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Congenital Rubella Syndrome in Lagos

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Fadahunsi, O. (1977). *Nigerian Journal of Paediatrics*, **5(1)**, 4. **Congenital Rubella Syndrome in Lagos.** Seventeen cases of congenital rubella syndrome were found among 190 children with congenital heart disease attending the Paediatric Clinic, Lagos University Teaching Hospital. This finding has confirmed that congenital rubella syndrome not only exists in this part of the world, but that it also manifests in the same devastating manner as elsewhere. The incidence of 9 per cent among the study population is, however, higher than would be expected in view of the opportunity which the rubella virus, like poliovirus has, to infect and render immune a majority of the population in any thickly populated urban area well before the child bearing age is reached. It is suggested that in Nigeria as well as in other parts of Africa vaccination against rubella should be included in all routine vaccination programmes.

GREGG (1941) was the first to describe the association of maternal rubella infection in early pregnancy with abnormalities in the offspring. The syndrome of congenital rubella has since become well recognised and its epidemiology studied in detail in most technically developed countries of the world (Sever, Nelson, and Gilkeson, 1965; Hortsmann *et al.*, 1965). Although clinicians in Africa have often recognised the syndrome in affected children, detailed epidemiological or clinical studies have been lacking, partly because these medical workers are pre-occupied by other diseased states which have much greater impact on infant morbidity and mortality. Two recent reports from East Africa (Sachdeva, 1973; Sebuliba, 1975) have however, drawn attention to this syndrome as an important health problem in that part of Africa.

The present study was prompted by the frequent recognition of clinical manifestations of congenital rubella among children attending the Paediatric Cardiac clinic, Lagos University Teaching Hospital, (LUTH), and the purpose was to determine the prevalence and clinical manifestations of the syndrome in these children.

Materials and Methods

During a two–year period all the patients diagnosed as cases of congenital heart disease were examined by the author for clinical features of congenital rubella syndrome. The type of associated congenital heart disease was confirmed by cardiac catheterisation in four of the children. Sera from eleven patients and their mothers were tested for rubella haemagglutination-inhibition (HAI) antibody using the method described by Dudgeon *et al.*, (1969).

Results

Incidence:

Among the 190 children with congenital heart disease seen during the two-year period, there were 17 with clinical features compatible with congenital rubella syndrome. Thus, in this small series, the incidence of the syndrome was 9 per cent.

The clinical features in these 17 children are summarized in Table I (*a* and *b*).

Age and Sex: Of the 17 patients 9 were males and 8 females. The ages ranged between 3 weeks and 6½ years with a mean of 2.2 years

"Gestational age and Birthweight": The 'gestational age' was described by the mothers as 'full term' in all the patients. In only six children were the birthweights known, and these ranged between 1.8. and 2.72 Kg (mean, 2.4Kg). In four of these six children the birth, weight was low, being 2.5 Kg or less. In the remaining 11 children whose birthweights were not known the parents decribed the children as being 'small or very small' at birth, and it may be concluded from these descriptions that they were also of low birthweight. It is worthy to note that a majority of children with congenital rubella syndrome have low birthweights (Lejarraga and Peckham, 1974).

Maternal age: The ages of the mothers at the time of delivery of the affected children ranged between 19 and 32 years, the mean age being 24.8 years. This age range is similar to that among 205 childbearing females studied in Lagos for rubella HAI antigen by Ransome-Kuti, and Marshall, (1968) 15 per cent of whom were found to be sero-negative.

Maternal rubella infection: A history was obtained of fever and a mild measles-like rash during the early months of pregnancy in 6 (35 per cent) of the 17 mothers. This compares with a positive history of less than 50 per cent reported by Brown, Hambling and Ansari, (1969). A positive history is said to be hardly obtained in more than 50 per cent of cases occuring in Caucasians (Dudgeon, 1975). Therefore, a positive history of 35 per cent in the present series may be considered high, since it is very difficult to recognise the German measles rash in dark-skinned persons.

Parity of the mothers and birth order of the patients: Sixteen out of the 17 (94 per cent) mothers were multiparous. Previous children of these 16 mothers were unaffected. The birth order of the 17 patients (Table I(*a*) shows that only 1 patient (case 6) was a first-born. Table II compares the pregnancy order in the present series with that in a recent British survey in which the highest number of affected children was among first-born (Marshall, *et al.*, 1976). These British workers have attributed the high percentage of primiparity among mothers of rubella babies to the fact that British multiparous mothers are more likely to have therapeutic abortion following clinical rubella in early pregnancy than their primigravid counterparts. In contrast to the British situation therapeutic abortion because of maternal rubella in early pregnancy is not commonly practiced in Nigeria. The finding of the highest incidence among the 3rd child in the present series probably reflects the natural history of rubella infection, whereby seronegative mothers usually acquire the infection from close contact with their infected children.

Physical growth: The weight was recorded in all the 17 patients, while the height and head circumference were measured in only 5 and 9 patients respectively (Table I(*b*). Plotted on the Boston Children's Medical Centre percentile chart, the weights of all the patients except cases 12,14, 17 were below the third percentile; the heights were below the third percentile in three of the five patients who had this measurement, while the head circumference was below the third percentile in four out of 9 patients. Furthermore, the weights and heights in this

TABLE I(*a*)

Clinical Features in 17 children with congenital Rubella Syndrome

Case No.	*Sex*	*Age (yr)*	*Mon. of birth*	*Birth-weight (kg)*	*Birth order*
1	F	15 mons	January	–	4th
2	F	$3\frac{1}{2}$	July	2.5	3rd
3	F	$1\frac{1}{4}$	February	2.7	5th
4	M	$6\frac{1}{2}$	August	2.8	3rd
5	F	$6\frac{10}{12}$	June	–	3rd
6	F	7 mons	September	–	1st
7	F	7 wks	September	2.4	3rd
8	M	$1\frac{1}{2}$	October	–	3rd
9	M	$1\frac{1}{2}$	May	–	3rd
10	M	9 mons	October	–	3rd
11	M	3 wks	November	–	4th
12	M	11 mons	January	–	2nd
13	M	4	August	–	6th
14	M	8 mons	November	–	4th
15	F	6 mons	January	1.8	3rd
16	F	$4\frac{1}{2}$	January	2.3	2nd
17	M	$3\frac{1}{4}$	May	–	2nd

series were considerably below those of 110 children with congenital heart disease reported from Ibadan by Janes and Antia (1975).

Rubella HAI antibody: Sera from 11 mothers and from their children were tested for rubella HAI antibody. The titres are shown in Table I(*b*). There were high antibody titres (16 and above) in 9 cases (81.8 per cent) consistent with the diagnosis of congenital rubella infection. In view of this high serological confirmation rate, it is concluded that diagnosis of congenital rubella infection in Nigerian children, may, in a majority of cases, be confidently based on the clinical features alone.

Seasonal Incidence

Figure shows that 12 (70 per cent) of the 17 cases of congenital rubella syndrome in this series were born between August and January. Thus the peak period of congenital rubella virus infection in Lagos appears to be the first quarter of the year, a period also reported from Ibadan by Antia (1974). In other countries the peak incidence of infection is reported to occur during October to March (Rose, Hewutt, and Milner, 1972; Dedgeon, 1975; Sebuliba, 1975).

Associated Congenital Malformations and other Disorders: Table III summarizes the associated congenital malformations in the present series.

TABLE I(*b*)

Clinical Features in 17 children with congenital Rubella syndrome

Case No.	Growth Percentile						Rubella HAI antibody titre	
	Wt. (kg)		Ht. (cms)		HC (cms)		Child	Mother
1	6.14	3rd	72	3rd	40.6	3rd	16 Consistent with Congenital Rubella	64
2	10.4	3rd	84.5	3rd	45.7	–	16 Consistent	64
3	4.82	3rd	–	–	40.5	3rd	16 Consistent	64
4	15.9	3rd	–	–	–	–	32 Consistent	256
5	15.5	3rd	–	–	–	–	8 Not consistent ? rare loss of antibody	64
6	5.6	3rd	–	–	40.5	3rd	16 Low titre ? Maternal origin	128
7	3.1	3rd	–	–	–	–	Not Tested	–
8	7.4	3rd	–	–	–	–	Not Tested	–
9	6.0	3rd	–	–	–	–	Not Tested	–
10	4.6	3rd	–	–	40.6	3rd	Not Tested	–
11	1.8	3rd	–	–	–	–	Not Tested	–
12	5.5	–	–	–	–	–	Not Tested	–
13	11.5	3rd	91.0	3rd	–	–	64 Consistent	64
14	5.85	–	–	–	41.9	–	64 Consistent	64
15	3.4	3rd	–	–	37.5	3rd	64 Consistent	256
16	12.0	3rd	92	3rd	46	–	16 Consistent	64
17	12.0	–	91	–	45	–	256 Consistent	256

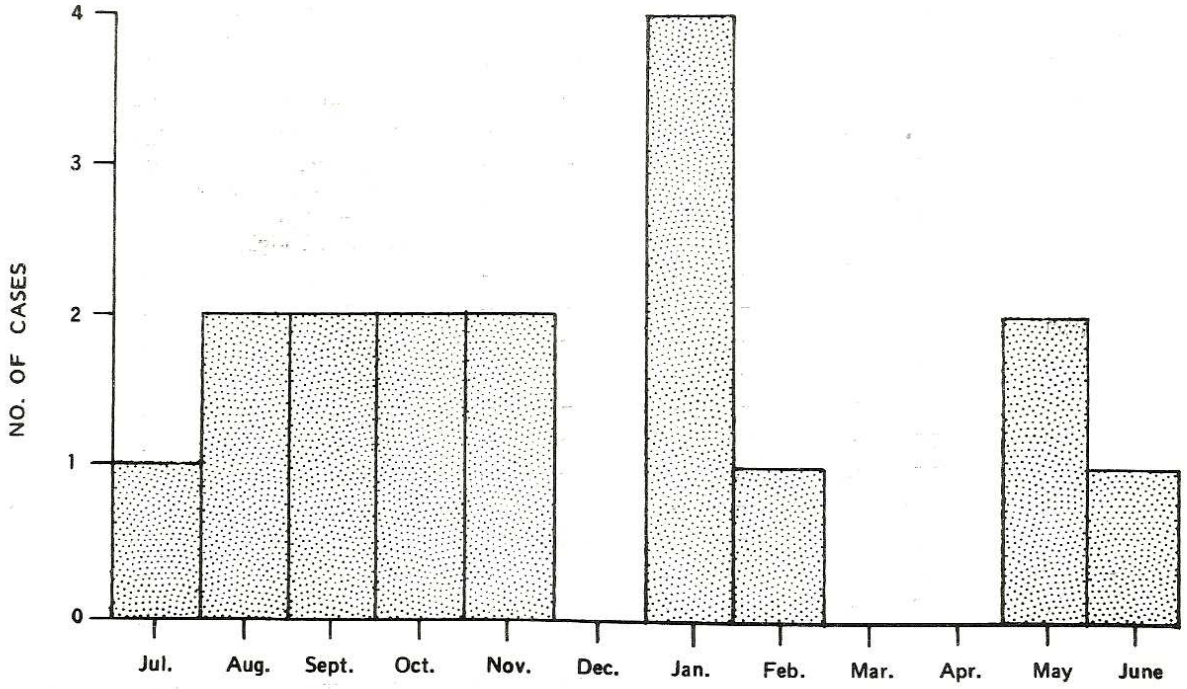
TABLE II

Pregnancy Order in the Present Series Compared to that in Britain

Pregnancy order	Present series		British series (Marshall et al., 1976)
	No. of cases	Per cent of total	Per cent of total
1	1	5.9	43.6
2	3	17.6	24.7
3	8	47.1	14.3
4	3	17.6	17.4
5	1	5.9	-
6	1	5.9	-

(*a*) *Heart defect:* There was clinical evidence of congenital malformation of the heart in all the 17 patients. Persistent ductus was the commonest lesion and occurred in 12 (70 per cent) of the patients. This finding is in agreement with that of Campbell (1961). Other lesions included pulmonary stenosis and ventricular septal defect.

(*b*) *Ocular defects:* There were cataracts and microphthalmia in 12 (70 per cent) of the 17 children. These defects were bilateral in seven patients, and unilateral in five. Two other patients (cases 6 and 8) had bilateral glaucoma and right corneal opacity respectively. Thus, 14 (82.3 per cent) out if the 17 patient had ocular defects resulting in serious visual impairment.



Month of birth of 17 children with congenital rubella syndrome.

(*c*) *Deafness:* Objective hearing assessment could be carried out only in the six patients aged more than three years and five of these were found to be deaf. Five others had no detectable hearing loss. There was some suspicion of deafness in two infants. Hearing defect in others could not be ascertained either because of too young an age or lack of testing opportunity. Deafness is said to be the only disability known so far to occur as a sole manifestation of congenital rubella syndrome (Marshall, 1973). Gumpel, Hayes and Dudgeon (1971), for instance, have reported that congenital rubella is the cause in as many as 59 per cent of children with congenital perceptive deafness attending a London clinic. Deafness may also develop much later in childhood in those cases of congenital rubella with no apparent deafness in earlier life (Dudgeon, 1975). The possibility therefore exists that congenital rubella accounts for a large proportion of deaf-mutes in the Nigerian community.

(*d*) *Neurological deficit:* Motor or mental retardation occurred in twelve (70 per cent) of the 17 children. In four of the mentally retarded children, the head circumference was below the third percentile for the age.

TABLE III

Associated congenital malformations in 17 children with congenital rubella syndrome

Case No.	*Malformations*				
	Cardiac	*Ocular*	*Deafness*	*CNS*	*Others*
1	PDA*	R. Cataract, Microphthalmia	Nil	Nil apparent	–
2	PDA*	L. Cataract	Yes	Motor delay, Mute	–
3	PDA VSD	Bilateral Cataract, Microphthalmia	Nil	Motor delay	–
4	PDA	L. Cataract	Unilateral	Nil apparent	Bilateral Cryptochidism
5	PDA	Nil	Nil	Mental retardation	–
6	PS (valv.)*	Bilateral Congenital Glaucoma	Probable	Delayed milestones	–
7	PDA	Bilateral Microphthalmia, Cataract, Retinopathy	Uncertain	Nil apparent	–
8	PDA	R. Corneal Opacity	Nil	Motor retardation	–
9	PS	Bilateral Cataract	Nil	Motor retardation	–
10	PDA	Bilateral Cataract	Yes	Hypotonia, motor and mental retardation	Low-set ears
11	VSD	Bilateral Cataract, Microphthalmia	Uncertain	Nil apparent	Bilateral inguinal hernia
12	PDA	L. Cataract	Uncertain	Motor retardation	–
13	PDA*	Nil	Yes	Mute, mental retardation	Bilateral inguinal hernia
14	PDA	Bilateral Cataract, Microphthalmia	Probable	Motor and mental retardation	–
15	PDA	R. Cataract Microphthalmia	Uncertain	Motor retardation	–
16	VSD	Bilateral Cataract, Microphthalmia,	Nil	Nil apparent	–
17	PS	Nil	Yes	Mute and hyperactive	–

PS = Pulmonary Stenosis;
PDA = Persistent ductus artoriosis;
VSD = Ventricular Septal defect
* Confirmed at Cardiac catheterisation.

Discussion

The present findings as well as those of Sachdeva (1973), and Sebuliba (1975) in East Africa confirm that clinical manifestations of congenital rubella are the same in Africa as elsewhere (Cooper and Krugman, 1967).

Although the number of subjects in the present series may be small the prevalence rate of nine per cent among children with congenital heart disease appears rather high. A similar high prevalence has been reported from Kampala in children with congenital heart disease (Sebuliba, 1975). Outside Africa the prevalence rate among children with congenital heart defect is reported to be 2 per cent (Campbell, 1961; Strarkova and Ebrahim quoted by Marshall, 1973). This relatively high prevalence rate in the African series is surprising since the proportion of women of child-bearing age susceptible to rubella infection in these African urban settings is

similar to that quoted elsewhere outside Africa (Rawls *et al.*, 1967; Marshall, 1969). It is also surprising that as high as 15 per cent of women of childbearing age in these African cities are usceptible to rubella infection because the present environmental conditions in most African urban areas encourage early contact with rubella virus. Thus, 100 per cent sero-immunity by adolescence among Nairobi city children has been reported by Hayden (1971) and this prevalence rate is perhaps, closer to expectations. Bracken and Stanfield (1971) have also shown that there is a high degree of immunity to the rubella virus infection in the female population of childbearing age as well as a high incidence of congenital rubella syndrome in Uganda. The present findings as well as those of Sebuliba in Uganda suggest not only that we have as large a reservior of susceptible women as elsewhere, but also that the incidence of maternal and foetal infections may be higher. These findings require further study and confirmation.

From the present experience there appears to be little difficulty in the clinical diagnosis of congenital rubella in affected children on clinical signs alone judging by the high (81.8 per cent) serological confirmation rate obtained in this series. The universal problem, more pronounced in the African setting is the recognition of rubella infection in a child or pregnant woman, as on this depends the planning of preventive measures against congenital rubella. Measures such as 'measles parties' for children and therapeutic abortion for the pregnant woman depend on reliable clinical diagnosis of german measles. The mildness of the disease, with little or no systemic disturbance, the difficulty in recognising the transient rash, and the non-specificity of the triad ot slight fever, rash and post-auricular lymphadenopathy, render preventive measures on clinical diagnosis of german measles very unreliable in tropical Africa where other diseases with the same signs are many, and facilities for laboratory confirmation unavailable in most medical institutions. Further studies in Nigeria are required to confirm that congenital rubella is a major health problem, and should this confirmation be made the adoption of the British policy (Dudgeon, 1975) of selective vaccination of all sero-negative adolescent girls with rubella vaccine is recommended.

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REFERENCES

Antia, A.U. (1974). Congenital heart disease in Nigeria: clinical and necropsy study of 260 cases. Arch. Dis. Childh., **49,** 36-39.

Bracken, P.M. and Stanfield, J.P. (1971). Rubella antibody in Uganda. *E. Afr. Med. J.*, **48,** 176-181.

Brown, T., Hambling, M.H., and Ansari, B.M. (1969). Rubella-neutralizing and haemagglutinin-inhibiting antibodies in children of different ages. *Brit. Med. J.*, **4,** 263-265.

Campbell, M. (1961). Place of maternal rubella in the aetiology of congenital heart disease. *Brit. Med. J.*, **1,** 691-696.

Cooper, L.Z. and Krugman, S. (1967). Clinical manifestations of postnatal and congenital rubella. Arch. Opthalmol., **77,** 434-439.

Dudgeon, J.A., Marshall, W.C., Peckham, C.S. and Hawkins, G.T. (1969). Clinical and laboratory studies with rubella vaccines in adults. *Brit. Med. J.*, **1,** 271-276

Dudgeon, J.A. (1975). Congenital rubella in the United Kingdom of Great Britain. In Infection of the fetus and newborn infant— Alla R. Liss, pp 23-34, Inc. New York.

Gregg, N.M. (1941). Congenital cataract following German measles in the mother. Trans. Ophth. Soc. Austral., **3,** 35-46.

Gumpel, S.M., Hayes, K., and Dudgeon, J.A. (1971). Congenital perceptive deafness: role of intrauterine rubell. *Brit, Med. J.*, **2,** 300-304

Hayden, R.J. (1971). Memorandum on the incidence of rubella in Nairobi children as revealed by antibody study. *E. Afr. Med. J.*, **48,** 658-661.

Hortsmann, D.M., Banatvala, J.E., Riordan, J.T., Payne M.C., Whittemore, R., Opton, E.M., and Florey, C. (1965). Maternal rubella and the rubella syndrome in infants., *Amer. J. Dis. Child.*, **110,** 408-415.

Janes, M.D., and Antia, A.U. (1975). Physical growth of children with congenital malformations of the heart and great vessels. Nigerian *J. Paed.*, **2**, 1-8.

Lejarraga, H. and Peckham, C.S. (1974). Birthweight and subsequent growth of children exposed to rubella infection in utero. Arch. Dis. Childh., **49**, 50-54

Marshall, W.C. (1969). Rubella vaccines. In Proceedings of the 23rd symposium on microbiological standardisation, London. p. 68; S. Kargar, Basel, Switzerland.

Marshall, W.C. (1973). The clinical impact of intrauterine rubella. In Intrauterine infections, pp. 3-22 Ciba foundation symposium 10, ASP, Amsterdam.

Marshall, W.C., Peckham, C.S., Dudgeon, J.A., Sheppard S., Smithells, R.W. and Weatherall, J.A.C. (1976). Parity of women contracting rubella in pregnancy. *Lancet*, **1**, 1231-1233

Ransome-Kuti, O. and Marshall, W.C. (1968). Personal communication.

Rawls, W.E., Melrick, J.L., Bradstreet, C.M.P., Bailey M., Ferris, A.A., Lehmann, N.I., Nagler, F.P., Furesz, J., Kono, R., Ohtawara, M., Halone, P., Stewart, J., Ryan, J.M., Strauss, J., Zdrazilek, J., Leerhoy, J., Von Magnus, H., Sohier, R. and Ferreira, W. (1967)., *Bull.* WHO, **37**, 79-88.

Rose, V., Hewitt, D. and Milner, J. (1972). Seasonal, influences on the risk of cardiac malformation. *International J. Epidemiol.*, **1**, 235-244.

Sachdeva, R. (1973). Congenital rubella syndrome at Mombasa. *E. Afr. Med. J.*, **50**, 146-152.

Sebuliba, P.S.K. (1975). Congenital rubella syndrome in Uganda children at Mulago Hospital. In the Child in the African Environment, growth, development and survival. Ed. Owor, R., Ongor, V.L. and Kirya, B.G. pp. 51-58.

Sever, J.L., Nelson, K.B. and Gilkeson, M.R. (1965). Rubella epidemic, 1964: effect on 6,000 pregnancies. *Amer. J. Dis. Child.*, **111**, 395-407.