ORIGINAL ARTICLE

EPIDEMIOLOGY AND OUTCOME OF CHILDREN LIVING WITH HIV IN A TERTIARY HOSPITAL: A 6-YEAR RETROSPECTIVE STUDY

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The authors declare that the data presented are original material and has not been previously published, accepted or considered for publication elsewhere; that the manuscript has been approved by all authors, and all authors have met the requirements for authorship.

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ABSTRACT

Introduction: Infection with HIV is multi-faceted and involves the interplay of medical, social, and economic factors thus, management of the disease continues to be a challenge to most physicians. The Philippines is experiencing a surge in cases since 2013. Understanding the local epidemiology of pediatric HIV may reveal opportunities to reduce or eliminate transmission through timely diagnosis.

Objective: This study was conducted to identify the features and outcome of children living with HIV in a hospital where a program for HIV treatment and monitoring was implemented.

Methodology: Medical records of all children <18 years of age diagnosed as pediatric HIV based on the World Health Organization case definition and enrolled in the STD/AIDS Guidance Intervention Prevention (SAGIP) Unit were reviewed. Data was analysed using descriptive statistics.

Results: Thirty pediatric HIV patients were included in the study. The most common mode of acquisition is by sexual transmission (57%) and most patients were male (76%), bisexual (47%), and heterosexual (47%). Weight loss (50%), rash (50%), fever (37%) and cough (37%) were the most common clinical findings. The most common opportunistic infections were tuberculosis (47%) and oral candidiasis (34%). Only 27 of 30 patients were started on antiretroviral therapy within 6 months from diagnosis. One patient showed resistance to a non-nucleoside reverse transcriptase inhibitor (NNRTI). There were 11 children who died of various opportunistic infections and its complications, while 2 were transferred to a different treatment hub after 6 months, and 1 lost to follow-up.

Conclusion: Sexual means of HIV transmission among adolescents is evident in this study. Weight loss, cough, rash, fever, and lymphadenopathy are common presenting features. Tuberculosis and oral candidiasis are the most common opportunistic infections and should alert physicians on possible HIV infection. A mortality rate of 37% was noted mostly in the first 6 months of initiating ART treatment.

KEYWORDS: *Pediatric HIV, Outcome, Profiles*

INTRODUCTION

The scale-up efforts on the program on prevention of maternal to child transmission (PMTCT) has contributed to the global decrease in pediatric HIV, with 2 million new infections averted since the year 2000. Although prevention of pediatric HIV has shown some success, based on the 2017 UNAIDS report where a steep decline in pediatric AIDS-related illness to about half from 2010 to 2016 (210,000 vs 120,000 cases) was seen, the same report showed a lag in pediatric HIV testing and treatment[1]. Global HIV trends have been decreasing, but the Philippines is experiencing an exponential increase of about 138% in cases since 2013[2]. Increase in pediatric HIV can be attributed to the following: increasing HIV infection in females of reproductive age leading to vertical transmission, lack of accessible testing facilities for infants <18 months thereby causing a delay in treatment, and earlier age of sexual debut in adolescent patients[1].

Clinical manifestations of pediatric HIV are varied and often non-specific[3]. A local study by Aro et.al. showed that 48% of children living with HIV (CLHIV) were 0-6 years old and majority were infected through vertical transmission (73%). The most common presenting signs and symptoms were cough, skin lesions and weight loss[4].

Understanding the local epidemiology of pediatric HIV and knowledge on the natural progression of the disease may reveal opportunities to reduce and eliminate transmission[3]. Identification of children infected with HIV will allow for timely and appropriate treatment and significantly improve quality of life. Knowledge of the epidemiologic and clinical profile may help clinicians meet the diagnostic and management challenges presented by CLHIV. There is paucity of data on the clinical profile and outcome of CLHIV in the Philippines and as HIV cases are increasing, data on CLHIV need to be updated. This study aimed to look into the epidemiology and outcome of children living with HIV in a hospital where an improved HIV diagnosis, treatment and monitoring program was implemented in the STD/AIDS Guidance Intervention Prevention (SAGIP) Unit of the University of the Philippines-Philippine General Hospital (UP-PGH).

METHODOLOGY

Ethics: Data was collected after approval of the study from the institutional Ethics Review Board.

Study Design and Population: A retrospective chart review of all pediatric cases <18 years of age at the time of HIV diagnosis and reported in the UP-PGH SAGIP Unit from January 1, 2012 to December 31, 2017 was done. HIV/AIDS diagnosis is based on the World Health Organization (WHO) case-definition of pediatric HIV/AIDS[5]. The SAGIP Unit is the hospital's facility which caters to STD/HIV/AIDS patients from all areas and facilitates inter-hospital and inter-departmental referrals.

Exclusion Criteria: Patients more than 18 years of age at the time of HIV diagnosis and those enrolled in the prevention of mother-to-child transmission (PMTCT) program who are born to HIV-positive mothers but with negative HIV-DNA PCR were excluded from the study.

Data Collection: Demographic and clinical data were obtained and recorded in a case report form. Data collected were age, sex, sexuality, residence, educational attainment and presenting signs and symptoms. Information on the child's HIV status, and marital status and respective professions of parents were noted. Maternal and birth history, mode of infant feeding, previous hospitalizations and relevant social history were collected. Pertinent laboratory tests (i.e., CD4, viral load, complete blood count, liver function tests) at the time of diagnosis and on follow-up were obtained. Information on Anti-Retroviral Therapy (ART) regimen including date started and duration of use, and occurrence of adverse events and its management were also obtained. Concomitant use of medications such as Cotrimoxazole and Isoniazid were noted. Clinical course and outcome of individual patients up to 6 months post-diagnosis were described.

Case Definition: HIV infection in patients >18 months to 18 years of age is defined as a positive

HIV antibody test confirmed by a second HIV antibody test and/or a positive virological test for HIV or its components confirmed by a second virological test obtained from a separate determination[5]. HIV status of patients <18 months was confirmed by at least one positive DNA-PCR test[5].

Mode of HIV transmission was determined by establishing maternal HIV status, as well as history of blood transfusion, use of injectable drugs and unsafe sexual practices.

Patients were stratified based on the WHO Staging System for pediatric HIV which classified an individual's status from asymptomatic to severely symptomatic.[5]WHO immunological classification for established HIV infection using CD4% based on age was also used to stage individual patients.[5]

Descriptive statistics was used for the following: demographic profile of patients, mode of HIV transmission, clinical presentation and clinical stage of the disease at the time of diagnosis. Quantitative variables were described using mean and standard deviation, while responses to qualitative variables were summarized as frequencies and percentages.

RESULTS

A total of 30 children were included in this study and median age at diagnosis was 16 years (2months being the youngest and 18 years being the oldest).

Sexual means was the most common mode of transmission in 57% of cases, with a mean age at diagnosis of 17.5 years (n=17). Perinatal transmission accounted for the remaining 40% (n=12). The mode of transmission was unknown in a 5-year-old male child who tested positive to 2 rapid HIV antibody tests and 1 HIV-ELISA test. He presented with prolonged fever, weight loss, cough and multiple lymphadenopathies. During his hospital stay, he had progressive respiratory distress with hypoxemia. He eventually died and autopsy revealed the presence of disseminated tuberculosis involving the lungs, pericardium, liver, spleen, pancreas, adrenals and kidneys. HIV testing of both parents and other siblings were negative.

In patients infected through sexual transmission (Table 1) majority were males (76%), mostly heterosexual (47%) or bisexual (47%). Sixty five percent came from urban areas. Their parents were mostly married (70%), high school graduates (47%), with unknown HIV status.

Table 1. Demographic Profile and Mode of Transmission of Children Living with HIV

Demographic Profile	N=30 (%)	Mode of transmission N=30(%)		
		Sexual 17(57%)	Perinatal 12 (40%)	Unknown 1 (3%)
Median Age at diagnosis (Range)	16 (0.17-18)			
Mean Age at diagnosis (range)		17.5 (15-18)	3.45 (0.17 – 7)	
Sex				
Male	21 (70.00)	13 (76%)	7 (58%)	1 (100%)
Female	9 (30.00)	4 (24%)	5 (42%)	-
Sexuality				
Bisexual	8 (26.67)	8 (47%)		
Heterosexual	9 (30.00)	8 (47%)		
Homosexual	1 (3.33)	1 (6%)		
N/A	12 (40.00)	-		
Residence				
Urban	18 (60.00)	11 (65%)	6 (50%)	1 (100%)
Rural	12 (40.00)	6 (35%)	6 (50%)	
Educational attainment (care givers)				
Elementary	2 (6.67)	1 (6%)	1 (8%)	-
Highschool	11 (36.67)	8 (47%)	2 (16%)	1 (100%)
College	3 (10.00)	1 (6%)	2 (16%)	-
N/A	14 (46.67)	7 (41%)	7 (60%)	-
Occupation of parents/guardian				
both unemployed	1 (3.33)	-	1 (8%)	-
1 parent employed	14 (46.67)	6 (35%)	8 (67%)	-
both parents employed	6 (20.00)	2 (12%)	3 (25%)	1 (100%)
N/A	9 (30.00)	9 (53%)	-	-
Marital Status of parents/guardian				
Not married				
Married	1 (3.33)	1 (6%)	-	-
Cohabiting	15 (50.00)	12 (70%)	2 (17%)	1 (100%)
Separated	3 (10.00)	-	3 (25%)	-
Widowed	5 (16.67)	2 (12%)	3 (25%)	-
N/A	5 (16.67)	1 (6%)	4 (33%)	-
	1 (3.33)	1 (6%)	-	-
HIV Status of Father				
Negative	8 (26.67)	5 (30%)	2 (17%)	1 (100%)
Positive	8 (26.67)	-	8 (67%)	-
Unknown	14 (46.67)	12 (70%)	2 (17%)	-
HIV Status of Mother				
Negative	7 (23.33)	6 (35%)	-	1 (100%)
Positive	12 (40.00)	-	11 (92%)	-
Unknown	11 (36.67)	11 (65%)	1 (8%)	-

In those infected through vertical transmission (Table 1), mean age at diagnosis was 3.45 years. Fifty eight percent were males, with an equal number of cases in urban and rural areas. Most patients have at least 1 employed parent (67%). Most parents were initially married (n=9) but 4 got widowed, 3 separated, and 2 remained married. Eleven out of 12 (92%) mothers were HIV positive except for one who was not tested because of non-disclosure of the HIV positive husband due to poor marital relationship. As for the fathers 8 out of 12 were HIV positive (67%), 2 (17%) were negative and 2 (17%) were of unknown status.

The most common presenting features (Table 2) in those infected through vertical transmission were fever (42%), cough (34%), weight loss (50%) and rash (67%). Most common physical findings (Table 2.1) were rashes (42%), weight loss (58%), fever (67%), and presence of abnormal chest findings (67%).

There is no significant difference on the clinical signs and symptoms in those infected through sexual transmission from those infected through vertical transmission, however, CNS symptoms and signs (18% and 29%) were more common in those who got infected sexually, and so is the presence of anal warts (12%), as seen in Table 2.

Table 2. Clinical Symptoms of Children Living with HIV (N=30)

Clinical Presentation	Vertical Transmission n(%)	Sexual Transmission n(%)	P-value (<0.05)
Fever	5 (42%)	6 (35%)	0.9302
Rashes	8 (67%)	7 (41%)	0.3292
Weight loss	6 (50%)	9 (53%)	0.8759
Cough/Chest findings	4 (34%)	7 (41%)	0.9679
Abdominal distention/ Organomegaly	2 (17%)	2 (17%)	1.000
Lymphadenopathy	5 (42%)	5 (29%)	0.7740
Jaundice	-	1 (6%)	1.000
Seizures/ CNS	-	3 (18%)	0.2436
Oral lesions	3 (25%)	2 (12%)	0.1626
Anal Warts	-	2 (12%)	0.1626

Table 2.1. Physical Examination Findings of Children Living with HIV (N=30)

Clinical Presentation	Vertical Transmission n(%)	Sexual Transmission n(%)	P-value (<0.05)
Fever	8 (67%)	8 (47%)	0.5050
Rashes	5 (42%)	9 (47%)	0.8250
Weight loss	7 (58%)	12 (70%)	0.7740
Cough/Chest findings	8 (67%)	9 (53%)	0.7216
Hepatomegaly	0	3 (18%)	0.3587
Lymphadenopathy	1 (8%)	2 (12%)	1.000
Seizures	0	5 (29%)	0.0588
Easy fatigability	0	5 (29%)	0.0588
Diarrhea	4 (33%)	5 (29%)	0.8221
Ear discharge	2 (17%)	1(6%)	1.000
Oral lesions	2 (17%)	0	0.1626
Vomiting	2 (17%)	0	0.1626
Abdominal distention	2 (17%)	0	0.1626

Nutritional status (Table 3) upon initial chart review were unknown in almost 30% of patients. In those with available data and where weight was obtained, 10 (34%) showed a normal weight for age, 7 (23%) were severely underweight and 4 (13%) were underweight. Height for age measurements in those with available data revealed that 13 (43%) had normal height for age, 7 (23%) were severely stunted, 2 (7%) were stunted and 8 (27%) were unknown due to lack of data.

Table 3. Nutritional Status of Children Living with HIV (N=30)

	N=30	%
Weight for Age		
Normal	10	34%
Underweight (Z score below -2)	4	13%
Severely Underweight (Z score below -3)	7	23%
Unknown	9	30
Height for Age		
Normal	13	43%
Stunted (Z score below -2)	2	7%
Severely Stunted (Z score below -3)	7	23%
Unknown	8	27%

Baseline laboratory tests were done in majority of patients prior to initiation of ARTs, however, follow-up diagnostics after initiation of ART was lacking (Table 4). The median CD4 count in patients infected through vertical transmission was 523.3 cells/mm3 and in those infected through sexual means, 161 cells/mm3 (Table 4).

Table 4. Laboratory Results before and after ART Treatment in CLHIV

	Sexual Transmission		Vertical Transmission	
Laboratory Tests	**Laboratory Results at the time of Diagnosis Median (n)**	**Laboratory Results after initiation of ART treatment Median (n)**	**Laboratory Results at the time of Diagnosis Median (n)**	**Laboratory Results after initiation of ART treatment Median (n)**
Viral Load	14, 512 (2)	12 (2)	2,542,229 (2)	39.4 (2)
CD4	161	264 (9)	523.3 (10)	1,149 (6)

Hem	120.9	133 (7)	104.1 (9)	97.8 (6)
Hema	0.36	0.39 (7)	0.31 (9)	0.29 (6)
WBC	7.0 (16)	7.77 (7)	9.8 (9)	5.42 (6)
Neutr	0.66	0.58 (7)	0.49 (9)	0.46 (5)
Lymp	0.21	0.32 (7)	0.38 (9)	0.43 (5)
Mono	0.11	0.084 (5)	0.06 (9)	0.086 (5)
Eosin	0.04	0.047 (4)	0.05 (9)	0.016 (5)
Platel	333	263 (6)	326 (9)	291.6 (5)
AST	45.18	42.19 (4)	59 (8)	34 (4)
ALT	34.99	39.26 (4)	56 .68 (8)	19.2 (4)
BUN	2.85 (8)	3.15 (2)	4.06 (5)	2.64 (3)
Crea	55.69	76.95 (6)	44.9 (6)	41.67 (3)
Total Chole	5.30 (8)	6.99 (3)	-	-
Trigly cerid	2.52 (7)	5.83 (3)	-	-
HBsAg n(%)	Non-reactive 13 (76.5) Reactiv	N/A	Non-reactive 6 (50) Reactive (0)	N/A
RPR n(%)	Non-reactive 11 (65)	N/A	Non-reactive (0) Reactive	N/A

Screening tests for other STIs in those infected sexually showed that only 1 in 17 (6%) was reactive to HBsAg and 3 (17.5%) were reactive to RPR. The laboratory findings before and after initiation of ART cannot be compared due to incomplete data.

Majority of patients infected by vertical transmission were at WHO clinical Stage I and II at the time of diagnosis (Table 5). In contrast, majority of those infected by sexual transmission were at WHO clinical Stage IV (53%). Using the CDC Surveillance staging which is based on initial CD4 count, most patients were at Stage 3 for both groups at the time of diagnosis, 77.78% and 67% respectively.

Follow-up staging after initiation of ART treatment showed that majority were at WHO Stage 1 (45%) and CDC Stage 1 (50%) in those infected through vertical transmission; the other group were mostly on WHO Stage IV (47%) and CDC Stage 3 (56%).

Table 5. Clinical and Immunological Staging of CLHIV before and after initiation of ART

	Sexual Transmission n=17		**Vertical Transmission n=12**	
CDC HIV Surveillance staging (based on CD4 count)	**At time of Diagnosis n (%)**	**After Treatment n (%)**	**At time of Diagnosis n (%)**	**After Treatment n (%)**
1	2 (16.5)	3 (33%)	1 (11.11)	3 (50.00)
2	2 (16.5)	1 (11%)	1 (11.11)	2 (33.33)
3	8 (67)	5 (56%)	7 (77.78)	1 (16.67)
Total	12	9	9	6
WHO Clinical and Immunologic staging	**At time of Diagnosis n (%)**	**After Treatment n (%)**	**At time of Diagnosis n (%)**	**After Treatment n (%)**
I	6 (35%)	6 (35%)	4 (33.33)	5 (45.46)
II	2 (12%)	3 (18%)	4 (33.33)	-
III	0	0	1 (8.33)	3 (27.27)
IV	9 (53%)	8 (47%)	3 (25.00)	3 (27.27)
Total	17	17	12	11*

**1 patient was lost to follow-up hence no clinical staging done*

A total of 42 opportunistic infections were recorded at the time of HIV diagnosis. The most common opportunistic infections as seen in Table 6 were were tuberculosis (35%), oral candidiasis (26%), Pneumocystis jiroveci pneumonia (14%), Toxoplasmosis (10%), and Cytomegalovirus infection (5%).

Table 6. Opportunistic Infections Present at the Time of Diagnosis

	Sexual Transmission N=22	**Vertical transmission** N= 20 (%)	**Total N=42 (%)**
Tuberculosis	9 (53%)	6 (50%)	15
Candidiasis	5 (29%)	6 (50%)	11
PCP pneumonia	3 (18%)	3 (25%)	6 (14%)
Toxoplasmo	3 (18%)	1 (8%)	4 (10%)
Others	2 (12%)	2 (17%)	4 (10%)
CMV	0	2 (17%)	2 (5%)

Only 27 of 30 patients (90%) were started on highly active antiretroviral therapy (HAART) as seen in Table 7. Twenty-five patients were started on treatment within 6 months from diagnosis while 2 patients started treatment after 6 months from diagnosis. Three patients who were not started on HAART were diagnosed with disseminated tuberculosis at presentation, hence, anti-tuberculous regimen was given first. These patients eventually died 2-3 days after the diagnosis of HIV infection was made.

Table 7. Highly Active Antiretroviral Treatment Regimens Used in Children Living with HIV (N=30)

HAART Regimens	**N (%)**
Lamivudine, Tenofovir, Efavirenz	14 (47%)
Lamivudine, Abacavir, Efavirenz	5 (17%)
Lamivudine, Zidovudine, Navirapine	3 (10%)
Lamivudine, Zidovudine, Efavirenz	2 (6.5%)
Lamivudine, Abacavir, Nevirapine	2 (6.5%)
Lamivudine, Abacavir, Lopinavir/ritonavir	1 (3%)
HAART not started	3 (10%)

Eighteen children were on Cotrimoxazole chemoprophylaxis for Pneumocystis jiroveci pneumonia (PJP). Seven patients who were >7 years old with CD4 count more than 200 cells were not given cotrimoxazole prophylaxis, while 5 patients were given Cotrimoxazole as treatment for PJP pneumonia. The diagnosis of PJP pneumonia was based on a high index of suspicion coupled with findings of respiratory distress and hypoxemia. One patient developed an adverse drug reaction to cotrimoxazole and prophylaxis was shifted to dapsone.

A total of thirteen patients (43%) were treated for tuberculosis, 7 (54%) were classified as Pulmonary TB and 6 (46%) diagnosed to have Disseminated Tuberculosis (Gastrointestinal, liver, lymph nodes, CNS). Six of 13 (46%) patients were classified as treatment completed, 1 (8%) as relapse after treatment, 3 (23%) with ongoing treatment and 3 (23%) died of complications of TB. One patient with disseminated tuberculosis developed multi-drug resistant TB and had secondary bacterial peritonitis; another patient with TB meningitis died of brain herniation; still another patient with unknown mode of HIV transmission died of probable bacterial pneumonia on top of disseminated tuberculosis.

For clinical course and outcomes during treatment, there were 3 reported adverse events for patients <10 years old and 2 events in those older than 10 years old (Table 8). Two events were attributed to zidovudine which manifested as severe and persistent anemia with a mean hgb of 70mg/dL; 1 related to nevirapine which presented as urticarial rash; 1 related to efavirenz which presented as severe headache and 1 with abacavir which presented as acute pancreatitis with abdominal pain, elevated serum lipase and amylase. Only one patient showed resistance to an NNRTI, Efavirenz.

The occurrence of opportunistic infections was noted to be high for all patients during the first 6 months of HAART. The most common diagnosis was tuberculosis in 4 patients followed by clinical

diagnosis of PCP (n=4), cryptococcal meningitis (n=2), CMV disease (n=1), oral candidiasis (n=1) and cerebral toxoplasmosis (n=1).

Eleven out of 30 (37%) HIV positive children succumbed to death secondary to AIDS-related infections and complications such as secondary bacterial infections, tuberculosis, and PJP pneumonia. There were 2 patients transferred to another treatment hub after more than 6 months of follow-up while 1 patient was lost to follow-up. The rest of the patients are continuously being seen and managed at the SAGIP Clinic.

Table 8. Clinical course, treatment and outcome of Children Living with HIV

Outcome	Vertical transmission	Sexual Transmission	Total (N=30)
Adverse Drug Reaction* (n=5) (HAART)	3 (60%)	2 (40%)	5 (17%)
Opportunistic Infection * (n=13)	6 (46%)	7 (54%)	13 (43%)
Mortality (n=11)	4 (36%)	7 (64%)	11 (37%)

** 1 patient may have 1 or more adverse event or opportunistic infection*

As seen in Table 9, baseline CD4 count as well as hemoglobin levels had significant negative correlation with the WHO clinical and immunologic staging (-0.4026, p-value=0.0061 and -0.4215, p-value=0.0014 respectively). The rest of the laboratory findings did not show any association with the clinical and immunological stage of HIV at the time of diagnosis.

Table 9. Association of Laboratory Findings with Clinical and Immunological Staging of CLHIV

Laboratory Findings	CDC HIV Surveillance staging		WHO Clinical and Immunologic staging	
	Kendall Tau	**p-value**	**Kendall Tau**	**p-value**
HIV Viral Load	*	*	*	*
CD4 Count	-0.4561	0.0015	-0.4026	0.0061
Hemoglobin	-0.2288	0.1354	-0.4215	0.0014
Hematocrit	-0.0523	0.7585	-0.1446	0.2800
WBC	-0.0523	0.7587	-0.0892	0.5119
Neutrophils	0.1765	0.2528	0.4000	0.0025
Lymphocytes	-0.2484	0.1042	-0.3877	0.0034
Monocytes	-0.0083	1.0000	-0.0290	0.8533
Eosinophils	-0.1538	0.4265	-0.2762	0.0671
Bands	-0.3571	0.1310	-0.1209	0.4668
Platelet count	0.1242	0.4287	0.0800	0.5579
AST	0.4667	0.0037	0.3587	0.0100
ALT	0.2417	0.1383	0.1558	0.2695
Total Bilirubin	0.0000	1.000	0.0000	1.000
Direct Bilirubin	0.0000	1.000	0.3000	0.5791
Indirect Bilirubin	0.0000	1.000	-0.3000	0.5791
Albumin	0.0000	1.000	0.1389	0.6102
BUN	-0.2857	0.2433	-0.4066	0.0323
Creatinine	0.1758	0.3504	-0.1368	0.3859
LDH	*	*	*	*

Total cholesterol	-0.4364	0.0508	-0.0545	0.8623
Triglycerides	-0.4222	0.0803	-0.2222	0.3774

DISCUSSION

Pediatric HIV has become a global public health problem affecting mostly children in resource poor areas of the world. In the Philippines, based on the latest report from the National Epidemiology Bureau of the Department of Health, from January 2013 to March 2018, there were 92 pediatric cases in those <15 years old with an increasing proportion of HIV positive cases in the 15-24-year age group (25% in 2006-2010 to 29% in 2011 to 2018).

Presence of HIV in the family can significantly impact on interpersonal relationships especially in a setting where family ties are strong. In a study done in Malawi on HIV status, gender and marriage dynamics showed that HIV status is a predictor of marital change and the relative risk of a divorce is three times higher for HIV positive compared to HIV negative women[6]. In this study, most parents of children affected by perinatal transmission were married (n=9/12), 4 were widowed, and 3 separated. Our data suggest that HIV positive individuals face risks of union dissolution from widowhood or separation.

Sixty percent of patients came from urban areas consistent with the report of Aro et.al. in 2012[4]. This may be attributed to the availability and accessibility of diagnostic and treatment facilities in urban centers.

Mother to child transmission (MTCT) is the most important source of HIV infection in children as seen in most studies[3,9]; however, in our study, sexual transmission outweighed MTCT, 57% vs 40%. This is in contrast to the findings of Aro et al. where MTCT was found to be the major mode of HIV transmission (73%)[4]. Results in this study is comparable with a UNAIDS report, where the number of adolescents 10-19 years living with HIV has risen by 30% between 2005 and 2016[1]. This may be due to various factors that puts the adolescents at an increased risk for HIV - early sexual debut, non-use of condoms, and preference for older sexual partners – all posing a greater risk for sexually transmitted infections and unintended pregnancies[10].

Risk factors found in a study done in Africa by Fernandez et al. include tobacco (34%), marijuana (28%), and alcohol use (22%) either on a weekly or daily basis[11]. In the Philippines, a study done in 2013 on adolescent sexual attitudes and behavior involving 1,412 participants showed that 27.7% engaged in premarital sex (PMS), compared to 18% back in 2000. Of those who engaged in PMS, 80% did not use a condom. Still in 2015 in an Integrated HIV Behavioral and Serologic Surveillance in the Philippines involving 9,498 males/transgenders having sex with males, 17% were in the 15-17-year age group while majority were 18-24 years of age (49%). More than half of the study population (58%) did not practice condom use and only 14% know their HIV status.

In this study, the mean age of diagnosis for patients infected through MTCT is 40 months with a median of 36 months. A later age of diagnosis was noted in India with a mean of 54 months, in Cameroon 71 months, and in Nepal 58 months [12-14] For patients infected through sexual transmission the mean age is 17.5 years with a median of 18 years. The youngest who became infected with HIV was at 15 years of age. In this study, 76% were males, 47% of which were bisexuals, 47% were heterosexuals and 6% homosexuals. This is in contrast to the findings in South Africa, where majority of adolescent patients were females (57%) and heterosexuals (83%)[15].

Only one case of HIV acquired thorugh MTCT received maternal ARV during her 2nd trimester. The infant received prophylaxis with Nevirapine for 6 weeks. Maternal viral load prior to ART was at 1,000,000 copies/ml and no repeat viral load was done prior to delivery. Maternal transmission of HIV has been well documented especially in the absence of effective intervention[13]. The implementation of

the PMTCT program has greatly reduced the incidence of HIV infection through vertical transmission. Failure of PMTCT program is usually attributed to late antenatal care, delay or omission of maternal ART initiation, and maternal seroconversion (or an initial false-negative HIV screening which later becomes positive prior to or during or after delivery) which leads to subsequent delay in maternal ART initiation[16]. ART started >24 weeks age of gestation may not allow adequate time for viral suppression by the time of delivery[17]. Although maternal ARV was started before the 3rd trimester for this case, the presence of high viral load may have contributed to the failure of PMTCT. Maternal illness may also contribute to insufficient levels of antibodies and inability to provide children with adequate natural passive immunity before birth[16], although in our case, there was no documented illness in the mother.

In this study, 11 out of 12 fathers of CLHIV infected perinatally were tested for HIV and 8 were positive. Paternal risk factors for HIV infection noted were multiple sexual partners, non-use or inconsistent use of condoms and IV drug use.[18]

There is a wide spectrum of clinical presentation of HIV infection in children. The common clinical findings in a study carried out in 4 hospitals in Yaoundé in 2002 were anemia (85%), prolonged fever (63%), chronic diarrhea lasting >1 month (46%), and weight loss or cachexia (43%)[19]. In India, the main clinical manifestations were pulmonary tuberculosis (55%), oral candidiasis (43%), recurrent respiratory tract infections (26%), and skin infections (21%)[20]. In our study, the most common clinical features were weight loss, cough, fever, and rashes. Presenting features in our study are almost similar and comparable with other studies done in resource limited settings [21-23].

Undernutrition is an important feature in HIV infected children in the developing world and remains to be one of the major causes of child morbidity[24]. Children with HIV infection can manifest with poor weight gain and may have failure to thrive[25]. In this study, majority presented with weight loss in 50% in those infected by vertical transmission and 53% in those infected by sexual transmission (Table 2). This can be due to multiple factors - poor nutrition, repeated bouts of infection or immunosuppression, along with poverty. Data in this study were comparable to the study by Sunguya et al. who found that among 213 HIV positive children 6-60 months old, 36.6% were stunted, 22.1% were underweight, and 13.6% were wasted[22].

Tuberculosis is the most common opportunistic infection seen in HIV infected children in developing countries[26]. Tuberculosis was also the most common opportunistic infection in our study at 47%. Mortality was higher in patients with disseminated TB at 67% comparable with reports of higher mortality in HIV co-infected TB patients in Ethiopia in 2016 (8.3% vs 2.5%, P=0.014) [26]. Oral candidiasis may be the first sign of HIV infection[27]. This was the second most common opportunistic infection noted in this study at 33%. Various studies have reported higher prevalence of candidiasis. Pruthvi et al. reported candidiasis in 71% of HIV positive patients, Nagalingeswaran et al. in 70%, Singh et al. in 65% and Anupriyawadhwa et al. in 50% of HIV positive patients[27-29]. Candidiasis has been used as a clinical marker of the disease as its frequency correlates with a low CD4 + T Lymphocyte count and a high viral load[30]. In our study, patients with oral candidiasis at HIV diagnosis had a higher mortality rate of 75%, and all of these patients had tuberculosis. In a local study by Manicad et al. on the prevalence of HIV infection in children using clinically directed selective HIV screening, there was a 1.6% prevalence of HIV in patients with tuberculosis and oral candidiasis[31].

Only 23 patients had initial hemoglobin determination and anemia was present in 53% of those tested. A study done in Ethiopia concluded that anemia was more prevalent and severe in patients with low CD4 T cell counts, patients infected with intestinal parasites, and HAART naïve patients[32-33]. However, another study in Ethiopia showed conflicting results[34]. In this study, 68% of those with anemia at the time of HIV diagnosis died.

However, a direct relationship between anemia and mortality cannot be established from this study due to presence of other comorbidities. Hemoglobin determination 6 months post ART was done in only 13 patients; hence, a significant correlation cannot be established with regard to improvement of anemia after ART.

CD4 count data in this study showed that majority had a CD4 counts of 0-199 (37%) followed by 200-399 (13%). CD4 cell count is a strong predictor of subsequent risk of AIDS or death in both untreated HIV-infected individuals and in those initiating combination ART (cArt)[35], although, the use of CD4 count along with viral RNA provides more information[36]. The higher the viral load and the lower the CD4 counts, the more susceptible the patient is to opportunistic infections such as pneumocystis jiroveci pneumonia, TB, oral candidiasis, toxoplasmosis, and cryptococcosis.

A significant negative correlation exists between the CD4 count and WHO Clinical Staging with a p value of 0.0061 as seen in this study. However, many patients who had complications of HIV/AIDS and those who died did not have baseline CD4 level and viral load in the data collected. Ideally, testing for viral load and CD4 should be part of the routine monitoring of patients with HIV, however, limiting factors in this study include the price and availability of the test, especially since baseline testing is not covered by the insurance system in the Philippines. Although baseline viral load was done in only 4 patients, CD4 count determination at the start of ART was done in majority of patients (63%). Because of the insufficient number of data obtained on follow up after initiating ART, CD4 count, viral load, level of immunosuppression, and development of symptoms cannot be correlated in this study.

The use of Cotrimoxazole as prophylaxis for various opportunistic infections in patients with HIV has been well documented[37]. In our study, cotrimoxazole prophylaxis was given to 60% of patients and it was withheld in 7 patients all with CD4 count of >200 cells. WHO treatment guidelines 2006 on the use of cotrimoxazole prophylaxis recommend the use of cotrimoxazole for CLHIV younger than 1 year of age regardless of CD4 percentage, children >1-year-old who are symptomatic or children with CD4 of <25%, and in children >5 years of age with CD4 <200 cells/mm3. The most common AIDS-defining condition in children is PJP pneumonia[37]. In this study, five patients were clinically diagnosed to have PJP pneumonia. This is noted to be high when compared to a study done in Nepal with only 1 case of PJP pneumonia out of 39 HIV-infected children[3]. The high incidence of PJP in this study could mean overdiagnosis due to lack of funds to have the diagnostics done as well as lack of readily available laboratory facilities for a definitive diagnosis.

The use of highly active antiretroviral therapy (HAART) in HIV treatment has led to dramatic improvements in the health of people with HIV/AIDS. ART reduces mortality as well as serious AIDS- and non-AIDS-related complications[35]. Previous recommendations for delayed ART were heavily influenced by drug toxicities, the potential for drug resistance and limited treatment options for patients who failed initial therapy. At present, therapeutic options have expanded, and the available agents are more potent, better tolerated, with lower toxicities compared to older agents. Most patients in this study (83%) were started with ART within 6 months from diagnosis and 2 patients after 6 months from diagnosis.

Various reports showed that adverse drug reactions (ADR) are associated with non-adherence to treatment, discontinuation of ART, treatment failure, and changes in ART regimens. ADRs in the form of anemia, rash, severe headache and acute pancreatitis were reported in 5 patients in our study. In Nicaragua where data on 692 HIV patients on ART were reviewed, there was a 6.4% incidence of ADRs, and the most common adverse events involved the central nervous (57%), gastrointestinal (27%) and dermatologic systems (18 %)[38].

The presence of opportunistic infections during the first 6 months of HAART was noted in 40% of patients in this study. Most common opportunistic infections noted were tuberculosis, cryptococcoma, CMV and PJP pneumonia among others. The pattern of opportunistic infections may be affected by the availability of ART to children infected with HIV. In a Nepalese study involving all age groups, oral candidiasis was the predominant opportunistic infection followed by streptococcal pneumonia, salmonella infection, cryptosporidial infection and tuberculosis[37].

From this data collected (2012-2017), there were 11 mortalities noted due to complications of AIDS. The most common cause of death was PJP and tuberculosis and most deaths occurred within 6 months from diagnosis.

This is comparable with reports of high mortality in children living with HIV within the first 6 months of initiating ART in Africa and Asia, with deaths resulting from TB and PJP [39-40]. However, a recent study done in Nigeria on the causes of death among HIV-infected children within the first 6 months of HAART cited tuberculosis (70%), sepsis/ undernutrition (10%) and severe pneumonia as contributing factors (6.7%)[41].

LIMITATIONS OF THE STUDY

The retrospective nature of the study was a major limiting factor. The forms used within the SAGIP Unit were also tailored for adult patients, and data pertinent to the pediatric population were found to be lacking. Due to limited advanced diagnostic facilities, recognition of opportunistic infections was mainly done by assessment of clinical features and indirect markers where applicable, which may have led to over or under diagnosis of various opportunistic infections. Lastly, because of the small number of HIV positive children reviewed in a single center, as well as the descriptive nature of this study, our findings may not be generalizable to similar settings.

CONCLUSION

In this study, sexual mode of transmission is the more common mode of acquiring HIV infection in children. Fever, weight loss, rash, cough and lymphadenopathy were the most common presenting features. Tuberculosis and oral candidiasis are the most common opportunistic infections present at the time of HIV diagnosis. HIV mortality is more common during the first 6 months of HAART initiation.

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