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Tuberculosis Infection in HIV-Positive Children Attending TB/HIV Clinic at Central Hospital Agbor, Delta State, Nigeria

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Abstract:
Tuberculosis infection in children has been a major setback to achieving the fourth Millennium Development Goal (MDG) of reducing child mortality rate by two-thirds by the year 2015. Children are the hope and future of any nation. Therefore, a cross-sectional study was conducted between January and April 2014 to survey tuberculosis infection in HIV positive children below five years of age attending TB/HIV Clinic at Central Hospital Agbor, Delta State, Nigeria. A total of eight three (83) children reregistered at TB/HIV clinic of the Hospital were randomly selected and screened for tuberculosis disease using structure and validated questionnaire containing both socio-demographic profile and disease symptoms. Information on sputum smear, chest X-ray and routine CD4 counts results were obtained from their case files. Of the eighty-three (83) children investigated, forty-five (45) had TB; a prevalence rate of 54.2 %. The analysis also revealed that majority of the children with TB/HIV infection were children whose mothers were HIV positive. Majority of the care-givers were mothers; (75.9 %) who were classified into class VI of the social economic class. Majority of the HIV positive children had CD4 count of 200-499 cells/µl. About 77.1% children were immunized with BCG vaccine and 15.9 % of the children had vaccine induced TB because their immune system was compromised. Only four (4) HIV infected children had extra pulmonary TB and the commonest symptoms presented by TB infected children were cough and weight loss. This study further confirmed the high prevalence rate of tuberculosis infection among HIV infected children. There is, therefore, the need to intensify awareness on prevention of mother to child transmission of HIV/AIDS infection (PMTCT) and to implement an early and active case finding for tuberculosis infection especially in children who are exposed.

Keywords: *Antiretroviral drugs, tuberculosis, cross-infection, children*

1. Introduction

Over the years, considerable improvement has been made towards eradicating human immunodeficiency virus (HIV) among children. However, the global burden of pediatrics HIV and acquired immune deficiency syndrome (AIDS) remains a challenge for healthcares workers around the world, especially in developing countries (Bamford and Lyall, 2015). This scenario is further aggravated by co-infections with tuberculosis (TB) especially in Sub-Saharan Africa.Presently, over a millions of children are infected with tuberculosis (TB) and 630,000 by HIV annually (Okechukwu and Okechukwu, 2011). In 2006, the death rate recorded annually from TB infection alone was over 250,000, while more than 56,000 deaths were projected to results from HIV infection globally (Raminez-Cardich et al., 2006; Selekman, 2006). TB/HIV co-infection has been a major setback to both TB and HIV infection control programmes. In the year 2000, of the approximately 8.3 million new TB cases diagnosed worldwide, it was estimated that 884,019 (11%) occurred among children especially in endemic areas (Nelson and Wells, 2004).

Due to the alarming rate of deaths occurring in children co-infected with HIV and TB, WHO, in 2013, established a strategy aimed at preventing mother-child-transmission (PMTCT) of HIV/AIDS. The objectives of PMTCT are to: reduce MTCT by 50% by 2010, reduce the prevalence of risky behavior that promotes MTCT, increase demand and uptake for HCT among women of reproductive age by 10%, prevent unintended pregnancy among HIV-positive women by 50%, improve access to safe delivery practices and to provide ART for HIV positive mothers and their children, and increase support for HIV-positive mothers to practice the infant feeding options of their choice (WHO, 2013). Reducing HIV/AIDS infection in children will drastically reduce the incidence of TB. This is because; TB Partners initiated an interim policy on collaborative TB/HIV activities captioned 'Fight Aids, Fight TB, Fight Now' (WHO, 2013) This policy, urged national governments and stake holders in health to build collaborative efforts aimed at reducing the morbidity and mortality from TB/HIV co-infection. Nigeria's Federal Ministry of Health (FMH) has adopted both policies and laid down a plan of action with guidelines for implementation (FMHN, 2011). The strategies for reducing the burden TB in People living with HIV (PLWH) in Nigeria include: establishing intensified TB case-finding, ensuring TB infection control in health care and congregate settings, providing isoniazid preventive therapy for latent TB infection in People living with HIV and AIDS (PLWHA) after excluding active TB (FMHN, 2011). The strategies for PMTCT in Nigeria include: VCT for HIV in antenatal and labour ward

settings, infant feeding counseling and support (FMHN, 2011). Though, these strategies have been implemented, not much have been achieved due to low access to ARV and DOTS therapy, high level of social stigma and discrimination and poverty.
In this study, the prevalence of Tuberculosis infection among HIV positive children under five years old attending TB/HIV clinic at Central Hospital Agbor, Delta state, Nigeria, was investigated. This is to provide basic support, national health information for further research and public health action.

2. Materials and Methods

2.1. Study Center

Central Hospital Agbor, Delta State, Nigeria, is the oldest and the largest paediatric hospital in the town attends to an average of 350 out-patients daily. In the in-patient section, there are 125 beds spread between 7 wards and emergency room. Apart from paediatric care, the hospital also offers the following services: Dental services, Ophthalmological services and HIV/AIDS Therapy among others.
The Hospital had received and still receives tremendous support from the state government in collaboration with Family Health International (FHI) and currently Global HIV/AIDS Initiative Nigeria (GHAIN) in setting up the machinery for prevention and treatment of HIV/AIDS in the areas of counseling and testing as well as providing anti-retroviral therapy for infected children and their parents.
The Hospital offers free medical services to all its patients in accordance with the state government policy. No fee is being taken for patients' card, consultation and even drugs. It also includes free accommodation and feeding.
The inclusion criteria for this study were the following:

- All HIV positive children registered at HIV/TB clinic of Central Hospital Agbor, Delta Sate.
- All children under five years receiving care for TB and HIV
- Children who are under DOTS treatment.

2.2. Study Population

The study population consisted of all children under five years old receiving care for TB and HIV at Central Hospital Agbor, Delta State during the study period. Most of the children were from HIV positive mothers who were also on treatment and those children whose status needed to be ascertained.

2.3. Methods of Data Collection

Questionnaires designed for the study were used for data collection. Information on socio demographic characteristics and key information on TB and HIV status were included in the form. Results of laboratory, radiological, and physical anthropometric measurement were retrieved from patients' file and recorded.

2.4. Ethical Considerations

The study protocol was, submitted to the Ethical Committee of the Delta State Hospital Management Board for permission and the protocol was approved. The mothers and/or caregivers of HIV/TB infected children were informed of the objectives of the study and they underwent an initial group counseling, during which informed consent procedure was introduced. During individual pre-assessment which followed group counseling, all subjects were guided through a detailed consent, which all signed.

3. Results

3.1. Marital Status of the Mothers / Care-givers

The analysis of marital status of the mothers / care-givers (Table 1) showed that 4 of the respondents were single, 66.3% were married, l2.0% were divorced/separated and 16.9% were widow or widower.

Marital Status	Frequency	Percentage (%)	Cumulative
Single	4	4.8	4.8
Married	55	66.3	71.1
Divorced/separated	10	12.0	83.1
Widow	14	16.9	100.0
Total	**83**	**100.0**	

Table 1: Distribution of Respondents by Marital Status (Mothers / Care-givers)

3.2. Educational Background of Care-givers / Mothers

From the analysis (Table 2), 7.3% of respondents had no educational training, 22 attended primary school, 12.2% attended junior secondary school, and 35 attended senior secondary school while 23.2% attended post-secondary school. Therefore, 4 1.5% of the respondents were illiterate while 58.5% were literate.

Educational Background	Frequency	Percentage (%)	Cumulative
None	6	7.3	7.3
Primary school	18	22.0	29.3
Secondary uncompleted	10	12.2	41.5
Secondary completed	30	35.4	76.8
Post-secondary	19	23.2	100.0
Total	**83**	**100.0**	

Table 2: Distribution of Respondents by Educational Background

3.3. Socio-Economic Status of Caregivers/Mothers

From the analysis in Table 3, 4.8% of the respondents were in social class 1, 18.1 % were in social class 11, 14.5% were in social class 111, 9.6% were in social class IV, 8.4% were in social class V while 44.6% were in social class VI. Therefore, 22.9% were in high social class while 77.1% were in low social class.

Social Class	Frequency	Percentage (%)	Cumulative
Socio-class I	4	4.8	100
Socio-class II	15	18.1	55.4
Socio-class III	12	14.5	47.0
Socio-class IV	8	9.6	37.3
Socio-class V	7	8.4	22.9
Sacio-class VI	33	44.6	4.8

Table 3: Distribution of Respondents by Socio-Economic Status

3.4. Care Givers and their Relationship to the Children

From the analysis, 75.9 % of the care givers were mothers, 13.3 % were fathers, 2.4 % were sisters, while 8.4% were others (Table 4).

Care -givers	Frequency	Percentage (%)	Cumulative
Mothers	63	75.9	75.9
Fathers	11	13:3	89.2
Sisters	2	2.4	91.6
Others	7	8.4	100.0
TOTAL	**83**	**100.0**	

Table 4: Distribution of the Care Givers by Relationship to Study Children

3.5. Ages of the Care-givers / Mothers

4.9% of the respondents were within the ages of 15-24, 30.5% were within the ages of 25-34, 45.1% were within the ages of 35-44 and 19.5% were within the ages of 45 years and above (Table 5).

Ages	Frequency	Percentage (%)	Cumulative
15-24	4	4.9	4.9
25-34	25	30.5	35.4
35-44	38	45.1	80.5
45 and above	16	19.5	100.0
TOTAL	83	100.0	

Table 5: Distribution of Care-givers By Age

3.6. Age Distribution of the Children

The analysis shows that, 6.0 % of the children were within the ages of 1-4 months, 10.8% were within 5-8 months, 10.8% were within 9-11 months and 72.3% were within 1-5 years of age (Table 6)

Children's Age	Frequency	Percentage (%)	Cumulative
1-4 months	5	6.0	6.0
5-8 months	9	10.8	16.8
9-11 months	9	10.8	27.7
1-5 years	60	72.3	100.0
TOTAL	**83**	**100.0**	

Table 6: Children's Distribution by Age

3.7. TB Status of Caregivers/Mothers

From the analysis of distribution of TB among caregivers / mothers, 44.6% of the caregivers/Mothers had TB while 55.4% do not have TB (Table 7).

Mothers' TB Status	Frequency	Percentage (%)	Cumulative
Positive	37	44.6	44.6
Negative	46	55.4	100.0
TOTAL	**83**	**100.0**	

Table 7: Distribution of Caregivers/Mothers Tb Status

3.8. HIV Status of Caregivers/Mothers

The HIV status of the caregivers/mothers results showed that 94.0% of Caregivers/Mothers are HIV positive while 6.0% of mothers are HIV negative (Table 8).

Mothers' HIV Status	Frequency	Percentage (%)	Cumulative
Positive	78	94.0	94.0
Negative	5	6.0	100.0
TOTAL	**83**	**100.0**	

Table 8: Distribution of Caregivers/Mothers HIV Status

3.9. Distribution of the Children by TB Status

It was confirmed that all the children were HIV positive, with 54.2% of the children having both HIV and TB, and 45.8% without TB (Table 9).

Children's HIV Status	Frequency	Percentage (%)	Cumulative
Positive	45	54.2	54.2
Negative	38	45.8	100.0

Table 9: Distribution of the Children by TB Status

3.10. Caregivers / Mothers still Alive and Contact Tracing

From the analysis, 83.1% of the children still had living mothers, while 16.9% of the mothers were late. Also 79.5% of the children had contact tracing, while 20.5% had no contact tracing. The analysis of the contacts tracing showed that 69.7% of the children contracted the infection from their mothers, 27.3% from their fathers, and 3% through other relations (Table 10).

Contacts	Frequency	Percentage (%)	Cumulative
Mother	46	69.7	69.7
Father	18	27.3	97.0
Other relations	2	3.0	100.0

Table 10: Distribution of Children by Contacts

3.11. Immunization Status and Co-Infection besides HIV and TB infection

From the analysis, 77.1% of the children had BCG vaccine while 22.9% do not have BCG vaccine. Further analysis of the age at which BCG vaccine was given to the children showed that 82.4% of the children had BCG vaccine at birth, 4.8% had it at 6 months of age, while 12.8% had it at one year and above. The result of analysis of Co-infection besides HIV and TB infection in the children showed that in 22.9% there was a co-infection apart from HIV and TB. While in 77.1 % there was no co-infection. The co-infections included broncho-pneumonia (27.7%), diarrhea (11.1%), hepatitis (5.6%), otitis media (5.6%), skin rashes (5.6%) and malaria (44.4%) in the children (Table 11)

Co-Infection	Frequency	Percentage (%)	Cumulative
Broncho-Pneumonia	5	27.7	27.7
Diarrhoea	2	11.1	38.8
Hepatitis	1	5.6	44.4
Otitis media	1	5.6	50
Skin rashes	1	5.6	55.6
Malaria	9	44.3	100.0

Table 11: Distribution of Respondents by Co-Infection

3.12. Route the Children Contracted TB

From the analysis, 15.9 % of the children contracted TB through vaccine administration, while 84.1% were through community acquired (Table 12).

Route of Tb Contraction	Frequency	Percentage %	Cumulative
Vaccine induced	8	15.9	15.9
Community acquired	37	84.1	100.0
TOTAL	**83**	**100.0**	

Table 12: Distribution of How Children Contracted Tb

3.13. Symptoms Presented by TB Patients

From the analysis, 11.1% had chronic cough, weight loss and prolonged fever, 51.1°/p presented with chronic cough, and weight loss only, 22.2% had chronic cough and fever while in 15.6%, there was no major symptoms (Table 13).

Symptoms	Frequency	Percentage (%)	Cumulative
Chronic cough, weight loss and fever	5	11.1	11.1
Chronic cough and weight loss alone	23	51.1	62.2
Cough and fever alone	10	22.2	84.4
No major symptoms	7	15.6	100.0
TOTAL	**83**	**100.0**	

Table 13: Distribution of Respondents by Disease Symptoms

3.14. CD4 Count Result

From the analysis, 21.6% of the children had CD4 count of less than 200, 72.4% had CD4 of 200-499, and 6.0% had CD4 of 500 and above (Table 14).

Cd4 Count	Frequency	Percentage (%)	Cumulative
Less than 200	18	21.6	21.6
200-499	60	72.4	94.0
Greater than 500	5	6.0	100.0
TOTAL	**83**	**100.0**	

Table 14: Distribution of Children by CD Count

3.15. Method of TB Diagnosis

From the analysis, 28.9% did chest X-ray test, 26.7% had sputum smear examination, and 44.4% did both sputum smear examination and chest X-ray (Table 15).

Method	Frequency	Percentage (%)	Cumulative
Chest X-ray	13	28.9	28.9
Sputum smear exam	12	26.7	55.6
Both method	20	44.4	100.0
TOTAL	**45**	**100.0**	

Table 15: Distribution of the Respondents by Tb Diagnosis

3.16. Type of TB Disease (Pulmonary/Extra-Pulmonary)

From the analysis, 95.6% of the cases were pulmonary TB, while 4.4% were extra-pulmonary TB (Table 16).

Tb by Site	Frequency	Percentage (%)	Cumulative
Pulmonary	43	95.6	95.5
Extra-pulmonary	2	4.4	100.0
TOTAL	**45**	**100.0**	

Table 16: Distribution of Respondents by Disease Type

3.17. Pulmonary Sputum Smear

From the analysis, 58.1% were sputum smear positive white 41.9% were sputum smear negative (Table 17).

Sputum Smear	Frequency	Percentage (%)	Cumulative
Positive	25	58.1	58.1
Negative	18	41.9	100.0

Table 17: Distribution of Respondents by Pulmonary Sputum Smear

3.18. Symptoms among Sputum Smear Positive

From the analysis, 80.0% had chronic cough, weight loss, and prolonged fever, 12.0% had chronic cough and weight loss alone, 8.0% had chronic cough, and prolonged fever alone, while none had no major symptom (Table 18)

Symptoms	Frequency	Percentage (%)	Cumulative
Chronic Cough, weight loss & fever	20	80.0	80.0
Chronic cough, weight loss alone	3	12.0	92.0
Chronic cough and fever alone	2	8.0	100.0
TOTAL	**25**	**100.0**	

Table 18: Distribution of Respondents by Symptoms among Sputum Smear Positive

3.19. Chest X-Ray Result

From the analysis, 48.2% had a positive chest X-ray result, while 5l.8% had a negative chest X-ray result (Table 19).

Chest X-Rays	Frequency	Percentage (%)	Cumulative
Positive	40	48.2	48.2
Negative	43	51.2	100.0

Table 19: Distribution of Respondents by Chest X-Ray

3.20. Symptoms among Chest X-Ray Positive Patients

From the analysis, 32.5% had chronic cough, weight loss, and prolonged fever, 50.0% had chronic cough, and prolonged fever alone, 10.0% had chronic cough, and fever alone, while in 7.5%, there was no major symptom (Table 20)

Symptoms	Frequency	Percentage (%)	Cumulative
Chronic Cough, weight loss & fever	13	32.5	32.5
Chronic cough, weight loss alone	20	50.0	82.5
Chronic cough and fever alone	4	10.0	92.5
No major symptoms	3	7.5	100.0

Table 20: Distribution of Respondents by Symptoms in Positive Chest X-Ray

3.21. Categories of TB Treatment among TB/HIV Positive Children

The analysis of categories of TB treatment among TB/HIV Positive Children revealed55.6% were in category I, 26.7% were in category II, and 17.8% were in category III (Table 21).

Categories of Tb Treatment	Frequency	Percentage (%)	Cumulative
I	25	55.6	55.6
II	12	26.7	82.2
III	8	17.8	100.0
TOTAL	**45**	**100.0**	

Table 21: Distribution of Categories of TB treatment among TB/HIV Positive Children

4. Discussion

This descriptive and cross-sectional study investigated the prevalence and pattern of tuberculosis infection among HIV positive children receiving care at TB/HIV clinic of Central Hospital Agbor Delta state during a period of 15 weeks. Mothers' health status as regards to their TB and HIV status was used as a yard stick to diagnose HIV and/or TB in children below 5 years, with no major symptom and sputum smear negative results. Responses to questions on signs and symptoms of TB among the care givers were used as an adjunct to sputum smear and chest X-ray.

The prevalence of TB in HIV infected children in this study was relatively high (54.2%). This is an indication of the strong association between TB and HIV infection in this environment. This finding is consistent with most studies done in Nigeria and other African countries (Luo et al., 1994; Madhi et al., 2001; Fairlie et al., 2011, Moyo et al., 2011). With this rate, it means that the TB incidence is grossly under reported because many sick children are not brought to health facilities, there is limited diagnostic capacity. Again, more than 95% of children with active TB have negative sputum smear which further supported under diagnosis. The symptoms of the disease recorded (cough and weight loss - 51.1%) in this study were the major and frequent symptoms seen among TB children were.

In terms of age distribution of these children, the largest number is within 1-5 years having up to 72.3%. This was consistent with earlier studies (Hesselling et al., 2007; Elliot et al., 2009; Madhi et al., 2000; Fairlie et al., 2011) that almost all childhood TB/HIV infections are acquired in-utero, intrapartum and early post-partum periods. But because of the long latency periods of the two infections, they develop later in life. This finding could also be attributed to their undeveloped immune response. Absence of HIV DNA polymerase chain reaction and presence of HIV maternal antibodies make diagnosis difficult in children under the age of 15-18 months. Findings from the socio-economic and educational status revealed that 77.l% of the caregivers were in low socio-class, while

58.5% were literate. This is consistent with the studies with previous reports that mortality and high prevalence rate was found among the educated and low socio-economic class (De Cock et al 2004; Rosen et al., 2004; Grassly et al., 2013; Corbett et al., 2013).
In terms of disease presentation, extra pulmonary TB was not frequent as reported in other studies (Luo et al., 1994; De Cock et al 2004; Odhiambo et al, 2006; Corbett et al., 2013). The proportion of extra pulmonary cases was 4.4%. In this study, there was a notable significant difference in the proportion of extra pulmonary disease among the co-infected patients. In immunocompromised patients, the proportion can increase to 50%. This is not consistent with studies done in Kenya (Odhiambo et al, 2006). Also, this study showed that 75.9% of the children's' care givers were their mothers and l3.3 % were their fathers. But in the United States and other Western world, these children are kept in Foster Care System which may be due to neglect, physical abuse; sexual abuse etc. Foster Care agencies periodically review their conditions with their Physicians. Another interesting finding is that 15.9 % of the HIV infected children contracted TB infection through BCG immunization. This agrees with the study that suggested that BCG immunization should not be recommended for children with HIV/AIDS for the risk of developing vaccine-induced TB (Mukadi et al., 2010)
HIV and TB are both public health burden. Their interrelation is well established and HIV infection aggravates tuberculosis, particularly in Sub-Saharan Africa. The HIV epidemic has increased tuberculosis incidence and deaths. It was reported globally that 9% of all new TB cases were attributable to HIV infection in 2010 (Mukadi, 2010). Other studies have shown that approximately two-thirds of new smear positive cases were directly attributable to HIV infection. National surveillance is important to indicate the magnitude and burden of both diseases. The sentinel data in many countries comprise HIV and TB co-infection rates in addition to HIV prevalence figures from antenatal care and blood donors. To control the problem, the WHO recommends the establishment of a coordinated strategy for both diseases. If not, millennium development goals may not be achieved.
The study indicates a need to further intensify HIV prevention and awareness rising within the TB control programme in developing countries. Health Counseling and HIV testing and raising awareness on the prevention of mother to child transmission of HIV/AIDS (PMTCT) will go a long way in reducing HIV infection which is the bedrock in increasing TB infection. The co-infection results in increasing need for hospitalization and extra costs for the care of infected children. The national programmes will not achieve the target set for reducing TB infection if the current situation of co-infection is not addressed.

4.1. Conclusion

This study has shown that there is relatively high prevalence rate of tuberculosis infection in HIV positive children less than five years attending TB/HIV Clinic at Central Hospital Agbor. The prevalence and pattern of presentation of TB disease among HIV infected children differ from that of adult because sputum smear result was negative in most cases and extra pulmonary TB was not frequent. This co-infection has resulted in an increasing need for hospitalization and extra costs for the care of infected children. The National programmes put forward by WHO will not achieve the target set for reducing TB infection if the current situation of co-infection is not addressed.

4.2. Recommendation

It is recommended that full TB and HIV screening test on children whose mothers are HIV and/or TB positive using multiple case detection methods such as chest x-ray, sputum smear microscopy, and HIV serological tests. The campaign on prevention of mother-to-child-transmission of HIV should be intensified by governments, stakeholders, and health workers in both urban and rural areas alike. Parents and caregivers should continuously be enlightened on the transmission and dissemination routes of TB as well as the possible ways by which children can get infected.

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