1	0	0	5981	5.3
	Darfur	443	3.8	22	1	382	8.9	0	0	4099	3.6
Total		1164798		4918		16073		692		615525	

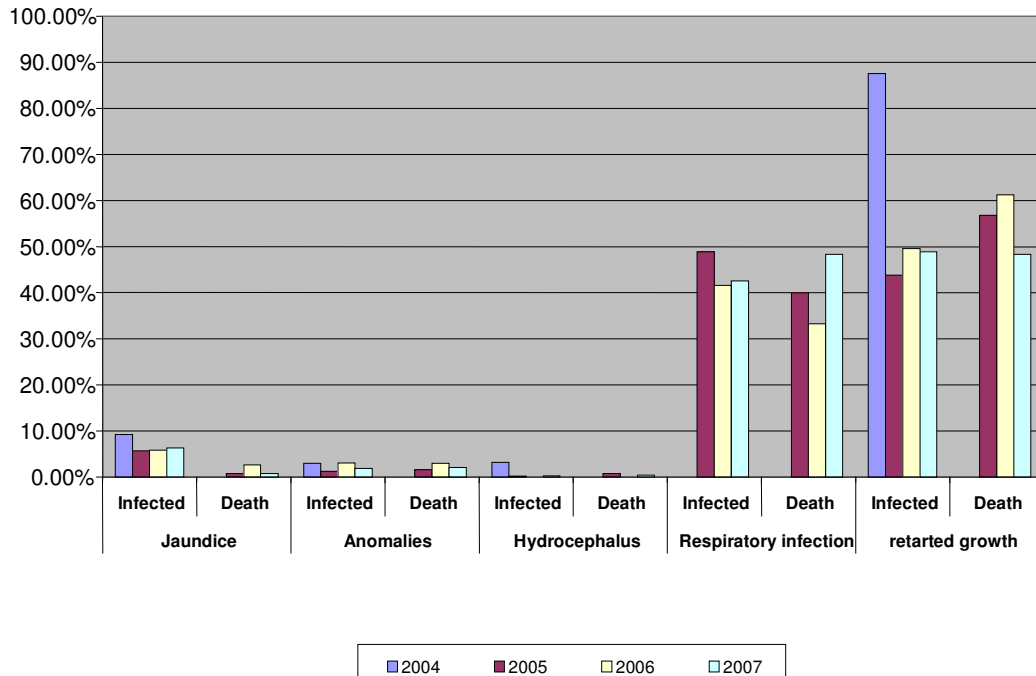


Figure 1: Congenital infections and deaths in females in Omdurman (2004-2007)

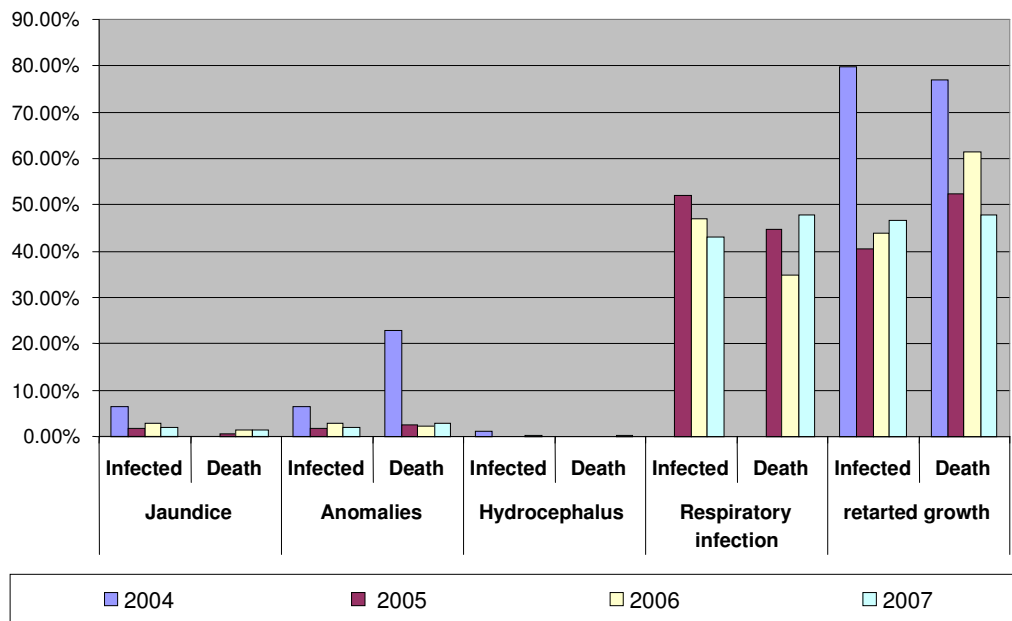


Figure 2: Congenital infections and deaths in males in Omdurman (2004 – 2007)

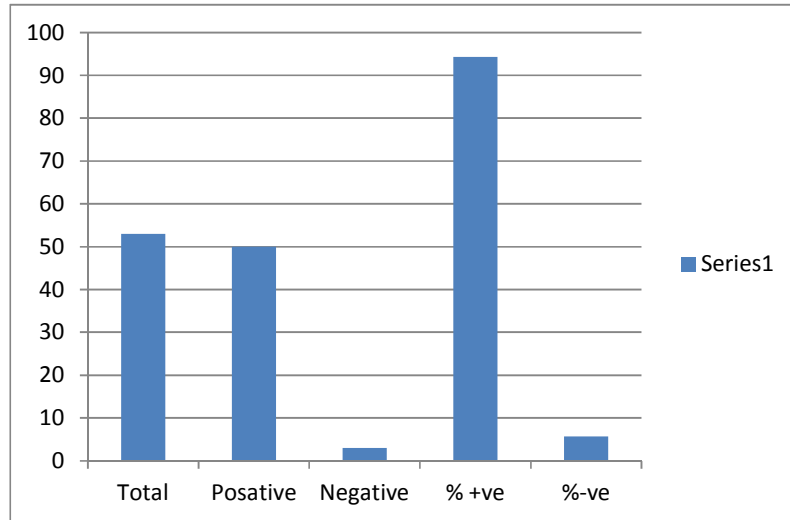


Figure 3: Cytomegalovirus IgM detected using ELISA in neonates samples in Khartoum State (2008).

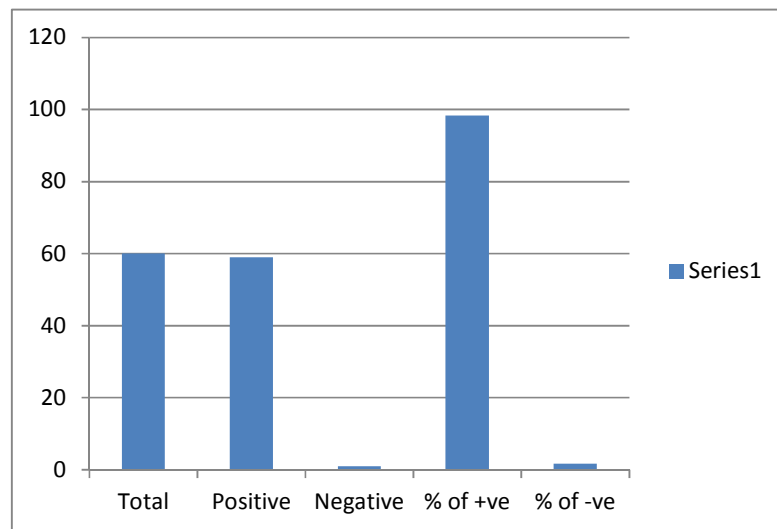


Figure 4: Cytomegalovirus IgG detected using ELISA in pregnant women samples in Khartoum State (2008).