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Prevalence of BCG scar among BCG-vaccinated children in a southern Nigeria tertiary hospital

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Abstract: *Background*: The burden of tuberculosis is high in Nigeria as in other developing countries. The administration of BCG vaccine to neonates is essential in the control of tuberculosis. A scar usually develops 6 – 8 weeks later at the site of vaccination, which can be used clinically as a proof of vaccination. Not all vaccinated infants however, develop a BCG scar.
Objectives: To determine the prevalence of scar formation post-vaccination and to unravel, if present, any factors responsible for scar failure.
Methods: Two hundred and fourteen children were consecutively recruited from those who presented for immunization in the University of Benin Teaching Hospital, Benin. The bio-data and other relevant information were obtained using a proforma. The anthropometric measurements of the children were obtained and the children were examined for presence of a BCG scar.
Results: Two hundred and six subjects (96.3%) had a post-vaccination BCG scar. About 72% of the subjects were vaccinated within the first week of life. The age at vaccination was significantly affected by gestational maturation (P=0.003) and birth weight (P=0.0001). Gestational maturation is a strong predictor of BCG scar formation post-vaccination (P = 0.007)
Conclusion: There is high prevalence of BCG scar formation in this study and gestational maturation is a strong predictor of BCG scar formation.

Introduction

Tuberculosis is an infectious disease which is prevalent in developing countries. In 2011, there were an estimated 8.7million new cases of Tuberculosis in the general population (13% co-infected with HIV) and 1.4million people died from the disease[1]. There were an estimated 0.5million cases and 64000 deaths among children in 2011.Africa and Asia have the highest burden of tuberculosis[1]. The African Region has approximately one-quarter of the world's cases, and the highest rates of cases and deaths relative to population. Nigeria is one of the 22 countries with a high burden of tuberculosis, with an incidence of about between 90,000 to 330,000 cases per year[1].

As part of control measures to reduce the burden of tuberculosis especially in children, the World Health Organization recommends vaccination with BacilleCalmette-Guerin vaccine at birth or first contact with health services, especially in developing countries.[2] The World Health Organization has emphasized this policy in recent years, because of consistent evidence that BCG protects against serious childhood forms of tuberculosis, even where it may not protect to a high degree against adult pulmonary form of the disease[2]. In various clinical trials the estimates of effectiveness have ranged from 80% protection to no benefit[3]. Despite its limitations, the BCG vaccine is the only currently available vaccine for the prevention of tuberculosis. Overall, more than 80% of all neonates and infants in countries where the vaccine is part of the national childhood immunization programmereceive the vaccine[4]. The coverage however, varies from country to country. The estimated BCG coverage for the year 2011, reported by the World Health Organization, revealed levels ranging from 54% in Ethiopia and 60% in Nigeria, to 99.5% in India and China[5].

The BaccilleCalmette-Guerin contains a live attenuated strain of Mycobacterium bovis which is administered intra-dermally over the left deltoid muscle. After a period of 6 – 8 weeks post-vaccination a swelling appears which increases in size and ruptures leaving behind a life-long puckered scar after healing. The presence of a BCG scar and the tuberculin skin test are utilized in clinical settings to determine those who have been immunized with the BCG vaccine. The tuberculin skin test is usually positive in people who have received the vaccine. Considering the fact that the tuberculin test

is also positive in those with the disease and those exposed to non-tuberculous mycobacteria infection, it is not specific for identifying those who have received the vaccine. Moreover, the result is often negative in immunocompromised (HIV, disseminated tuberculosis, malignant conditions) individuals, even those who had previously been vaccinated, due to cutaneous anergy.

In the absence of a vaccination card the BCG scar may thus be the only option left to clinically determine vaccination status. It is however, noted that not all vaccinated children develop a scar.[6]Different studies world-wide have reported varying prevalence rates of the presence of BCG scar in vaccinated children. A study in Karachi, involving 250 infants, reported presence of scar in 80.4% of the infants.[6]However in this study, the age at vaccination, gestational age and other characteristics of the children were not evaluated in order to find the possible reason for the absence of scar formation. A study in Northern Nigeria reported a 95.1% prevalence of scar formation.[7]This study however, evaluated only 41 children. Another study in Northern Nigeria evaluated 296 children between the ages of 3 – 59months receiving immunization in a Teaching Hospital and two Primary Health Centers. Only 55.7% of the vaccinated children had a BCG scar.[8] This study is aimed at evaluating infants in Southern Nigeria to determine the prevalence of scar formation and to unravel, if present, any factors that may be associated with BCG scar formation.

Materials and method

This is a cross-sectional study carried out between June and September, 2012 at the University of Benin Teaching Hospital, Benin-city, Edo State. The Hospital offers curative and preventive services to patients from Edo State and the neighbouring States of Delta, Ondo, Bayelsa, Ekiti and Kogi. Immunization services take place in the General Practice Clinic and the Institute of Child Health, on a daily basis from Monday to Friday, except on public holidays. The immunization units of the General Practice Clinic and Institute of Child Health vaccinate about 1000 children respectively annually.
Ethical clearance for the study was obtained from the Ethical Committee of the University of Benin Teaching Hospital. A verbal consent was obtained from the parents and caregivers of the subjects after explaining the objectives and the harmless nature of the study.

The subjects were consecutively recruited from children attending the General Practice Clinic, who had been previously vaccinated with BCG and have presently come for subsequent vaccines in the National Programme on Immunization schedule. Information on the bio data such as age, sex, and gestational age were obtained using a proforma. Information on birth weight, age at receipt of BCG vaccine and place of vaccination were also obtained. Subjects delivered before 37 completed weeks of gestation from the mothers last menstrual cycle were classified as preterm; those between 37 and 42 completed weeks of gestation as term while those delivered after 42 completed weeks were classified as post-term. The weight of the subjects was measured with an infant weighing scale, Way master^{R} made in England, calibrated to the nearest 50gm; the length was assessed with an infantiometer while the head circumference was measured with a non-elastic measuring tape. The left upper arm around the deltoid was examined for presence of a BCG scar. The subjects were classified nutritionally using the WHO weight for age z-score growth charts. Subjects with z-score of less than –3 were classified as severely under-nourished; between –3 and –2 as moderately under-nourished; between –2 and +2 as normal; while above+2 as overweight.[9]The data collected was recorded in Microsoft Excel spreadsheet and transported to SPSS version 19 for analysis. Univariate analysis was conducted for all variables to assess their distribution. Continuous variables were summarized using means and standard deviations while categorical variables were summarized using proportions.
Chi-square test was used to determine association between categorical variables. P-value of less than 0.05 was considered statistically significant.

Results

A total of two hundred and fourteen subjects comprising 117 (54.7%) males and 97 (45.3%) females were recruited for the study. The mean age of the subjects was 4.33 ± 2.54 months. The ages of the subjects ranged from 6weeks to 15months. The age group of 6weeks – 6 months formed the bulk (90.7%) of the study population. The general characteristics of the study population are as shown in table 1.

Table 1: General characteristics of the study population

Characteristic	n	%
Gender		
Male	117	54.7
Female	97	45.3
Age (in months)		
1.5 – 6	94	90.7
7 – 12	16	7.5
≥13	4	1.9
Age at vaccination (days)		
1 – 7	151	71.9
8 – 14	35	16.7
15 – 21	9	4.3
22 – 28	3	1.4
≥ 29	12	5.7
Gestational Maturation		
Pre-term	15	7.1
Term	186	88.6
Post-term	9	4.3
Birth weight category		
Low birth weight	13	7.6
Normal birth weight	137	80.1
High birth weight	21	12.3
Place of vaccination		
Private Hospitals	21	9.9
UBTH	180	84.9
Other Public Hospitals	11	5.2
Nutritional status		
Overweight	11	5.2
Normal	190	88.8
Underweight	8	3.7
Severe malnutrition	5	2.3

Majority of the subjects (71.9%) were vaccinated within the first week of life while 16.7% were vaccinated between the 8th and 14th day of life. Twelve (5.7%) subjects were vaccinated after one month of life. Among those vaccinated within the first week of life 9.3% and 10.6% were vaccinated on the 1st and 2nd day of life respectively. Majority of them (44.4%) were vaccinated on the 7th day of life. A greater proportion (26.7%) of pre-term infants were vaccinated after 4weeks of age in comparison to the term (9.3%) and post-term (0%) subjects as shown in table 2. This difference was statistically significant (P=0.003). Similarly, a greater proportion (30.8%) of the subjects with low birth weight were vaccinated after 4weeks in comparison to normal birth weight (0.7%) and high birth weight (4.8%) babies. This difference was also statistically significant (P=0.0001). The above findings indicate that prematurity and low birth weight are significantly associated with late presentation of the study population for BCG vaccination.

Table 2: Association between age of vaccination and gestational maturity and birth weight

	Age at vaccination (days)			χ^2	P-value
	0 – 14 n(%)	15 – 28 n(%)	≥29 n(%)		
Gestational maturity					
Pre-term	9(60)	2(13.3)	4(26.7)		
Term	165(90.7)	9(4.9)	8(4.4)	16.28	0.003
Post term	9(100)	0(0)	0(0)		
Birth weight category					
LBW	7(53.8)	2(15.4)	4(30.8)		
NBW	130(94.9)	6(4.4)	1(0.7)	35.93	0.0001
HBW	18(85.7)	2(9.5)	1(4.8)		

Evaluation of the nutritional status of the study population, as shown in table 3, showed normal nutrition in 190 (88.8%) subjects; 5.2% were overweight while 2.3% had severe malnutrition.

Presence of scar post-vaccination was observed in 206 of the subjects, giving a prevalence of 96.3%. There was absence of scar in 8 (3.7%).Evaluation of the factors related to scar formation showed a statistically significant difference (p = 0.011) among subjects in the various gestational age groups as shown in table 3. Absent scar formation was highest among the post-term (22.2%) in comparison to the term (3.2%) and pre-term (0%) subjects. The presence of BCG scar was not significantly associated with the place of vaccination; chronological age at vaccination, nutritional status, birth weight, and gender of the subjects.

Table 3: Association between BCG scar formation and some variables.

Variables	Presence of scar n(%)	Absence of scar n(%)	P-value
Gender			
Male	110(94)	7(6)	0.057
Female	96(99)	1(1)	
Gestational Maturity			
Pre-term	15(100)	0(0)	
Term	180(96.8)	6(3.2)	0.011
Post-term	7(77.8)	2(22.2)	
Age at vaccination (days)			
1 – 14	180(96.8)	6(3.2)	
15 – 28	11(91.7)	1(8.3)	0.509
≥29	12(100)	0(0)	
Birth weight categories			
Normal	134(95)	7(5)	
Low birth weight	13(100)	0 (0)	0.415
High birth weight	21(100)	0(0)	
Place of vaccination			
UBTH	173(96.1)	7(3.9)	
Other GovtHosp	10 (90.9)	1 (9.1)	0.619
Private Hospitals	21(100)	0(0)	
Nutritional status			
Over-weight	11(100)	0(0)	
Normal	182(95.8)	8(4.2)	0.789
Underweight	8(100)	0(0)	
Severe mal-nutrition	5(100)	0(0)	

Discussion

The WHO recommendations for routine use in EPI schedule and available data on BCG vaccine effectiveness indicate that the vaccine should be administered as soon as possible after birth and before 1 month of age for maximumprotection.[11]In this study, 71.9% of the subjects were vaccinated within the first week of life, while 5.7% were vaccinated after one month of age. Previous studies showed variable rates at reception of BCG vaccination. A study from Sri Lanka reported 99% reception of BCG within the first week of life[12]. The very high rate of vaccination within the first week of life in the Sri Lankan study may be due to high awareness of the need for BCG immunization which is reflected in the high BCG coverage of almost 100%[11] as against 49.7% in Nigeria where this study was carried out.[12]A similar study[7] from the Northern part of Nigeria reported a lower percentage (36.2%) of BCG vaccination within the first week of life. This difference might be due to a lower BCG coverage in the Northern part of Nigeria compared to Southern Nigeria, where our study was carried out, as shown in the National Demographic Health Survey in Nigeria[12].

It was observed from this study that birth weight and gestational age significantly influenced the age of BCG vaccination. These two factors are closely related as preterm neonates will most likely have a low birth weight. Weight is usually a limitation in the commencement of immunization in Nigeria since, from observation in most immunization centres, a minimum weight of 2kg is insisted upon by health workers before administration of BCG. The same practice of late vaccination of Low birth

weight infants have also been reported in Guinea-Bissau[13]. According to the World Health Organization, pre-term infants in developing countries should be vaccinated with BCG at a post-conceptional age of 40weeks. Since establishing the correct gestational age is a challenge in most developing countries, the birth weight rather than gestational maturity is utilized in defining when BCG is administered. This has varied implications for the low birth weight infant, since failure to vaccinate children with BCG at birth has been reported to contribute to lower BCG vaccination coverage among low birth weight children.[13]Early vaccination of Low Birth Weight infants with BCG has also been reported to reduce mortality rate by 17% in a randomized control trial in Guinea-Bissau[14]. Late reception of BCG in the few patients (1%) reported in Sri Lanka was ascribed to illness which resulted in the children being admitted in the Special Care Baby Unit[11]. The gestational age and birth weight may be contributory as both are common reasons for admission into the neonatal unit.

The prevalence of scar formation from our study indicate that the presence of a BCG scar can be utilized as a reliable clinical evidence of BCG vaccination, in the absence of immunization card, as most of the studied population (96.3%) developed a scar post-vaccination. This observation is comparable to the findings from Peru[14]and India[15]where the prevalence of scar formation was 99% and 90.2% respectively. This observation is, however, at variance with the study of Mustapha et al[8] in Northern Nigeria where the prevalence of scar formation was 55.7%. This difference might be accounted for by the different age groups in Mustapha's study and these other studies. Mustapha et al studied children between the ages of 3 – 59months as against 6weeks – 15months in our study, with children between the ages of 6weeks – 6months forming the bulk (90.7%) of the study population. The studies from India and Peru similarly studied younger children vaccinated from birth to 3months of age and were followed up until 6months.There has been documented evidence of waning of BCG scar post-vaccination in children followed up from infancy to fourteen years of age[17]. The possibility therefore, of disappearance of the BCG scar in the older children among the subjects in Mustapha's study could have contributed to the lower prevalence of scar formation reported. Other factors which include use of a non-potent vaccine, faulty vaccination techniques and lack of maturation of the immune system are documented factors that may contribute to failure of scar following vaccination[15]. It is difficult to ascertain if these factors contributed to the difference in the prevalence of scar formation.

Presence of BCG scar was not significantly affected by sex, birth weight, age at vaccination, nutritional status and centre of vaccination. Santiago et al[15], similarly, did not find any association between scar formation and sex, birth weight, age at vaccination and nutritional status. There was however, a significant association between development of BCG scar and gestational age in our study, as a higher proportion of the post-term infants showed absence of scar post-vaccination. The possible reason for this finding is not quite apparent as previous studies relating gestational age and scar formation post-vaccination are at variance. Preterm neonates are more likely to show absent scar formation compared to term and post-term neonates due to poor immune response as reported by Sedaghatianet al[18] in the United Arab Emirates. A study in India[19] among preterm babies delivered less than 35weeks gestation and vaccinated at birth and at 38 – 40 weeks post-conception did not show any statistically significant difference in scar formation. The small number of post-term infants in our study may affect the interpretation of this finding and thus affect the deductions made.

Limitations of the study

Mothers' information on birth weight and gestational age was utilized in absence of information from the case file. The accuracy of this information might not be completely reliable.

Conclusion

This study shows a high prevalence of BCG scar formation post vaccination in early childhood and gestational age is a strong predictor of BCG scar formation post-vaccination.

Author's contributions

AOA: Conceptualization, methodology, planning and data collection, analysis and writing of the manuscript.

OOW: Methodology, planning and data collection, analysis, proof reading of the manuscript.

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References

1. World Health Organization. Global tuberculosis report 2012. World Health Organization 2012. Available at http://www.who.int/tb/publications/global_report/gtbr/2_main.pdf.
2. Fine PE, Carneiro IA, Milstien JB, Clements CJ. Issues relating to the use of BCG in Immunization programs: a discussion document. Geneva, Switzerland: *Department of Vaccines and Biologicals, World Health Organization, 1999: 1 – 45.*
3. Kernodle D. "Decrease in the effectiveness of BacilleCalmette-Guerin Vaccine against Pulmonary Tuberculosis". *Clin Infect Dis 2010; 177*

4. World Health Organization. BCG vaccine, Geneva, Switzerland. World Health Organization 2013. Available at http://www.who.int/bilogicals/areas/vaccine/bcg/en
5. World Health Organization. Reported estimates of BCG coverage. World Health Organization2013. Available at http: // www.apps.who.int/immunization_monitoring/globalsummary/timeseries/tscoveragebcg.html.
6. Sherjil A, Iqbal J. Absence of scar formation in infants after BCG vaccination. *Prof. Med J 2006;13 (4):637-41*.
7. Wammanda RD, Gambo MJ, Abdulkadir I. Age at BCG administration during routine immunization. *J Comm Med Prim Healt Care 2004;16(1):33-5.*
8. Mustapha MG, Garba MA, Rabasa AI, Farouk AG. Prevalence of BCG scar formation among BCG vaccinated apparently healthy U-5 children and its correlation with Mantoux skin test induration in Maiduguri, Nigeria. *Niger Med J 2008;49(4):84-7*.
9. WHO Global Database on Child Growth and Mal-nutrition. World Health Organization Geneva, 1997. http:// www.whqlibdoc.who.int/hq/1997/WHO_NUT_97.4.pdf.
10. World Health Organization. EPI Schedule report. World Health Organization 2006. http:// www.who.int/immunization/sage/3_EMRO_1_EPI_Schedule_Report.pdf
11. Srisaravanapavanathan N, Dissanayake NN, Sarathchandra J. BCG vaccination scars of children under five years in a tertiary care hospital. *Sri Lanka J Child healt 2008; 37: 81 – 4.*
12. National Population Commission (NPC) Nigeria and ICF Macro. 2009. National Health Demographic Health Survey 2008. Abuja, Nigeria: National Population Commission and ICF Macro.
13. Roth A, Jensen H, Garly ML,Djana Q, Martins CL, Sodemann M, Rodrigues A, Aaby P. Should low birth weight infants receive BCG at birth? Community survey from Guinea-Bissau. *PIDJ 2004; 23: 544-50*.
14. Aaby P, Roth A, Ravn H, Napirna BM, Rodrigues A, Lisse IM, Stensballe L, Diness BR, Lausch KR, Lund N, Biering-Sorensen S, Whittle H, Benn CS. Randomized trial of BCG vaccination at birth to Low Birth Weight children: beneficial non-specific effects in the neonatal period. *JID 2011;204:245 – 52*.
15. Santiago EM, Lawson E, Gillenwater K, Kalangi S, Lescano AG, Du Quella G, Cummings K, Cabrera L, Torres C, Gilman RH. A prospective study of Bacillus Calmette-Guerin scar formation and Tuberculin skin test reactivity in infants in Lima, Peru. Pediatrics 2003;112;e298. http:// pediatrics.aappublications.org./content/112/4/e298.full.html.
16. Surekha RH, Vijayalakshmi V, Sunil k, Lakshmi KA, Suman LG, Murthy KJR. Cell mediated immunity in children with scar-failure following BCG vaccination. *Ind-Ped 1998;35:123 – 7*.
17. Channabasava R, Mohan VM, Suryanarayana , Murthy MSK, Shashidhara AN. Waning of BCG scar and its implications. *Ind J Tub. 1993;40:137–44.*
18. Sedaghatian MR, Karduoni K. Tuberculin response in preterm infants after BCG vaccination at birth. *Arch Dis Child 1993; 69: 309 – 11.*
19. Thayyil-Sudham S, Kumar A, Singh M, Paul VK, Deorari AK. Safety and effectiveness of BCG vaccination in preterm babies. *Arch Dis Child Fetal Neonatal Ed. 1999 July 81(1); F64 – F66.*

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Empiric antibiotic prescription among febrile under-five Children in the University of Port Harcourt Teaching Hospital, Rivers State, Nigeria.

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Abstract: *Background:* More than 97% of febrile infants and young children have self-limiting viral infection and therefore, would not require antibiotics. Over prescription of antibiotics increases antibiotics exposure and development of resistance among patients. There is need to evaluate empiric antibiotic prescription in order to limit its use to only febrile children with bacterial infection.
Aim and Objectives: The aim of this study was to determine the prevalence of empiric antibiotic prescription among febrile under-five, post neonatal children presenting in the children outpatient clinic of the University of Port Harcourt teaching hospital.
Method: Febrile Children aged 29 days to <60 months who presented in the outpatient clinic were recruited from September 2010 to January 2011. Their weight, biodata, symptoms, Physician's diagnosis, and names of antibiotic prescribed were entered into a predetermined proforma and analysed.
Result: A total of 362 children with male to female ratio of 1.03:1 were studied. Two hundred and eighty three (78.2%) febrile children received empiric antibiotic prescriptions. The most frequent antibiotic prescribed was amoxicillin 80 (28.3%). Children aged 1-12months received the highest number of prescriptions 113 (80.7%). There was no significant relationship between age, temperature level, weight for age, number of symptoms and frequency of antibiotic prescription ($p>0.05$). Upper respiratory tract infection (83.7 %) and diarrhea (55.9%) were significantly associated with empiric antibiotic prescription ($P=0.05$ and 0.002 respectively).
Conclusion: Empiric antibiotic prescription for febrile under-five children is a common practice in UPTH. Physicians should therefore reduce the frequency of antibiotics prescription in febrile children unless there is clinical evidence of bacterial infection.

Key words: Empiric Antibiotics, Fever, post neonatal under-five, Nigeria

Introduction

Acute febrile illness among infants or young children is a common clinical scenario, accounting for up to 30% of paediatric clinic consultation[1]. More than 97% of non-toxic but febrile infants and young children have self-limiting viral infection therefore would not require antibiotics[2]. In Uganda, antibiotic was prescribed empirically to 59.5% of febrile, under-five children while in Netherland, it was prescribed to 26.5% of febrile children aged 1month to 6years[3,4].

The Integrated management for childhood illnesses (IMCI) guideline for management of febrile children in Malaria endemic areas recommended use of antibiotics when any of the following is present: General danger signs, stiff neck or any sign of severe malaria[5]. The National institute for health and clinical excellence (NICE) guide lines for management of febrile children in the United Kingdom recommends empiric antibiotic be given to children with suspected serious bacterial infection.[6] Considering that the prevalence of bacterial infections among febrile children in ambulatory clinic setting is 1.1% in the United States of America, few febrile children would actually require empiric antibiotics prescription[7].

It is important to monitor antibiotic usage in order to protect their efficacy[8]. This is because improper antibiotic usage, increases antibiotic exposure among humans and animals. This directly increases antibiotic resistance by promoting emergence of resistant bacteria strains.[9,10]

If this continues unchecked it would ultimately cause increased mortality from treatable diseases. In management of the febrile child, there is a need to evaluate empiric antibiotic treatment in order to limit its use to only children at risk of bacterial infection[11].

The aim of this study was to determine the prevalence of empiric antibiotic prescription among febrile under-five, post neonatal age children presenting in the children outpatient clinic of the University of Port Harcourt teaching hospital. We also set out to identify the factors on which physicians base their decision to prescribe empiric antibiotics and to identify the pattern of antibiotics prescription. It is hoped that consideration of findings from this study may lead to better founded and consequently, diminished empiric antibiotic prescriptions. This will ultimately help to protect available antibiotics from the emergence of resistant bacteria strains, threatening to render them ineffective.

Subjects and Methods

This was a prospective study that was carried out in the Children's outpatient clinic (CHOP) of the University of Port Harcourt Teaching Hospital (UPTH) between September 2010 and January 2011. The University of Port Harcourt Teaching hospital is a tertiary hospital located in Southern part of Nigeria. The children outpatient clinic runs both general and specialist paediatric services. The general paediatric clinic is covered mostly by Resident doctors and House officers with access to review cases with the Consultant Paediatrician. Ethical clearance for the study was obtained from the Ethics Committee of the University of Port Harcourt Teaching Hospital. Written informed consent was obtained from parents or guardian. The minimum sample size of 362 was calculated using a bacteraemia prevalence rate of 38.2% among febrile infants in a children emergency ward in Nigeria[12]. All the children that presented to the clinic and met the inclusion criteria within the study period were consecutively recruited. The criteria for inclusion into the study was age one month to < 5years, and axillary temperature ≥ 37.5°C. Children that had initially received antibiotic were excluded. The temperature and weight of all the children were measured and recorded in a structured data collection form. Each child was given a code prior to their scheduled consultation by the physician. In order not to influence the patients' prescription, the attending physicians were not informed that their prescriptions were being recorded. After being attended by the physician, they were seen in a separate room where data was collected by interviewing the caregivers. Sociodermographic information regarding age, sex, address was obtained. Clinical information including the number of symptoms the subject presented with, Physician's diagnosis, number and names of antibiotic prescribed if any was obtained from the patient files. The questionnaire was filled by the investigator. Any antibiotic prescribed prior to laboratory evidence of any bacterial infection was defined as Empiric antibiotic prescription.
Their nutritional status was determined using the Gomez classification[13].

Statistical analysis was done using EP Info version 3.5. Chi- squared test and Fishers Exact test were used to test for significant associations between proportions. Comparison of means was done with the student's t test. A p value of 0.05 or less was considered statistically significant

Result

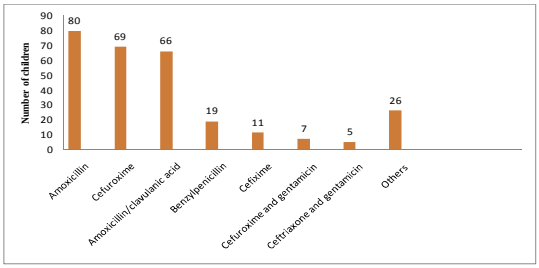
Three hundred and sixty two children who met the inclusion criteria were enrolled into the study. There were 184 (50.8%) males and 178 (49.2%) females, giving a male to female (M:F) ratio of 1.03: 1. They were aged 1 to < 60 months (mean 21.1 ± 15.4 months). The mean age of the male subjects was 20.8 ± 15.07 months, while that of the females was 21.4 ± 15.8 months (p=0.15). The median age for all the subjects was 18 months and the modal age was 24months. Two hundred and fifty eight (71.3%) children were aged ≤ 24months. The mean temperature of the study population was 38.2 ± 0.6°C (range 37.5 - 40.8 °C). One hundred and ninety children had axillary temperatures within the range of 37.5 - 38 °C. Seven had temperature >40°C(Table 1).

Table 1: Temperature and age distribution of the study population

Temp (°C)	Age in months (%)					Total (%)
	1-12	>12-24	>24-36	>36-48	>48-<60	
37.5-38.0	85(44.7)	54(28.4)	31(16.3)	10 (5.3)	10(5.3)	190(100)
>38.0-38.5	31(35.6)	29(33.3)	12(13.8)	5(5.7)	10 (11.5)	87(100)
>38.5-39.0	13(34.2)	16(42.1)	6(15.8)	1(2.6)	2(5.3)	38(100)
>39.0-39.5	9(30.0)	11(36.7)	8(26.7)	1(3.3)	1(3.3)	30(100)
>39.5-40.0	2(20.0)	5(50.0)	0(0)	0(0)	3(30.0)	10(100)
>40.0	0(0)	3(42.9)	1(14.3)	1 (14.3)	2(28.6)	7(100)
Total (%)	140 (38.7)	118 (32.6)	58(16.0)	18 (5.0)	28(7.7)	362(100)

Two hundred and sixty seven (73.8%) children had normal nutritional status. 1st, 2nd and 3rd degree malnutrition was seen in 72(19.9%), 21(5.8%) and 2(0.6%) respectively. The mean weight of the study population was 11.2 ± 4.5kg. Two hundred and eighty three (78.2%) febrile children received prescription for empiric antibiotics from the consulting physician. The most frequent antibiotic prescribed was amoxicillin in 28.3% of children (Fig 1). Antibiotics prescribed less than five times were grouped under others and they include ampicllox, ceftazidime, ceftriaxone, cephalexin, ciprofloxacin, erythromycin, septrin, ampicillin/ sulbactam and chloramphenicol. Most children 257(90.8%) received one antibiotic while two antibiotics were prescribed in 25(8.8%) and 3 in a single prescription.

Fig 1: Names of Empiric antibiotics and frequency



Children aged 1-12months received the highest number of prescriptions (80.7%) and frequency of antibiotic prescription decreased with age (Table 2). Although the difference was not statistically significant (P=0.76).

Table 2: Age distribution of children given empiric antibiotics

Age (months)	Empiric antibiotics Yes (%)	Empiric antibiotics No (%)	Total
1-12	113(80.7)	27(19.3)	140(100)
>12-24	93(78.8)	25(21.2)	118(100)
>24-36	44(75.9)	14(24.1)	58(100)
>36-48	13(72.2)	5(27.8)	18(100)
>48-<60	20(71.4)	8(28.6)	28(100)
Total	283(78.2)	79(21.8)	362(100)

χ^2 =1.86 df=4 P=0.76

All children with temperature >39.5-40.0^{o}C received empiric antibiotics (Table 3). There was however, no significant relationship between temperature level and the frequency of empiric antibiotic prescription (P=0.2)

Table 3: Relationship between temperature and empiric antibiotic prescription

Temperature range (^{o}C)	Empiric antibiotic Yes(%)	Empiric antibiotic No(%)	Total
37.5-38.0	143(75.3)	47(24.7)	190(100)
>38.0-38.5	71(81.6)	16(18.4)	87(100)
>38.5-39.0	31(81.6)	7(18.4)	38(100)
>39.0-39.5	24(80.0)	6(20.0)	30(100)
>39.5-40.0	10(100)	0(0)	10(100)
>40.0	4(57.1)	3(42.9)	7(100)
Total	283(78.2)	79(21.8)	362(100)

χ^2 =6.4, df=5, P=0.2

Children with second degree malnutrition received the highest number of prescriptions for empiric antibiotics (Table 4). Only two children however had third degree malnutrition. Nutritional status was not significantly related with the frequency of prescriptions (P=0.55)

Children that presented with 3 and ≥5 symptoms received the highest number of empiric antibiotics prescription (Table 5), while 72.75% of children that presented with fever and no other symptom where given empiric antibiotic prescription. The number of symptoms the patient presented with was not significantly related to the frequency of empiric antibiotic prescription.

Table 4: Nutritional status and empiric antibiotic prescription

Nutritional status (Gomez)	Empiric antibiotic Yes(%)	Empiric antibiotic No(%)	Total
Normal	210(78.7)	57(21.3)	267(100)
1st degree malnutrition	54(75.0)	18(25.0)	72(100)
2nd degree malnutrition	18(85.7)	3(14.3)	21(100)
3rd degree malnutrition	1(50.0)	1(50.0)	2(100)
Total	283(78.2)	79(21.8)	2(100)

χ^2 =2.0, df=3, P=0.55

Table 5: Number of symptoms excluding fever and antibiotic prescription

No of symptoms excluding fever	Empiric antibiotic Yes(%)	Empiric antibiotic No(%)	Total
0	16(72.7)	6(27.3)	22(100)
1	55(76.4)	17(23.6)	72(100)
2	108(77.1)	32(22.9)	140(100)
3	70(83.3)	14(16.7)	84(100)
4	29(76.3)	9(23.7)	38(100)
≥5	5(83.3)	1(16.7)	6(100)
Total	283(78.2)	79(21.8)	362(100)

χ^2 =2.08, df=5, P=0.83

Febrile Children who had upper respiratory tract infection (URTI) presenting only as either cough or catarrh or both were given empiric antibiotic prescription in 83.7% of their consultations. Those who had diarrhoea received prescription for empiric antibiotics in 55.9% of their consultations (Table 6). Diagnosis that occurred in less than 9%(32) of the study population was not evaluated because of the small sample size. URTI and diarrhoea were significantly associated with increased antibiotic prescription (P=0.05 and 0.002 respectively).

Table 6: Clinical diagnosis and frequency of antibiotic prescription

Clinical diagnosis	Empiric antibiotic Yes(%)	Empiric antibiotics No(%)	P value
URTI	118(83.7)	23(16.3)	0.05
Tonsillitis	41(87.2)	6(12.8)	0.1
Pneumonia	33(86.8)	5(13.2)	0.2
Diarrhoea	19(55.9)	15(44.1)	0.002

Discussion

An overall frequency of 78.2% for empiric antibiotic prescription among febrile under-five children is high. This high frequency of antibiotic prescription is similar to 72.2% reported among similar age group in Tanzania, another African country[14]. African countries with developing economies could have similar challenges in their health sector. In such settings, challenges with laboratory services ranges from delay in laboratory results to complete absence of laboratories. Results of laboratory investigations to confirm infection usually takes more than 24 hours. This necessitates a second

visit or often the patient is lost to follow up. This situation makes the physician to opt for empiric antibiotic prescription. A study done in the Netherland among febrile children reported a lower antibiotic prescription rate of 26.5%[4]. In the Netherland study a practice guideline for the management of febrile children was used.[15] This guideline does not recommend routine use of antibiotics in children with fever without an apparent source. This adherence to the guideline could have contributed to the lower frequency of antibiotic prescription. Also the mean temperature of the Netherlands study was lower than our study (37.9 vs 38.2^{o}C respectively). The lower temperature could mean that the study population in the Netherlands study was at a lower risk of bacterial infection than our study population. Previous studies have demonstrated that high temperatures in association with young age increases the likelihood of bacterial infection[6,16].

Amoxicillin and cefuroxime were the most frequently prescribed antibiotics in this study. Amoxicillin, a narrow spectrum penicillin has been reported in Tanzania, Nigeria and America as one of the common antibiotics used in paediatric practice[14,17,18]. The high use of cefuroxime, a broad spectrum cephalosporin in our study shows a growing pattern of clinicians choosing more expensive and broader spectrum antibiotics in their practice. Similar trend has also been reported in USA and it raises serious concerns about the overuse of broad-spectrum antibiotics, particularly for patients for whom antibiotic therapy is not indicated at all[18]. The recommended principle for rational antibiotic prescription includes: Choosing a drug that has efficacy in treating or preventing the disease but leaves other bacteria in the body intact and one that is available, convenient and inexpensive[19,20].

The risk of bacterial infection is higher in younger children due to immaturity of the immune system.[21] knowledge of this fact may encourage physicians to prescribe empiric antibiotics more often in this age group. However, even among febrile young children there is an urgent need for classification based on risk for bacterial infection using clinical guidelines. In Europe and America these guidelines are already available[6,15,22]. These guidelines use both clinical and laboratory parameters in risk assessment for bacterial infection. This is based on the assumption that results of these laboratory tests are available to the physician during the index consultation. In a resource poor setting however, this is not the case, so an assessment for risk of bacterial infection in a febrile child is often made without the use of any laboratory results.

The highest antibiotic prescription rate was found among children with temperature range of 39.5-40°C. The combination of young age and hyperpyrexia may have contributed to the 100% antibiotic prescription seen in this group of children. This is because in our study, children with temperature range of 39.5-40°C were much younger (70% < 24mths) while those with temperature >40°C were older (57% > 24mths), as shown in Table 1. Although hyperpyrexia has been documented to be associated with higher risk for sepsis, guidelines on management of febrile children recommends that, height of body temperature alone should not be used to identify children with high risk for bacterial infection but the age of the child should also be taken into account[6,7,16].

Febrile Malnourished children could receive higher antibiotic prescriptions as they have a higher risk of bacterial infection[23]. This was the case in our study as children with 2nd degree malnutrition received the most antibiotics. The number of symptoms did not significantly affect the rate of antibiotic prescriptions. This finding is not surprising as increased symptoms could have meant more system involvement in the on-going pathology but does not differentiate between viral and bacterial aetiology.

In our study 83.7% of children who had common cold were prescribed antibiotics. This directly contravenes WHO and IMCI treatment guidelines, which discourages the use of antibiotics in children with common cold[5,24]. In Tanzania 68.9% of children with common cold were prescribed antibiotics, while in USA 29.6% of children received antibiotic for acute respiratory tract infections when it was not indicated[14,18]. Antibiotics do not reduce the severity or duration of illness in viral infections. Thus their use in viral illness exposes a patient to the risks of side effects from a medication without any benefit. Antibiotics are also not recommended for acute watery diarrhoea[5,24]. Our study however reported 55.9% antibiotic prescription rate in management of diarrheal diseases. Similar high frequency of antibiotic prescription has been reported in other low income countries.[14,25,26]

Conclusion

In conclusion, empiric antibiotic prescription for febrile under-five children is very high in UPTH. This finding has also been reported in studies conducted in other low income countries. Such high rate of empiric antibiotic prescription would lead to increased development of resistant strain of bacteria to the present antibiotics and threatens the end of antibiotic era. There is a need to protect available antibiotics by rational prescription only when they are indicated. The use of available practise guidelines in the management of febrile children would help reduce inappropriate antibiotic prescription in febrile children. The campaign to protect these antibiotics needs to be actively brought to low income countries. These countries have a higher prevalence of infectious diseases and as such would have greater mortality should these drugs be rendered inactive.

We recommend implementation of current evidence based practice that advocates for prior documentation of evidence of bacterial infection by laboratory testing before antibiotic prescription for febrile children. The

febrile child at urgent need for empiric antibiotic should however receive it while laboratory testing to document bacterial infection is being done. We acknowledge the need for locally useful clinical detector/screening tools which could be used in the absence of sophisticated laboratory methods to identify the febrile child at risk of serious bacterial infection. There is no doubt that classifying children based on their risk assessment for bacterial infection prior to commencing antibiotics will, identify the small group of children that need urgent commencement of empiric antibiotics and at the same time, limit the irrational use of antibiotics. This practice may reduce development of antibiotic resistance and reduce the cost of healthcare.

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References

1. Eskerud JR, Laerum E, Fagerthun H, Lunde PKM, Naess AA. Fever in general practice Frequency and diagnoses. *Fam Pract. 1992;263–269.*
2. Jaskiewicz JA, McCarthy CA, Richardson AC, et al. Febrile infants at low risk for serious bacterial infection—an appraisal of the Rochester criteria and implications for management. Febrile Infant Collaborative Study Group. *Pediatrics.1994;94:390–6.*
3. Batwala V, Magnussen P, Nuwaha F. Antibiotic use among patients with febrile illness in a low malaria endemicity setting in Uganda. *Malar J 2011;10:377.*
4. Elshout G, Marijke K, Johannes C, et al. Antibiotic Prescription in Febrile Children: A Cohort Study during Out-of-Hours Primary Care. *J Am Board Fam Med 2012; 25: 810-818.*
5. World Health Organization. International Management of childhood Illnesses chart book for primary health Care Level. 2nd ed. 2004; 7-17.
6. Richardson M, Lakhanpaul M. Assessment and initial management of feverish illness in children younger than 5 years: summary of NICE guidance. *BMJ 2007;334:1163–4.*
7. Stanley R, Pagon Z, Bachur R. Hyperpyrexia among infants younger than 3 months. *Pediatr Emerg Care 2005; 21(5):291-4. [PMID:15874809]*
8. Morris K Battle against antibiotic resistance is being lost. *Lancet Infect Dis.2007; 7(8):509.*
9. Magee JT, Pritchard EL, Fitzgerald KA et al. Antibiotic prescribing and antibiotic resistance in community practice: *retrospective study, 1996–8. BMJ 1999; 319: 1239–40.*
10. Hay AD, Thomas MM, Montgomery A, Wetherell M, Lovering A, McNulty C. The relationship between primary care antibiotic prescribing and bacterial resistance in adults in the community: a controlled observational study using individual patient data. *J Antimicrob Chemother. 2005;56: 146-153.*
11. Finkelstein JA, Christiansen CL, Platt R, Fever in Pediatric Primary Care: Occurrence, Management, and Outcomes. *Pediatrics 2000; 105(2): 260 -266.*
12. Ayoola OO, Adeyemo AA, Osinusi K. Concurrent bacteraemia and malaria in febrile Nigerian infants. *Trop Doc 2005; 35 (1):34-6.*
13. Gomez F, Ramos GR, Frenk S, Cravioto MJ, Chavez R, Vasquez J. Mortality in second and third degree malnutrition. *J trop pediatr Afr child health 1956; 2:*
14. Gwimile JJ, Shekalaghe SA, Kapanda GN, Kisanga ER. Antibiotic prescribing practice in management of cough and/or diarrhoea in Moshi Municipality, Northern Tanzania: cross-sectional descriptive study. *Pan Afr Med J 2012; 12:103.*
15. Berger MY, Boomsma LJ, Albeda FW, et al. The standard of the Dutch College of General Practitioners on children with fever. *Huisarts en Wetenschap 2008;51:287–96.*
16. Lee GM, Harper MB. Risk of bacteraemia for febrile young children in the post-Haemophilus influenzae type B era. *Arch Pediatr Adolesc Med 1998; 152 (7):624-8.*
17. Oshikoya KA, Chukwura HA, Ojo OI. Evaluation of outpatient paediatric drug prescriptions in a teaching hospital in Nigeria for rational prescribing. *Paediatr Perinat Drug Ther 2006;7:183-8*
18. Hersh AL, Shapiro DJ, Pavia AT, Shah SS. Antibiotic Prescribing in Ambulatory Pediatrics in the united states. *Pediatrics. 2011;128 (6):1053-1061.*
19. Iyalomhe GBS, Iyalomhe SI, Eholor RE. Antibiotic prescription and resistance: A contemporary literature review. *Int J Med Med HYPERLINK "http:// www.academicjournals.org/ journal/IJMMS" Sci. 2011; 3(14): 376-380.*
20. World Health Orgarnization, The Rational Use of Drugs - Report of the Conference of Experts, Nairobi 25-29 November 1985, World Health Organization, Geneva.
21. Baker MD. Evaluation and management of infants with fever. *Pediatr Clin North Am 1999; 46(6):1061-72.*
22. Baraff LJ, Bass JW, Fleisher GR, Klein JO, McCracken GH Jr.,Powell KR, et al. Practice guideline for the management of infants and children 0 to 36 months of age with fever without source. Agency for Health Care Policy and Research. *Ann Emerg Med 1993;22:1198–210.*
23. Schaible UE, Kaufmann SH. Malnutrition and Infection: Complex Mechanisms and Global Impacts. *Plos Med 2007; 4(5):115.*
24. World Health Organization. Pocket book of hospital care for children guidelines for the management of common illnesses with limited resources. 2007; 72-81, 109-130
25. Hoan le T, Chuc NT, Ottosson E, Allebeck P. Drug use among children under 5 with respiratory illness and/or diarrhoea in a rural district of Vietnam. *Pharmacoepidemiol Drug Saf. 2009 ;18(6):448-53.[PMID:19326362]*
26. Siddiqi S, Hamid S, Sauerborn R et al. Prescription practices of public and private health care providers in Attock District of Pakistan. *Int J Health Plann Manage. 2002; 17: 23-40.*

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CASE REPORT

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Conjoined twins in Edo state of Nigeria; a report of the first surviving set

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Abstract: The term conjoined twins refers to babies who are physically joined at some point. It is a rare condition with an estimated incidence of 1 per 200,000 live births. We report our experience with conjoined twins over a twelve year period in tertiary hospital in Nigeria and a case of the first set of conjoined twin survivors in Benin City, Nigeria. Over the last twelve years (1999-2011), three cases of conjoined twin have been recorded in our teaching hospital. A set of **t**horacoomphalopagus twins (females) were delivered in 1999 and they survived for only 36hrs. Another set of female omphalopagus twins were delivered in 2009 and survived a separation surgery. A third set of female **t**horacoomphalopagus was delivered in another institution same year and referred to our unit but they only survived for 48 hours.
The first surviving twins were omphalopagus, sharing a single liver, and common bile duct emptying into a common duodenum. The stomach, as well as the jejunum was normal and unshared. Surgical separation of the liver was done and biliary reconstruction procedure performed for twin II. A three -year follow up showed good outcome.

Introduction

The care of conjoined twins continues to pose a daunting medical challenge that includes adequate care of pregnancy, well planned delivery, critical care in early neonatal life, advance surgical intervention and last but not the least is the ethical issues[1,2]. We report our experience with conjoined twins over a twelve year period in a tertiary hospital in Nigeria and a case of the first set of conjoined twin survivors in Benin City, Nigeria. The incidence of conjoined twins in Nigeria is unknown; however an article published in 2001 suggests that over the preceding 60 years there were 12 published cases nationwide,[3] excluding our own cases. The cases seen in our center have so far not been reported perhaps because this center had not recorded any survival of conjoined twins since its existence three and half decades ago. Therefore under reporting may be due to the poor prognosis and stigmatization associated with this condition.

Conjoined twining is one of the most fascinating human malformations but it is not exclusive to our specie as it has also been reported in other mammals, reptiles, birds and fishes.[4] The term conjoined twins refers to babies who are physically joined at some point. It results from incomplete splitting of monozygotic (identical) twins after 12 days of embryogenesis. Some authors recently had postulated that it actually results from "fusion" of stem cells of already separated embryo[4]. Conjoined twinning occurs sporadically with no risk in future pregnancy. Overall the condition is rare with an estimated incidence of 1 per 200,000 live births[4]. Though there are more live born females conjoined twin with a female to male ration of 3:1, however this condition occur more in male foetuses as evidenced by its higher rates in male stillborn. Male conjoined twins are also more likely to die shortly after birth, implying that female conjoined foetuses have better chance at survival than their male counterparts.
The site of union forms the basis of the terms used for classifying conjoined twins: Thoracoomphalopagus (joined at the chest, abdomen or both) – 74%
Thoracopagus or xiphopagus (joined at the chest) - 40%
Omphalopagus (joined at the abdomen) - 34%
Pygopagus (joined at the buttocks) – 18%
Ischiopagus (joined at the ischium) – 6%
Craniopagus (joined at the head) – 2%
A rare type occurs when one incompletely formed (parasitic) twin is dependent on the well-formed one. This is known as heteropagus twinning. The term "pagus" is a Greek word which means "that which is fixed"
The term Siamese twins comes from Eng and Chang Bunker (1811-1874), the famous conjoined twins from Thailand (previously known as Siam). They were thoracopagus twins and were exhibited in circus shows around the world before settling in the United States, where they married two sisters and had nearly two dozen children. They were successful businessmen and lived up to 63 years. There have been several other reports of

conjoined twins in different parts of the globe. In Nigeria the earliest report of conjoined twins were born in Sokoto on 20th December 1935 to a 25 year old para 3 woman at home.[5] They shared only abdominal wall and skin, but no shared internal organs. They were readily separated at the General Hospital in Sokoto by a British missionary doctor.[5] Twenty years later the Kano omphalopagus twins Tamonotanye and Waiboko, were separated in London by Ian Ard.[6] Since then there have been sporadic, howbeit scanty, reports of conjoined twin from the country, but a three year survival follow up of the survivors is generally scarce. Since the first documentation in 1935 till date, 18 cases have so far been reported as summarized in table 1. There are, nonetheless, some cases of conjoined twins that were found in the Nigerian news reports that never made the medical literature, Table 2

Table 1: Summary of conjoined twin reported from Nigeria

Place of delivery	Author(s)	Type of Conjoin Twins	No of pairs	Place of surgery	Outcome	
		Twin I Twin II				
Sokoto	McLaren, 1936	Omphalopagus	1	Sokoto General Hospital	S	S
Kano	Aird, 1945	Omphalopagus	1	Hammersmith, UK	S	D
Port Harcourt	Holgate and Ikpeme, 1956	Omphalopagus	1	Enugu General Hospital	S	S
Kaduna	Stigglebout, 1958	Thoracopagus	1	-	Still Born	Still Born
Ibadan	Gupta, 1966	Pygopagus	1	Hammersmith, UK	S	D
	Omokhodion et al, 2001	Thoracopagus	1	UCH, Ibadan	D	D
Warri	Bankole et al, 1972	Ischiopagus	1	UCH, Ibadan	D	D
Zaria	Mabogunje, 1978	Omphalopagus	1	ABUTH, Zaria	D	D
	1980	Thoracopagus	1		Still Born	Still Born
	1980	Dicephalus	1		Still Born	Still Born
	Sathiakumar et al, 1990	Pygopagus	1		S	D
NDU Sule	Mabogunje and Lawrie, 1978	Heteropagus	1		S	-
Anambra	Iroku and Anah, 1990	Pygopagus	1	UNTH, Enugu	D	D
Lagos	*2003	Thoraco-abdomino pagus	1	John Hopkins, Baltimor	S	S
Ile-Ife	Adejuyigbe et al, 2005	Ischiopagus	2	OAUTHC, Ile-Ife	S	S
Enugu	Ekenze et al, 2009	Omphalopagus	1	Germany	S	S
Maiduguri	Auwal et al, 2011	Ischiopagus	1	UMTH, Maiduguri	S	S
*Total			18			

*Total excluded the conjoined twins seen at the UBTH between 1999 and 2011

Table 2: News reports of Nigerian conjoined twins

Gender	Date	Birth place	Extent of joining	Place of surgery	Website
??	2005	Owerri	Chest Abdomen Pelvic girdle Genitalia		www.allafrica.com/stories/200503040379.html
F	2013	Oturkpo	Abdomen		www.newsinnigeria.org/2013/18
F	2012	Kano	Pyopagus Heart Chest to abdomen	India	www.punchng.com
F	2013	Nasarawa	Upper intestines		www.news2.onlinenigeria.com
M	2013	Enugu	Thoracoomphalopagus One heart Joined genitals		www.nigerianuniversitynews.com/2013/06
F	2011	Jos	Parasite twin – no head Chest down 3 legs One liver	Ibadan	www.enownow.com www.dailytrust.info/index.php/city-news/2010
M	2013	Abuja	One intestine		-abuja www.nigerianmonitor.com
F	2004	Abakaliki	??		www.business,highbeam.com/3548/article-IGI -121544947

Surgical separation of conjoined twins that results in the death of one, or both, of the twins raises complex moral, ethical and legal issues. Where organs such as brain or heart are shared there is a great risk of one or both twins dying if attempt is made at separation. Indeed, any shared organ is often not shared equally and the question often arises as to who should be left with what. Of particular concern is the potential for homicide charges against doctors.[2] The parents of the Manchester twins, Mary and Jodie born in 2000, refused to grant permission for surgery, despite the judges' ruling in favour of surgery. A circumstance, where Mary was sacrificed at surgery, was argued by some as "a murder Mary to save Jodie".[7]

Over the last twelve years (1999-2011), three sets of live conjoined twins were documented in our teaching hospital. The hospital has an average annual delivery rate of 1,600 and serves as a major referral center for a population of approximately six million people. There were two thoracoomphalopagus and one omphalopagus twins. One set of the thoracoomphalopagus twins was delivered elsewhere. Both sets of thoracoomphalopagus twins died within 48 hours following birth.

Case

The surviving twins were delivered on the 9th of September 2009 at 02:48hrs to a young couple at the University of Benin Teaching Hospital, in Benin City, Edo State which is in the South-South part of Nigeria. Their mother, a 29 year old lady registered this first pregnancy at our health facility at the 19th week of gestation. Obstetric ultrasound scan done at her antenatal booking revealed that she had a set of omphalopagus twins. The antenatal period remained otherwise unremarkable until the 34th week of gestation when she went into spontaneous preterm labour. She was delivered of live female omphalopagus twins by an emergency Caesarian Section (Fig 1). The twins were both small-for-dates. They had a combined birth weight of 3.4kg but the Apgar Scores were good. They were joined at the level of the xiphisternum to a point just above the umbilicus. There was a small exomphalos with separate umbilical cords. They both had mild respiratory distress syndrome which resolved within 72hrs following delivery. On the third day of life they developed jaundice requiring phototherapy: the highest bilirubin levels were 13.2 for twin 1 and 13.5mg/dl or twin 2. They were treated for Escherichia coli sepsis with ciprofloxacin and gentamycin guided by the antibacterial sensitivity. By the third week of life they had shown evidence of full recovery and had regained their combined birth weight. From the fourth week they were on full milk feeds and had satisfactory growth.

Thoraco-abdominal CT scan revealed that they both shared a single liver and proximal part of the gut. Twin I had dextrocardia without any functional abnormality. Extensive evaluation of the other systems was normal.

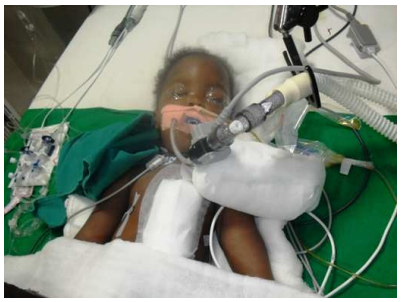
They remained in our newborn unit, until the age of nine months. Their combined weight was 9.8 kg, and a separation surgery was then performed at the Narayana hospital in Bangalore, India. Findings at surgery included a single liver that was "fused" in the midline with separate blood supplies. There was a common gallbladder and bile duct that emptied into a common duodenum which extended up to about 20cm in length. Each twin had her own stomach and jejunum. The liver was divided and biliary reconstruction procedure done for twin II. The duodenum was shared between the two by resection and re-anastomosis. The twins required initial mechanical ventilation and were weaned off by the 4th day. Post surgery they remained stable and were transferred back to the UBTH (fig 2). Physical therapy was instituted to enable them "catch-up" with their motor development that was hitherto made difficult whilst conjoined.

Twins I and II weighed 4.7kg and 4.8kg respectively after surgery. At 2 years postnatal age they weighed 8.5 and 8.6kg respectively while at 3 years they weighed 13.4kg and 13.6kg. Their psychomotor development was compatible with their age at 18 months using the Bailey Developmental Scale. Thorough clinical and laboratory re-evaluation at age three, paying particular attention to the cardiovascular, digestive and renal systems of the twins yielded normal findings.

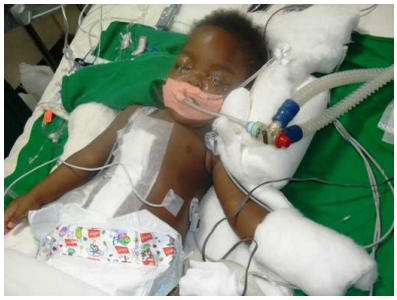
Fig 1: The conjoined twins at two weeks of life

Fig 2: After surgery

Twin I



Twin II



Discussion

This case is a report of the first surviving conjoined twins in a decade of conjoined twins history in this center. Overall reporting of conjoined twins is low in the country. Review of available literature showed that 18 cases have been reported across the country in the last 76 years from 1935 to 2012. Five cases, 28%, were reported from a single center in the North, Zaria,[8] while the other cases were reported from Ibadan,[3] Ife,[9] Enugu[10] and few tertiary health centers in other parts of the country. The higher report from Zaria may be due to the heightened interest of the workers. None so far has been reported from Benin and some other tertiary centers across the country to enable a more countrywide data review. In contrast, 22 cases were reported from a single institution in Philippines, over a 30 year period (1974-2006).[11] An institution in Sao Paula, Brazil reported 14 cases over a 25 year period further reflecting

possible underreporting in Nigeria.[12] It is hoped that this report will be an important contribution to the few existing publications in the country. Although a small number of centers in the country have reported survival of conjoined twins, of note is that information on follow up morbidity and mortality were generally lacking. Our surviving conjoined twins were followed up for catch-up growth, psychomotor development, presence of organ dysfunction and possible late complications of the surgery. All these parameters turned out to be normal at the age of three years. Due to the complexity of the surgical separation, a follow up to evaluate long term survival and quality of life is useful reviewing surgical intervention in the future. In the recent case of separation of heteropagus twins in Maiduguri,[13] the twins had major reconstructive surgery, consequently, long term follow up of these twins will be complementary to our knowledge.

All three sets of conjoined twins seen at our center were females, which is in keeping with the female preponderance noted in the literature. Four out of the six babies suffered early neonatal deaths while 2 (index twins) survived at 3-year follow up. Due to paucity of data it is difficult to say, with any degree of accuracy, what the still birth rate or neonatal death rate for conjoined twins in the country is. Three of the reported 18 pairs where still born, all the reported live born had surgery, 11 in Nigeria and 4 abroad (Table I). Six out of the eight babies (75%) operated abroad survived (one baby was sacrificed to save the other twin). Twelve out of 22 babies (54%) operated in Nigeria survived. Success rate was fairer with ischio/pygopagus twins (58.3%) and poor with thoraco/omphalopagus twins, especially when internal organs are shared.

A careful review of the current case with surgeons in our institution and consult with other surgeons within and outside the country informed the choice of having the surgery done abroad to improved the chances of survival of both twins considering the shared organs. This reflects the need to build on the already existing capacity to handle such cases.

While some have questioned the decision to separate conjoined twins "when two are born as one",[2] having the twins separated may seem justified if it is adjudged that one or both twins would die without separation. This is the case in some heteropagus twin situations in which the parasite twin may die and/or cause the host twin serious physiologic embarrassment due to vascular, biliary or enteric anastomosis. Even though our omphalopagus twins are likely to survive into adulthood, the decision to separate was preferential because of the expected favourable outcome following surgery. In contrast to reports from other parts of the world, the author is unaware of any report of adult conjoined twins in the country. This situation may not be surprising as these babies might have been deprived of care and left to die largely because of stigma, poverty and ignorance. The current case required a lot of psycho-social support for the young parents who had initially abandoned these babies. On the contrary the Biddenden Maids, born in England in 1100, were famous and lived for 34 years. The Siamese twins were also wealthy and famous in the United States. We suggested that providing national awareness, special government support and opening national conjoined twins' registry will go a long way in improving the outcome of these babies, especially when surgery pose a survival risk to one or both twins.

Conclusion

There is under reporting of conjoined twins in Nigeria compared to other parts of the world. Experience from available literature showed that these can be largely prevented by demystifying the condition, providing more awareness and support for the families. These measures will go a long way to improving reporting as well as enhancing the survival of these babies. Secondly paediatricians and surgeons in Nigeria might want to review their decisions to separate when the risk to one or both twins is greater than the risk without the procedure.

Authors' contribution

Amuabunos AE, Eregie CO, Omoigberale AI Effiong V: All managed the patient and reviewed the manuscript

Conflicts of interest: None

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References

1. Davis C. Separating conjoined twins: a medical and criminal law dilemma. *J Law Med. 2010;17 (4):594-607.*
2. Gillett G. When two are born as one: the ethics of separating conjoined twins. *J Law Med. 2009;17 (2):184-9.*
3. Omokhodion SI, Ladipo JK, Odebode T O, *et al* The Ibadan conjoined twins: a report of omphalopagus twins and a review of cases reported in Nigeria over 60 years. *Ann Trop Paediatr. 2001;21 (3):263*
4. Spencer R. Conjoined twins: theoretical embryologicbasis. *Teratology 1992;45:591–602.*
5. McLaren DW. Separation of conjoined twins. *Brit Med J 1936; ii:971*
6. Aird I. The Conjoined Twins of Kano. *Brit. Med. J 1954 ;1: 831*

7. Paris JJ, Elias-Jones AC. "Do we murder Mary to save Jodie?" An ethical analysis of the separation of the Manchester conjoined twins. *Postgrad Med J. 2001;77 (911):593-8.*
8. Mabogunje OA, Lawrie JH. Conjoined twins in West Africa. *Arch Dis Child 1980; 55:626–30.*
9. Adejuyigbe O, Sowande OA, Olabanji JK, *et al*. Successful separation of two pairs of conjoined twins in Ile Ife, Nigeria: case reports. *East Afr Med J. 2005;82 (1):50-4.*
10. Ekenze SO, Ibeziako SN, Adimora GN, *et al*. Ruptured omphalocele in thoracoomphalopagus conjoined twins. *Int Surg. 2009;94(3):221-3.*
11. Saguil E, Almonte J, Baltazar W, *et al* Conjoined twins in the Philippines: experience of a single institution. *Pediatr Surg Int. 2009 ;25 (9):775-80*
12. Berezowski AT, Duarte G, Rodrigues R, *et al* Conjoined twins: an experience of a tertiary hospital in Southeast Brazil. *Rev Bras Ginecol Obstet. 2010;32(2):61-5.*
13. Abubakar AM, Ahidjo A, Chinda JY, *et al* The epigastric heteropagus conjoined twins. *J Pediatr Surg. 2011;46(2):417-20*

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CASE REPORT

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Unusual presentations of childhood acute lymphoblastic leukaemia: A case report

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Abstract: Childhood acute lymphoblastic leukaemia, (ALL) is increasingly reported to present in an atypical fashion which may have significant implications for treatment outcomes and survival. This case report presents a Nigerian child who's clinical and radiological features together with effusion cytological findings were suggestive of metastatic neuroblastoma. However, a definitive diagnosis of ALL was established following a bone marrow aspiration study that revealed abnormal cellularity consistent with L1 morphological subtype. Unfortunately, the child was discharged against medical advice before definitive therapy could be commenced.

Key words: Atypical presentations, metastatic neuroblastoma, childhood acute lymphoblastic leukaemia.

Introduction

Acute lymphoblastic leukaemia (ALL) is a malignant haematological condition that arises from an acquired somatic mutation in a lymphoid progenitor cell[1]. This mutation may occur at various points in the development of the lymphoid progenitor. Malignant proliferation and accumulation of lymphoid blasts in the bone marrow and some extramedullary sites such as the liver, spleen, skin, testes (in males) and even the central nervous system (CNS) is the hallmark of this disease.
ALL accounts for up to 30% of childhood cancers in Caucasians[2], thus it is among the most common paediatric malignancies.

Clinically, ALL may have diverse patterns of presentation; typically its clinical presentation is related to bone marrow failure and extra medullary effects of the disease. As such common symptoms range from those arising secondary to cytopaenias (including anaemia, leucopaenia and thrombocytopaenia) to those due to organ/ system infiltration such as lymphadenopathy and hepatosplenomegaly. Increasingly, unusual presentation of childhood ALL is being documented in literature and cases presenting with back pain and vertebral compression[3], stroke[4], absence of blasts in the peripheral blood[5], obstructive jaundice[6], and isolated masseter muscle involvement[7] have been variously reported.
We report here a case of ALL presenting with atypical features, in a Nigerian child to highlight challenges of diagnosis.

Case Report

A 4- year- old male Nigerian was seen at the Nnamdi Azikiwe University Teaching Hospital, Nnewi, with a 14- week history of recurrent fever, multiple facial swellings with enlargement of the head and protrusion of the eyes, (fig. 1). There was also a history of significant weight loss and nasal discharge that occasionally was blood tinged.

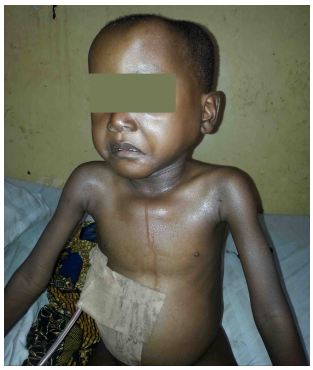

Fig1: Showing head and anterior chest wall swellings

General examination was significant for marked weight loss, moderate mucosal pallor, significant generalized lymph node enlargement and bipedal pitting oedema. Three discrete masses were noted on the left part of the frontal bone, left part of the jaw and anterior chest wall, measuring 10cm, 6cm and 9cm in their longest diameters respectively. These swellings were globular, firm to hard in consistency, non mobile, non tender and were neither attached to overlying skin nor showed any differential warmth.

Bilateral parietal bossing along with coronal sutural diathesis was also noted. The anterior fontannel was

patent and normotensive, measuring 2cm x 2cm. He had no signs of meningeal irritation and muscle tone and power were normal globally.

His abdomen was uniformly distended with palpably enlarged, firm and tender liver, 10cm below the right costal margin. Ascites was present and demonstrable.
Chest examination was significant for reduced chest expansion and stony dull percussion notes over the right hemi thorax with absence of breath sounds in both the right mid and lower zones.
A provisional clinical diagnosis of neuroblastoma metastatic to the right hemi thorax and the head region was considered.

An abdomino-pelvic ultrasonographic examination showed a right sided supra renal mass while a chest radiograph demonstrated right sided pleural effusion, the cytology of which revealed hypercellular smears showing sheets of medium sized cells with high nucleocytoplasmic ratio, in a dirty background. The neoplastic cells have coarse chromatin pattern. Overall features were suggestive of a malignant (round) blue cell tumour, probably neuroblastoma. These findings reinforced metastatic neuroblastoma as the most probable diagnosis.
The patient was seronegative for HIV 1 and 2, while haemoglobin electrophoresis confirmed AA haemoglobin phenotype. Complete blood count was significant for severe anaemia (Haematocrit was 0.17L/L), moderate leucocytosis (white cell count of 20.8 x 10^9/L) and mild thrombocytopaenia (platelet count of 76 x 10^9/L). Blood film and bone marrow cytology were however in keeping with ALL, L1 morphological type (figs 2 and 3). Flow cytometric analysis of peripheral blood cells showed positivity for CD 45, an extended immunophenotypic profile as well as cranial computed tomography (CT) scan could not be done because of the non availability of funds.

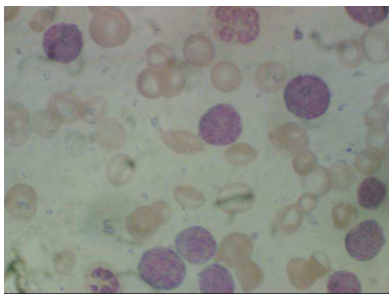

Fig 2: Bone marrow film, showing L1 lymphoblasts

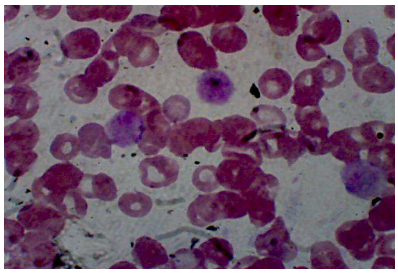

Fig 3: Peripheral blood film, showing lymphoblasts

Supportive treatment including blood product transfusions were commenced while work up including biopsy of the masses was planned as a prelude to definitive chemotherapy for ALL. However, further care was abruptly terminated as child was discharged against medical advice.

Discussion

Atypical presentations of ALL have reportedly constituted an enormous challenge, in terms of diagnosis, especially in resource poor settings. However, advances in diagnostic protocols, especially in the realm of immunophenotyping and relevant molecular diagnostics have greatly enhanced diagnostic precision in such atypical cases[3-6]. While such levels of diagnostic accuracy is desirable, the application of basic cytological techniques for the analysis of appropriate specimens has continued to provide valuable information in resource poor settings. In this patient, bone marrow study was able to establish a diagnosis of ALL.

Our patient presented with head enlargement, facial and anterior chest wall swellings. Typically children with ALL tend to present with extra medullary organ enlargement owing to infiltration by lymphoblasts and while the liver, spleen and testes are the most frequently affected organs, other less common extra medullary sites have been reported in the literature. Coronal sutural diathesis as well the patent anterior frontannel observed in this patient may be an indication of CNS infiltration by lymphoblasts; a CT scan however was not done to confirm this. Wimperis et al[7] in 1992 described two children with ALL in whom isolated masseter muscle involvement was the only presenting feature of the disease. Accurate diagnoses of the cases were hinged on the use of immunophenotyping and immunogenotyping. Indeed, such extended panel of diagnostic tools have proved useful in establishing diagnoses in similar atypical cases of ALL presenting as vertebral compression[3], stroke[4], absence of blasts in peripheral blood[5] and obstructive jaundice[6].

The initial diagnosis in this child was metastatic neuroblastoma based on his age and the clinical presentation of multiple masses in the head region and chest and reenforced by the ultrasonographic finding of a supra renal mass together with the pleural effusion cytology report. However, in this patient, peripheral blood and bone marrow cytology were both in keeping with ALL of the L1 morphological type. Besides, the demonstration of CD 45 lineage antigen supported the haematopoietic origin of this malignant condition. In a recent case study, D'angelo *et al*, [8] reported ALL co-existing with neuroblastoma in a 3 year old girl, as different disease entities. We had entertained the possibility of this phenomenon at a stage in the management of this child prior to bone marrow investigations; in point of fact, biopsied tissue sample of one of the masses had been scheduled but later considered unnecessary.

Advances in ALL treatment have ushered in an individualized, tailored and risk adapted approach, utilizing a myriad of chemotherapy options with or without haematopoietic stem cell transplantation. Treatment

stratification is commonly based on the biologic features of individual disease[2]. Utilizing the risk adapted protocol, Pui *et al*, [9] suggested that prophylactic cranial irradiation, which has been a component of the standard treatment of childhood ALL, may safely be omitted. Unfortunately our patient did not stay long enough in our care to receive any definitive treatment; he was not followed up to the community.

Conclusion

Childhood ALL may present in a rather atypical manner. A high index of suspicion, complimented by appropriate diagnostic tests is essential in making early and accurate diagnoses in cases of ALL with atypical presentations.

Conflict of Interest: None
Funding: None

Limitation of this report

A biopsy and histology of the body masses, including that on the adrenals (preferably via ultrasound guide) might have been a more definite way to rule out the possibility of neuroblastoma co-existing with ALL in this child, this was however not done.

References

1. Provan D, Singer CRJ, Baglin T, Dokal I. Oxford Handbook of Clinical Haematology. Oxford University Press, New York. 3rd Ed. 2009.p132.
2. Lo Nigro L. Biology of childhood acute lymphoblastic leukaemia. *J PediatrHematol Oncol. 2013;35:245-52.*
3. Hafiz MG, Islam A, Siddique R. Back pain and vertebral compression: an unusual presentation of childhood acute lymphoblastic leukaemia. *Mymensingh Med J 2010; 19:130-6.*
4. Ege MJ, Meyer LH, Debatin KM, Stahnke K. Co-incidence of recurrent hemiparesis and detection of acute lymphoblastic leukaemia in a 4 year old girl: one or two disease. *KlinPediatr. 2009;221:386-9.*
5. Cogulu O, Karapinar DY, Karaca E, Aydinok Y, Ozkinay F. Unusual course of an acute lymphoblastic leukaemia case with i (9q) as a sole cytogenetic abnormality. *Leuk Res. 2006; 30:1461-3.*
6. Alvaro F, Jain M, Morris LL, Rice MS. Childhood acute lymphoblastic leukaemia presenting with jaundice. *J Paediatr Child Health. 1996;32:466-8.*
7. Wimperis JZ, Brandt LJ, O'Connor S, Marcus R, Broadbent V. Unusual presentation of common acute lymphoblastic leukaemia antigen-positive extra medullary disease in childhood. Two patients with isolated masseter muscle involvement. *Cancer.1992 15;70:8897-901.*
8. D'angelo, Grigoli A, Sementa AR, Tropia S, Alaggio R, Arico M. Simultaneous diagnosis of acute lymphoblastic leukaemia and peripheral neuroblastic tumour in a child. *J PediatrHematol Oncol. 2012;34:75-5.*
9. Piu CH, Campana D, Pei D, Bowman WP, Sandlund JT, Kaste SC *et al*. Treating childhood acute lymphoblastic leukaemia without cranial irradiation. *N Engl J Med. 2009;360:2730-41.*

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CASE REPORT

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Diphtheria in a 13 year old adolescent girl: Management challenges

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Abstract: ***Background:*** Diphtheria is an acute toxic infection which is associated with a high morbidity and mortality and can pose management challenges especially in the absence of proper diagnostic and therapeutic facilities.
Case report: A.S. was a 13 year old girl who presented with fever of five days duration, dysphagia and neck swelling of 4 days duration and sore throat and hoarse voice of 3days duration. Her illness started a day after returning from a 4-day holiday youth camp. She received only oral polio vaccine immunization in childhood. Significant physical examination findings included a swollen neck, a greyish membrane covering the soft palate and uvula with haemorrhagic spots. The pharynx, anterior nares and the nasal turbinates were inflamed and erythematous.
A working diagnosis of respiratory diphtheria was made. Throat swab microscopy showed club shaped Gram positive baccilli. Appropriate culture medium for C. diphtheria was not available.
She received intravenous crystalline penicillin and metronidazole and lateroral erythromycin in an isolated ward. On the 6th day of admission she developed cardiac and neurologic complications– bradycardia (PR=40bpm), hypotension (BP=70/40mmHg), drooling of saliva and paraparesis. Electrocardiography confirmed a complete heart block. She died on the 11th day of admission while efforts were being made to raise funds for a cardiac pace maker.
Conclusion: Management of this vaccine preventable disease requires a high index of suspicion and diphtheria antitoxin should be made readily available.

Introduction

Diphtheria is an acute toxic infection caused by *Corynebacterium* species, typically *Corynebacterium diphtheriae* and rarely toxigenic strains of *Corynebacterium ulcerans*[1,2,3]. The classic disease affects the upper respiratory tract with the formation of an adherent gray-white pseudomembrane in the infected place followed by systemic symptoms caused by elaboration of an exotoxin produced by the bacillus[1,4]. The disease progresses rapidly with a case fatality rate as high as >20% in acute disease states if there is no sufficient diagnostic procedure and therapy option[1]. Therefore it requires a high index of suspicion. The most dominant factor causing death is myocarditis and diphtheria myocarditis incidences related to nasopharyngeal diphtheria is 10-20% with a death rate as high as 50-60%[5].

The emergence of immunization program changed the epidemiology of the disease and reduced its prevalence worldwide. In the Western world, diphtheria is near eradication level in most countries[6]. Also, in many African countries with a high diphtheria immunization coverage rate, the incidence of diphtheria has decreased by >95% across the region in the past 10 years[6]. In Nigeria also, reported cases of diphtheria has been declining even with just low to moderate coverage with DPT3.[7] Accordingly, there has been no reported case from Our centre in the past 10 years.

However, recently there are pockets of sporadic cases being reported in Nigeria. Sadoh et al[8] reported nine cases of diphtheria in children who were aged between 11months and 10years in the University of Benin Teaching Hospital (UBTH) between 2008 and 2010, while Oyeyemi et al[9] reported ten cases of diphtheria in children aged 3-13years in the Federal Medical Centre Katsina on two clusters of diphtheria outbreak between 2009 and 2010 involving three contiguous local government area in Katsina State. In this case we report a 13 year old girl who died from probable diphtheria myocarditis and the diagnostic and management challenges encountered.

Case Report

AS was a 13 year old girl who presented at the Children Out Patient Clinic of the University of Port Harcourt

Teaching Hospital with complaints of fever of five days duration, dysphagia and neck swelling of four days duration, sore throat and hoarse voice of three days duration. Her illness started a day after returning from a four-day holiday youth camp. She received amoxicillin capsules before presentation. She had never been immunized except for Oral Polio Vaccines which she received on National Immunization Days (NIDs).

Physical examination revealed a lethargic child in painful distress with a bull neck, hoarse voice, and drooling saliva. Throat inspection showed a thick greyish membrane covering most part of the soft palate and hanging down over the uvula with areas of haemorrhagic spots. The pharynx was erythematous, the anterior nares and the nasal turbinates were inflamed and plugged with blood crusts. (Fig 1) She had a good volume and regular pulse with a rate of 82 beats per minute, a blood pressure of 100/70mmhg and normal heart sounds. She had no neurological deficits.

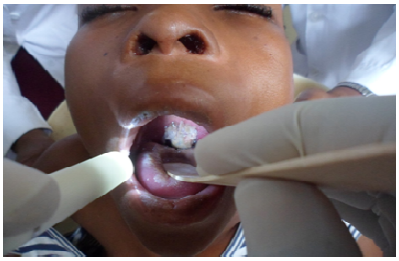

Fig 1: Greyish adherent membrane in the soft palate and uvula, and the haemorrhagic exudates in the nostrils

A diagnosis of probable respiratory diphtheria was made. Microscopy of the throat swab and swab of the anterior nares showed club shaped Gram positive rods. Culture using Tellurite salt agar could not be done as this was not available. She was reviewed by the Otorhinolaryngologist while the State Disease Surveillance and Notification (DSN) unit was notified.

She was nursed in an isolation room, received intravenous crystalline penicillin at 0.4MU/kg/day in 4 divided doses, intravenous Metronidazole at 8mg/kg/dose every 8hours, intra venous fluid, oral toileting with saline water and bed rest. All close contacts were counseled especially on the need to immunize all under-5 children whose last DPT dose was more than 12 months ago and were placed on Tablets Erythromycin – 500mg qds for two weeks.

By the 6th day of admission, she developed cardiovascular complications – bradycardia (PR=40bpm) and hypotension (BP=70/40Hg). She received 20mls/kg of normal saline over 30minutes, intravenous hydrocortisone and Atropine with no apparent clinical improvement. Her condition deteriorated and by the 7th day of admission her pulse rate dropped further down to 24bpm and the power in the lower limbs was reduced to grade two. A diagnosis of Diphtheria Toxic cardiomyopathy (Heart Block) and neuropathy (Para paresis) was made. An electrocardiogram confirmed a Complete Heart Block. (Fig 2) Parents were counselled on the need for an urgent pacemaker. Efforts were ongoing to raise fund for a pacemaker before she died on the 11th day of admission.

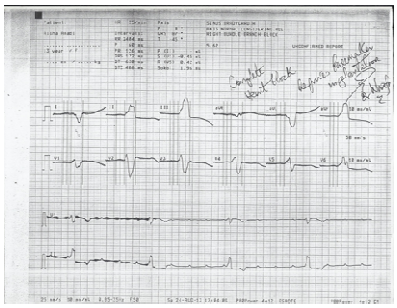

Fig 2: ECG tracing of AS showing complete dissociation of the p wave and QRS complex which are widened (172ms), idioventricular rhythm with rate of 25/mm and a giant T wave inversion

Discussion

Diphtheria is an acute toxic infection caused by *Corynebacterium diphtheriae*, an aerobic, non-encapsulated, Gram positive bacillus.[1] *C. diphtheriae* is an exclusive inhabitant of human mucous membranes and skin. It spreads primarily by airborne respiratory droplets, direct contact with respiratory secretions or exudates from infected skin lesion. Incidence peaks during the dry season with majority of the cases occurring in unimmunized children below 15 years of age. Diphtheria occurs by entry of C. diphtheriae into the nose or mouth. After a 2-4 day incubation period, toxins are secreted which leads to toxin-mediated tissue necrosis. This coupled with local inflammatory response produces patchy exudates which later forms fibrinous exudates and a tough adherent membrane.[4] Respiratory embarrassment may follow extension of disease into larynx or tracheobronchial tree.

Our patient never had DPT vaccine and hadjust returned from a crowded youth camp. These are strong risk factors for respiratory diphtheria. She also presented with features typical of probable respiratory diphtheria like sore throat and dysphagia, progressive neck swelling, haemorrhagic and inflamed nasal turbinates and an adherent greyish white membrane hanging down the pharynx. The early presentation and short duration of these symptoms confirms the short incubation period and rapid progression of the disease as this child at presentation within five days of disease onset was already very ill and lethargic.

Complications remain the greatest cause of morbidity and mortality following infection with diphtheria. Complications secondary to the elaborated diphtheria toxin are the most common. Toxic cardiomyopathy most commonly occur in the second week of the disease but can appear as early as the first or as late as the sixth week of illness[1,10]. Toxic cardiomyopathy occurs in 10–25% of patients with respiratory diphtheria and is responsible for 50–60% of deaths[1]. Neurologic complications appear after a variable latent period, are predominantly bilateral and are motor rather than sensory and usually resolve completely. Paralysis of the soft palate is common and generally appears in the third week. Our patient developed features of myocarditis by the second week of disease onset and bilateral motor weakness of the lower limbs by the third week which is in line with disease

progression. This early onset of cardiac manifestation is associated with rapid disease progression and is a poor prognostic feature as was the case of our patient. Drooling of saliva and hoarse voice in this patient may be due to sore throat and dysphagia or to paralysis of the soft palate.

A diagnosis of diphtheria may be described as "probable" or "confirmed". It is probable if the case meets the clinical description or confirmed if a probable case is laboratory confirmed or linked epidemiologically to a laboratory confirmed case. A clinical description is an illness characterized by laryngitis or pharyngitis or tonsillitis, and an adherent membrane on the tonsils, pharynx and/or nose. However, persons with positive *C. diphtheriae* cultures and not meeting the clinical description (i.e. asymptomatic carriers) should not be reported as probable or confirmed diphtheria cases. Our patient met the criteria for probable diphtheria but could not be confirmed. Our centre and many others in Nigeria lack the appropriate capacity and skills for the isolation of this organism and this does have several deleterious effects on the management and surveillance of this vaccine preventable disease.

A lot of challenges were encountered in the management of this patient. Once diphtheria is suspected, management entails isolation of the patient, use of specific antitoxin and antibiotics, management of complications, supportive care and chemoprophylaxis for close contacts of patient. The first management challenge was lack of specific diphtheria antitoxin. The use of specific antitoxin is vital in halting disease progression. Antitoxin can neutralize circulating toxin or toxin that is absorbed to cells but is ineffective once cell penetration has occurred. Specific antitoxin is the main stay of therapy and should be administered as early as possible by intravenous route and in a dosage sufficient to neutralize the free toxin. Unfortunately as important as this is in the treatment of patient with diphtheria this anti toxin is unavailable in the country. Only a probable diagnosis could be made in this case as it could not be bacteriologically confirmed by the appropriate culture medium. This challenge may not be limited to our centre as many other centres contacted to assist with the culture also admitted not having the culture medium.

Antibiotics are indicated to clear the causative organism and thereby halt toxin production, and prevent transmission of organisms to contacts. Our patient received intra venous crystalline penicilline and metronidazole which have very good coverage for diphtheria but did not respond to it. This was probably because the disease has reached an advanced stage before presentation and elaborated toxins may have fixed to tissues which are not affected by antibiotics. Management of complications was also challenging. Our case developed both cardiac and neurologic complications both of which may have contributed to the mortality. Although she was diagnosed of having complete heart block, lack of funds and unavailability of the pacemaker made this management option not available

Primary prevention in form of active immunization as DPT vaccine at 6,10, 14 weeks of age and booster dose at 15-18 months and again between 4-6 years of age is recommended. The National Programme on Immunization (NPI) presently does not provide booster doses but a high coverage rate in infancy provides significant disease protection. Unfortunately, our case received neither the primary vaccine nor booster dose. This buttresses the need to reinforce and ensure full coverage of primary immunization by checking immunization cards as a requirement for school enrolment.

All household contacts and those who have had intimate physical contact with a patient are closely monitored for illness through the 7-day incubation period. Antibiotic prophylaxis is given, regardless of immunization status using erythromycin (40-50 mg/kg/day) for 7-14 days or a single injection of benzathine penicillin.[1] This was done for all close contacts of our patient including the managing team. Unfortunately, it was not possible to trace the asymptomatic carrier from whom our patient contracted the disease, neither was it possible to trace other adolescents that participated in the youth camp for possible development of symptoms.

Conclusion

In conclusion, diphtheria, a vaccine preventable disease (VPD) is a disease with rapid progression and requires a high index of suspicion. Facilities necessary for the diagnosis and treatment of this disease especially diphtheria specific antitoxin should be made readily available in Nigeria. Parents and caregivers of children should utilize the opportunity of free immunizations to vaccinate their children, for indeed, prevention is better than cure.

Conflict of interest: None
Funding: None

References

1. Stephen B E. Diphtheria In: Behrman RE, Kliegman RM, Jenson HB, Stanton BF. (editors) Nelson Textbook of Pediatrics, 18th edition. Philadelphia: W.B. Saunders Company, 2007. 1153-1157.

2. Seto Y, Komiya T, Iwaki M, Kohda T, Mukamoto M, Takahashi M. Properties of corynephage attachment site and molecular epidemiology of *Corynebacterium ulcerans* isolated from humans and animals in Japan. *Jpn J Infect Dis. 2008;61:116–22*

3. De Zoysa A, Hawkey PM, Engler K, George R, Mann G, Reilly W. Characterization of toxigenic *Corynebacterium ulcerans* strains isolated from humans and domestic cats in the United Kingdom. *J Clin Microbiol. 2005;43:4377–81*

4. Vitek CR, Wharton M. Diphtheria toxoid. In: Plotkin S, Orenstein W, Offic P, (editors). Vaccines. Amsterdam: Elsevier Inc.; 2008: 139–56.
5. Ralph DF, Barbara WS, Pratip KN. Diphtheria In: Feigin RD, Cherey JD. (eds) Textbook of Pediatric Infections Diseases, 6th edition. Philadelphia: W.B. Saunders company, 2009. 1393-1395.
6. WHO World Health Organization Immunization, Vaccines And Biologicals. Vaccine preventable diseases Vaccines monitoring system 2013 Global Summary Reference Time Series DIPHTHERIA
7. Oyeyemi BO, Suleiman AO, Suleiman BM, AjetomobiA, Ibrahim A. A report on two clusters of diphtheria outbreak involving three contiguous local Government Area in Katsina state, Nigeria. Proceedings of the 42nd Annual General and Scientific Conference of the Paediatric Association of Nigeria (Panconf), 2011. Jan 11-15 Abuja, Nigeria. P 12
8. Sadoh AE, Okhakhu A, Omuemu V, Lofor PVO, Osarogiagon W, Oviawe O, Diphtheria in Nigeria: Is there resurgence. Proceedings of the 42nd Annual General and Scientific Conference of the Paediatric Association of Nigeria (Panconf), 2011. Jan 11-15 Abuja, Nigeria. Pg 40-41

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CASE REPORT

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Incidental finding of dextrocardia with situs inversus totalis in a day old neonate: Case report and review of the literature

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Abstract: Dextrocardia with situs inversus are rare congenital anomalies which can be asymptomatic and compatible with normal life. They are characterized by mirror images of all intra-thoracic and intra-abdominal viscera. Our aim is to report an incidental finding of dextrocardia with situs inversus in a neonate with neonatal sepsis. A day-old male term neonate presented with features of infection. Physical examination revealed cardiac apex on the 4th right intercostal space, along the mid-clavicular line. Chest radiograph and abdominal ultrasound confirmed the diagnosis of dextrocardia with situs inversus. Bilateral cervical ribs were also seen on chest radiograph. He was managed with antibiotics and discharged. Newborn babies should have a thorough physical examination after delivery before discharge to enable early diagnosis of congenital anomalies for appropriate referral.

Key words: Dextrocardia, neonate, neonatal sepsis.

Introduction

Dextrocardia (also called looping defect) is an abnormal congenital positioning of heart on the right side[1]. Situs inversus totalis also called situs transversus, is a congenital condition in which major visceral organs are reversed or mirrored from normal positions. Many people with situs inversus are unaware of their unusual congenital anomaly until they seek medical attention for unrelated conditions[1]. Individuals with dextrocardia and situs inversus totalis may have associated congenital heart malformations[2], primary ciliary dyskinesia or splenic malformations.[3]
We describe a case of dextrocardia with situs inversus totalis in a one day old neonate with neonatal sepsis, the first case to be reported in Gusau, Zamfara State, Nigeria.

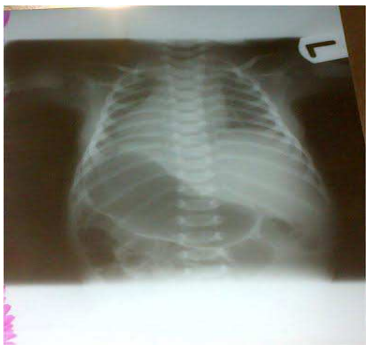
Case report

A 24 hour old male term neonate presented with complaints of refusal to suck, fever, convulsion and bloody stool of few hours duration. He had associated abdominal distension, but no vomiting or bleeding from any other site. Pregnancy was supervised, uneventful, no maternal risk factors of sepsis. Delivered at a general hospital and cried immediately after birth. He was not examined by a paediatrician after delivery as none is available at the hospital.

On examination he was not febrile and not pale. Cardiovascular system examination revealed full volume pulses, regular with apex beat at 4th right intercostal space mid clavicular line. He had normal heart rate with first and second heart sounds. Abdomen was full, soft, not tender and no organ was palpable. Rectal examination revealed finger stained with bloody stool.

Chest X-ray showed normal heart size with apex located to the right in keeping with dextrocardia. Hepatic shadow was noted on the left and possible splenic shadow on the right. There were cervical ribs bilaterally.
Abdominal scan demonstrated liver on the left while the spleen was on the right. Demonstrable bowel loops were slightly distended but otherwise normal.
Full blood count showed leucocytosis, random blood sugar and serum electrolytes were normal. Blood culture did not yield any growth. Cerebrospinal fluid analysis was in keeping with bacterial meningitis and gram negative cocobacilli were seen on microscopy. However, cerebrospinal fluid culture yielded no growth.

Fig 1: Radiograph showing the cardiac apex pointing to the right and the hepatic shadow on the left.



Echocardiography was not done as it is not available in our hospital
Diagnosis of early onset neonatal sepsis with meningitis was made with background Dextrocardia and situs solitus inversus. He was managed on nil per os, antibiotics, anticonvulsants and intravenous fluid; however blood transfusion was not required. Bloody stool stopped on 5th day of admission and he remained stable and was discharged by 10th day. Echocardiography in another centre was not done by the parents as requested and baby was lost to follow up at age of 3 months despite adequate counselling of parents.

Discussion

Dextrocardia with complete situs inversus is rare, usually discovered incidentally in otherwise normal subjects[2]. Mirror-image dextrocardia with situs inversus occurs in 1 in 10, 000 of the general population.[1,2]
Most neonates delivered in the hospitals are not examined especially by paediatricians as is the case of this index baby, to detect such cases in neonatal period. It may be discovered in infancy because of associated anomalies but often remains asymptomatic and discovered by chance in adult life.[4]Many people with this condition are unaware of their unusual anatomy until they seek medical attention for an unrelated condition.[1]This anomaly may not be diagnosed until late life in some cases and it is associated with primary ciliary dyskinesia and splenic malformations.[3]

It has been shown that the incidence of congenital heart malformations is higher in patients with dextrocardia and situs inversus than in patients with normal situs solitus.[2]This is due to the fact that dextrocardia with situs inversus is merely a mirror image of the normal situs solitus,[2] hence any associated cardiac malformations are usually mirror images of similar malformations in people with the normal situs solitus.[2]In isolated dextrocardia, in which the heart is on the right side without inversion of the abdominal viscera, malformations of the heart are almost always invariably present.[2]It has been postulated that even though the factors responsible for situs inversus are not clear[2] autosomal recessive gene, maternal diabetes, cocaine use and conjoined twinning are implicated.[5,6]

A case of dextrocardia with situs inversus occurring early in life has only been reported in a three day old neonate[7]. Some cases of dextrocardia have been reported in Nigerian children and adults which were mostly incidental findings. Ekpe al[7] reported on dextrocardia with situs inversus co existing with neonatal intestinal obstruction in a three day old neonate. A 14 year old child was incidentally found to have dextrocardia with situs inversus when he was evaluated for chronic sinusitis at Enugu.[8]

Danbauchi and Alhassan[9]. in Zaria reported two cases of dextrocardia with situs inversus; a 35-year-old man that presented for the first time with respiratory symptoms but no cardiac symptoms and a 14-year-old who presented with cardiac symptoms.
Dextrocardia with situs inversus have also been reported in cadavers in medical schools during dissection in Nigeria[10] and India.[11] An unusual occurrence of dextrocardia with situs inversus have been reported in two generations of families in India; affecting a father and his two sons following consanguineous marriage.[2]

Conclusion

An incidental finding of dextrocardia with situs inversus in a newborn is reported and the need for clinicians to have high index of suspicion is highlighted due to its asymptomatic nature. Clinicians should look for this anomaly when reporting or viewing chest x-rays. Newborn babies should have a thorough physical examination after delivery before discharge to enable early diagnosis of congenital anomalies for appropriate referral.

Authors contributions
Garba BI and Aminu MS: Conceptualised the case report.
Onazi SO, Musa A, Adelakun MB and Sule MB : Literature review.
Sule MB Ultrasound.
Garba BI and Aminu MS: Manuscript writing

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References

1. Tabry IF, Calabrese J, Zammar H et al. Case report: off-pump total myocardial revascularization for dextrocardia and situs inversus. *Heart Surg Forum 2001; 4: 251–3.*
2. Chib P, Grover DN, Shahi BN. Unusual occurrence of dextrocardia with situs inversus in succeeding generations of a family. *J Med Genetics 1977;14:30-2.*
3. Nawaz A, Matta H, Hamchou M, Jacobez A, Trad O, Al Salem AH. Situsinversusabdominus in association with congenital duodenal obstruction: a report of two cases and review of literature. *Pediatr SurgInt 2005; 21: 589–92.*
4. Uchenna DI, Jesuorobo DE, Anyalechi JI. Dextrocardia with situsinversustotalis in an adult Nigerian: a case report. *Am J Med Med-Sci 2012;2(3):59-61.*
5. Agirbashi M, Hamid R, Jennings HS, Tiller GE. Situs inversus and hypertrophic cardiomyopathy in identical twins. *Am J Genetics 2000;91:327-30.*
6. Distefano G, Romeo MG, Grasso S, Mazonne D, Sciacca P, Mollica F. Dextrocardia with and without situsviscerum in 2 siblings. *Am J Med 1987;27:929-34.*
7. Ekpe EE, Uwah U, Nyong EE. Dextrocardia with situs inversus co existing with neonatal intestinal obstruction. *Port Harcourt Med J 2008;2(2):177-80.*
8. Maduebuchi CJ, Amuche UF, Uzodinma EC. Situsinversustotalis in a child with chronic sinusitis. *Open J Paed 2013;3:236-8.*
9. Danbauchi SS, Alhassan MA. Case report: dextrocardia with situs inversus; two cases presenting differently. *Niger Postgrad Med J 2002; 9: 248–52.*
10. Ofusori DA, Okwuonu CU, Ude RA, Adesanya OA. Dextrocardia and situsinversustotalis in a Nigerian cadaver: a case report of a rare anomaly. *Int J Morphol 2009;27 (3):837-40.*
11. Dabbiru R,NarreddySR, KuppiliVMM. Dextrocardia with situs inversus- a case report. *Int Jour Anat Variat 2011;4:88-9.*