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Negative Outcomes (Default, Loss to Follow-Up and Death) Among HIV-1 Mother-to-Child Infected Infants in the Gambia. What Are the Majors Associated Risk Factors?

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Abstract – Background: Late antiretroviral therapy (ART) initiations for pregnant women together with their attritions from ART adherence during pregnancy through breastfeeding, was found significantly contributing to mother-to-child transmission (MTCT) of HIV-1 infections in the Gambia. Despite, studies to determine the outcome of these infants overall, infants infected through MTCT are lacking.

Aims: To determine negative outcomes (defaults, loss to follow-up and deaths) among HIV-1 mother-to-child infected infants and major risk factors associated to their negative outcomes in the Gambia.

Methods: A descriptive retrospective study which involved retrospective data collection and analysis on HIV-1 infected infants who had their samples collected from 2015-2019 and were tested for EID. STATA version 13 software was used for the data analysis, with frequencies and percentage reported for categorical variables and relationship between two categorical were examined using Fisher's exact test.

Results: From 2015-2019, 95/1420 HIV exposed infants were found PCR DNA HIV-1 positive. Among these infected ones, immigration factors (IF) was found major associated factors to defaults, whereas miss-opportunity (MOF) factors was found major associated factors to loss to followed-up and lack of accessed to ART initiation deaths.

Conclusions: A proxy 2015-2019 MTCT national HIV-1 prevalence of 6.7% (95/1420) was found in the Gambia, with majority of these infants who died were not initiated on ART found primarily, associated with MOF. Therefore, the needs to focus on HIV infected mother-infant pairs with MOF characteristic(s) could significantly reduce lack of access to ART initiation mortality risks of infants infected through MTCT in the Gambia.

Keywords – Early infant diagnosis, Human immunodeficiency virus-type 1 (HIV-1), ART, MTCT, Loss to follow-up, default, death, The Gambia;

I. INTRODUCTION

Globally, about 3.4 million children below the age of 15 years were reported living with HIV [1] and about 600,000 newly infected annually [2]. In 2010, about 390,000 of the global HIV infected children under-15 years were reported got infected through mother-to-child transmission (MTCT) [2]. Furthermore, about 330,000 newly infected infants in 2011 were also as a result in MTCT [3]. Therefore, this trend could be sufficient enough to confirm MTCT was the driving force of global infancy and childhood HIV infection epidemic. This is manifested in several studies as MTCT accounts for up to 95% of infants and children infected with HIV globally [1, 2]. Nonetheless, complete implementation and enforcement of prevention of mother-to-child transmission (PMTCT) of HIV infection services (early HIV

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screening detection among pregnant women and immediate universal ART initiation for infected ones, together with their adherence to ART during pregnancy through breastfeeding) can prevent or significantly reduce MTCT. This is reported in clinical trials to less than 2% among HIV infected non-breastfeeding mothers and less than 3% among those breastfeeding [4]. Furthermore, a study report in the Gambia also revealed 0% (0/64) among infected pregnant women that received HIV prophylaxis then initiated on ART during pregnancy through breastfeeding [5]. Therefore, complete implementation and enforcements of PMTCT of HIV infection services as described above is highly required in the region. Ultimately if prioritize and enforce effectively, could result in the attainment of global public health aims in the virtual elimination of MTCT and also increases the well-being of HIV infected mothers and their exposed infants.

Fortunately, Sub-Saharan Africa accounts for up to only 10% of the global population, but with over 79 % of the global HIV prevalence and about 92% and 90% prevalence in infected pregnant mothers and their infants respectively [5, 6, 7]. Furthermore, over 80% of all under five HIV/AIDS related mortalities among which, one-third of them die in the first year of life and half before the age of 2 years in the region [2, 6]. Therefore, in addition to the required complete implementation and enforcement of PMTCT services described above, early diagnosis of HIV exposed infants and immediate initiations of universal ART for infected ones; together with intensify follow-up mechanisms to ensure their retention in care and treatment also requires public health attention in the region. These are associated with improved prognosis and prevent or significantly reduce infancy or childhood HIV related morbidity and mortality risks [6]. However, despite World Health Organization (WHO) recommended ART for all HIV infected pregnant and postnatal women, together with their infected infants regardless to their immune status or clinical staging [8, 9 10, 11] nonetheless, late initiation of ART for infected pregnant women and their default from ART during pregnancy through breastfeeding, are grossly reported major contributing factors to MTCT in the region including the Gambia [4, 5, 11, 12]. Whereas, polymerization chain reaction (PCR) assay mainly utilize in molecular diagnosis of these before 18 months age, due to probable interference of persistent maternal antibodies with the used of antibody test kits/reagents [3, 7, 8, 13], is challenged by cost, training and infrastructure requirements for their availability or sustainable utilization in many laboratory settings in the region [7, 13]. Furthermore, although decline in MTCT has been observed in the region nonetheless, about 150,000 children were reported newly infected in 2015 alone [8], together with only 51% of the 1.6 million African HIV exposed infants had access EID testing in 2015 (14). Combination of these challenges consequently, may have result in a third of HIV related infancy death in the first year of life and half before 2 years of age in the region, either without or poor access to EID of HIV infection, a bench-mark for immediate universal ART initiation for infected ones [6, 14, 15]. Therefore, it could be emphasized that prioritizing complete implementation and enforcement of PMTCT-EID services requires public health attention in the region. However, HIV infected mothers with characteristic(s) of high risk factors to MTCT in the region including the Gambia as described above, are reported significantly contributing to either preventing or delaying sample collection from their high risk HIV exposed infants; or either prevent or delayed ART initiation for their confirmed infected ones; or either default from ART by both mother-infant pairs; and or their loss to follow-up either after their high risk exposed infants sample collection or after ART initiation for their confirmed infected ones [6, 15]. Combination of which too could ultimately, increases their infant's chances of HIV related morbidity and mortality risks. Nonetheless, ensuring EID of HIV infection among exposed infants and immediate ART initiation for infected ones can significantly improve prognosis and prevent or reduces their chances of mortality risk in maintain in care and treatment [6, 7, 13, 14]. Therefore, in ensuring this evident-based the Gambia government prioritized establishment of a functional molecular laboratory at the central laboratory of the country in 2015[16]. This was accompanied by national adoption of WHO test and treat guideline for PMTCT and HIV infected infants [16, 17] as described above. Despite, 6.4% (7/109) prevalence of HIV-1 in MTCT between May to July 2016 was observed as result in the major contributing factors to MTCT described above. Most importantly, the survival and ART status outcome of these infants is a gap of study in the Gambia.

Subsequently in 2019, one urban and three rural health facilities were also capacitated with Point-of-Care (POC) molecular platform. This was done primarily, to decentralized required EID testing services and monitor responses to ART (HIV Viral load count) by all confirmed HIV infected persons in care and treatment, together with molecular diagnosis of tuberculosis. Currently there are 56 health facilities that includes private facilities/clinics inaugurated for both PMTCT and EID DBS sample collection services, together with 10 ART health facilities/clinics among the 56 facilities across the country [17]. The mode of sample collection (dry blood spot (DBS)) from HIV exposed infants

utilized in the country is in line with WHO recommended practice. This enables increase up-take in sample collections and preparations even at less equipped health facilities/posts purposely, to augment the benefits of PMTCT-EID services and mitigate infancy HIV/AIDS related deaths [6, 7, 13, 14]. However, despite among the objectives of the Gambia national HIV/AIDS strategic plan 2014-2020 is to reduce MTCT from 10% to 3% in 2020 [17]. Nonetheless, underscoring May-July 2016 prevalence of 6.4% in MTCT , together with the established challenging risk factors in PMTCT services observed significantly contributing to MTCT in The Gambia as discussed above, studies to determine the outcome of these infants overall, infants infected through MTCT are lacking since the inception of PMTCT-EID services in the Gambia. Therefore, we aimed to determine defaults, loss to followed-up and deaths among HIV-1 mother-to-child infected infants and their associated risk factors.

II. Material And Methods

2.1 Study design and population:

A descriptive retrospective study which included retrospective data collection and analysis on all HIV exposed and infected infants in the Gambia, with the aimed to describe infected ones status on adherence to universal ART from initiated date and provide major associated risk factors to their negative ART status outcome (death, default and loss to follow-up). In the Gambia, treatment folders are provided for all HIV infected persons particularly, infected pregnant and postnatal mothers in care and treatment in order, to track lack of maternal follow-up, scheduling EID appointments and document status on adherence to ART among other essential HIV services. Therefore, status on adherence to universal ART by HIV-1 infected infants for this study, were categorized directly either according to ART status comments in treatment folders of the ones enrolled in care and treatment or mother's treatment folders of the ones not enrolled as follows:

Complete adherence: (Represents PCR DNA-HIV-1 infected infants who were found either greater than or equals (≥) 6 months or less than (<) 6 months on adherence to universal ART from initiated date).

Default: (Represents PCR DNA-HIV-1infected infants who stop receiving universal ART at any moment from initiated date).

Loss to follow-up: (Represents PCR DNA-HIV-1infected infants whose mothers were communicate and visited but either cannot be trace, or trace but had denied universal ART initiation for their infants despite, upon their receipt of infants test results).

Death: (Represents PCR DNA-HIV-1 infected infants who had died either before or after ART initiation).

Whereas, associated contributing factors to default, loss to follow-up and deaths were categorized base on direct description of comments either from treatment folders or situational analysis on each PCR DNA-HIV-1 positive data collected from testing labs and were found at ART clinics as follows:

Health services factor (HSF): (Represents PCR DNA-HIV-1 infected infants whose mother were HIV negative in registers and the infants cannot be trace; or infected infants whose test results were received and documented as negative results, thus prevented the infant from access to ART initiation; or missing registers to confirmed infected infant's mother HIV and ART status).

Immigration factors (IF): (Represents PCR DNA-HIV-1 infected infants whose mother-infant pair traveled out of the area/country where they are enrolled in care and treatment beyond their clinic appointment dates).

Miss opportunity factors (MOF): (Represents PCR DNA-HIV-1 infected infants whose mothers have not received any form of ART or only received shortcut of ART during pregnancy through breastfeeding; or had denied ART initiation for their infected infants despite, upon their receipt of infants test results).

Stigma/decimation Factor (SDF): (Represents PCR DNA-HIV-1 infected infants whose mother-infant pair stops universal ART as a result in fear of possible discloser of their status to husbands).

Natural Factor (NF): (Represents PCR DNA-HIV-1 infected infants whose mothers died either before or after initiation of ART for their infants; or divorce of parents resulting in lack of accessed to their infected infants).

2.2 Ethical consideration:

The study is an extract of a main thesis project which was approved by the Gambia Government/MRC Joint Ethics Committee (Ref no. R01900v2). However, approval was obtained from the director of health services to access study sites. Furthermore, as the study was conducted through a retrospective data collection, informed consent was not obtained from participants. However, all data were anonymized prior to analysis.

2.3 Study sites:

Fifteen (15) PMTCT health facilities namely: SOS and Sibanor clinics; Serekunda, Banjulinding, Bajakunda and Janjangbureh major health centers; Brikama/Hand-on-Care, Soma, Essau and Basse district hospitals; Bansang, Bwiam, Serrekunda and Farafeni general hospital; together with Edward Francis Small Teaching hospital; were accessed for the study. The sites were selected and accessed based on their registration of at least one PCR DNA-HIV-1 infected infant tested from the central and 4 study sites laboratories (Brikama/Hands-on-Care, soma, Bansang and Basse) capacitated for EID testing services in the Gambia.

2.4 Sample size:

All HIV exposed and infected infants who had their DBS samples collected from 2015 to 2019 and were tested for EID of HIV-1 infection.

2.5 Sampling method:

Total number of HIV exposed infants who had their sample collected from 2015-2019 and were tested for EID of HIV infection, were quantified and documented from the five capacitated testing laboratory records mentioned in study sites above. Those tested PCR DNA-HIV-1 positive, laboratory data were extracted and follow-up at their respective collected site where their mothers were enrolled in PMTCT care and treatment. Infants who were initiated on ART, treatment folder's comments were reviewed and extracted status on adherence to receipts of universal ART from initiated date. For those who were not initiated despite with the receipt of their test results at ART clinics, their mother's treatment folder comments were reviewed and extracted status on ART adherence then linked to their infant's status. This is because they are the primary caregivers whose statuses on adherence to universal ART can ultimately influence their infant's status.

2.6 Inclusion and Exclusion Criteria:

All PCR DNA HIV-1 infected infants who had their sample collected from 2015 to 2019 and were tested for EID of HIV-1 infection, together with quantified PCR DNA HIV-1 negatively tested ones under the period reviewed. However, infected infants who had records of their test results only available at testing laboratories, but neither in clinic registers nor in treatment folders, were excluded in determining associates risk factors to negative outcomes as described above. Furthermore, the Real-Time PCR and POC molecular platform used in the Gambia can only detect the HIV-1 infection, thus the study excludes HIV-2 exposed and infected infants.

2.7 Data collection and analysis procedure:

Since PMTCT/year numbers of HIV infected mothers are the same number given to their exposed infants in the Gambia therefore, PCR DNA-HIV-1 positive PMTCT/year numbers with their center names and date tested were extracted from the central laboratory records, together with quantification and documentation of PCR DNA-HIV-1 negatives numbers. The same procedures were also conducted at the four testing sites mentioned above. Extracted PCR DNA-HIV-1 positive numbers, together with their collected health facility/clinic names were used to link mother-infant pairs in their respective collected sites PMTCT-ART and Infant's ARV registers (PA&IAR). This was done to verify and linked the extracted PMTCT/year numbers from the testing laboratories records to their respected infants, confirmed receipt and record of test results, together with extraction of infant's gender and mother's nationality. Two to five days of data collection and verification by the researcher, laboratory staff, ART service providers and social workers was conducted. This depended on the number of HIV-1 infected infants registered by each above study sites. For those confirmed in the registers and were enrolled in care and treatment, their treatment folders as described in study design above were reviewed to extracted status on universal ART adherence from initiated date. For unconfirmed ones either as test results not received or received but not recorded in the registers, their mother's treatment folders were reviewed for confirmation. If results were confirmed in their mother's treatment folders and their infants were enrolled in care and treatment, their infant's treatment folder were reviewed and extracted status on universal ART adherence from initiated date. But if not enrolled in care and treatment, their mother's treatment folders were reviewed to extracted status on adherence to ART, then linked to their infant's status also as previously described in sampling methods above. However, for PCR DNA HIV-1 positive PMTCT/year numbers with their health facility/clinic names records found only in testing laboratories records as described above, were documented as HIV-1 infected infants against the collected health facility/clinic name. Thus, they were not included in determining associated risk factor to negative ART status outcomes as described in the inclusion and exclusion criteria. However, PCR DNA-HIV-1 infected infants whose status on universal ART adherence were confirmed default, loss to follow-up or death during the study, associated contributing factors were documented as discussed in study design and population above. Nonetheless, for those whose associated factors to ART adherence status were not in records, they were documented as unidentified factors (UF).

Collected data were then entered in excel spread sheet and imported in STATA version 13, cleaned for analysis at statistically significant level of 0.05%. Frequencies and percentage were reported for categorical variables. Relationship between two categorical were examined using Fisher's exact test an alternative to Chi-Square test, because the expected frequencies in the cells were less than 5. The two-sided p-values of the test are reported in the Tables of the analysis.

III. Results

The study quantified 1420 HIV exposed infant samples were collected from 2015-2019 and tested for EID of HIV-1 infection. Of this sum, 95 (6.7%) were PCR DNA-HIV-1 positive from 15 health facilities among which, 42 (49.4%) are female, 43(50.6%) male and the gender for the remaining 10 were unknown/missing. Majority (69/95; 81.2%) of these infants were Gambians and others Senegalese (10/95; 11.8%), Nigerian (4/95; 4.7%) and Guinean (2/95; 2.3%), whilst the remaining 10 nationality were also unknown/missing. Furthermore, among the 95, 7 of them test results were found only in laboratory records, thus their ART status were unidentified/missing whereas, 25/88 (28.4) and 12/88 (13.7%) were found had greater than or equals to (≥) 6 month and less than (<) 6 months respectively on ART adherence from initiated date to the end of our data collections in March 2020 , together with 12/88 (13.6%) were found defaulted, 20/88 (22.7%) loss to followed-up and 19/88 (21.6%) not initiated on ART as characterized in table 1.

Table 1: Characteristics of PCR DNA HIV-1 infected infants in the study population on gender, nationality, and ART status.

Variable	N = 95/1420 (6.7%)
Gender: n (%)	
Female	42 (49.4)
Male	43 (50.6)
Missing, n	*10*
Nationality: n (%)	
Gambian	69 (81.2)
Senegalese	10 (11.8)
Nigerian	4 (4.7)
Guinean	2 (2.3)
Missing, n	*10*
ART status: n (%)	
≥ 6 months	25 (28.4)
Default	12 (13.6)
Not initiated on ART	19 (21.6)
Loss to follow-up	20 (22.7)
< 6 months	12 (13.7)
Missing, n	7

NB: ART: Antiretroviral therapy; <: (less than) 6 months on adherence to ART from initiated date; ≥: (greater than or equals to) 6 months on adherence to ART from initiated date.

Furthermore, among the 95 PCR DNA-HIV-1 infected infants, 43 (70.5%) were found alive and 18 (29.5%) death, while 34 of them survival status was unknown/missing as characterized in table 2. At statistically significant level

(p=<0.001), HIV-1 infected infants with known survival and ART status includes: 24/25 (96.0%) of those found ≥ 6 months on ART adherence, only 1 (4.0%) was found death during adherence; all the 12 (100. 0%) found < 6 months on ART adherence were found alive; among the overall 12 (13.6%) defaulters, only 4 (57.1%) were found alive but not in care and treatment, together with 3 (42.9%) found deaths; among the overall 20 (22.7%) found loss to followed-up, only 3 (100.0%) were found alive but also not in care and treatment; and among the overall 19 (21.6) found not initiated on ART, 14 (100.0%) were found death, while the remaining 5 survival status were unknown as characterized in table 3.

Table 2: Characteristics of PCR DNA HIV-1 infected infants on survival status.

Survival status: n (%)	
Alive	43 (70.5)
Death	18 (29.5)
Missing, n	*34*

NB: Missing (Unidentified survival status)

Table 3: Characteristics of PCR DNA HIV-1 infected infants on survival and ART status.

Variable	**Survival status**		**P value**
	Alive	Death	
ART status: n (%)			<0.001
≥ 6 months	24 (96.0)	1 (4.0)	
Default	4 (57.1)	3 (42.9)	
Not initiated on ART	0 (0.0)	14 (100.0)	
Loss to follow-up	3 (100.0)	0 (0.0)	
< 6 months	12 (100.0)	0 (0.0)	

NB: ART: Antiretroviral therapy; <: (less than) 6 months on adherence to ART from initiated date; ≥: (greater than or equals to) 6 months on adherence to ART from initiated date.

In addition, at statistically significant level (P = <0.001), among the overall 12 (13.6%) defaulters, associated contributing factors to defaults of 3 (18.8%) were unknown/missing, but the study found immigration factors (IF) associated with defaults of 5 (50.0%) and natural factors (NF) found associated with defaults of 2 (66.7%), together with stigma and discrimination factors (SDF) also found associated to defaults of 2 (100.0%); among the overall 20 (22.7%) found loss to follow-up, associated contributing factors to the loss to followed-up of 10 (56.1%) of them were also unknown/missing, but IF was found associated to the loss to-followed-up of 3 (30.0%), while miss-opportunity factor (MOF) was found associated to loss to followed-up of 6 (42.9%) and natural factors (NF) found associated to loss to followed-up 1 (33.3%); among the overall 19 (21.6%) not initiated on ART, associated contributing factors to lack of access to ART by 4 were unknown however, health service factors (HSF) was found associated to lack of access to ART by 6 (85.7%), while IF was found associated to lack of accessed to ART by 2 (20.0%) and MOF was found associated to lack of accessed to ART by 7 (50.0%);. HSF was also found associated to the paused (discharged) on adherence to universal ART by 1 (14.3%) out of the 12 found < 6 months on ART adherence and MOF was found associated to the stopped of adherence to ART by 1(7.1%) out of the 25 found ≥ 6 months on ART adherence. Overall,

14 were found affected by MOF, 10 affected by IF, 7 affected by HSF, 3 affected by NF and 2 affected by SDF among HIV-1 infected whose associated factors to their negative ART status outcomes were known as described in table 4.

Table 4: Associated contributing factors in respect to ART status among PCR DNA HIV-1 infected infants.

Variable	**ART status of the HIV-1 infant**					**P-value**
	Complete adherence	Default	Not initiated on ART	Loss to follow-up	AFST	
Associated reasons: n (%)						<0.001
HSF	0 (0.0)	0 (0.0)	6 (85.7)	0 (0.0)	1 (14.3)	
IF	0 (0.0)	5 (50.0)	2 (20.0)	3 (30.0)	0 (0.0)	
MOF	1 (7.1)	0 (0.0)	7 (50.0)	6 (42.9)	0 (0.0)	
NF	0 (0.0)	2 (66.7)	0 (0.0)	1 (33.3)	0 (0.0)	
SDF	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	
UF	0 (0.0)	3 (18.8)	4 (25.1)	10 (56.1)	0 (0.0)	

NB: **HSF** (health services factors), **IF** (immigration factors), **MOF** (miss-opportunity factors), **NF** (natural factors), **SDF** (stigma and discrimination factors), and **UF** (unidentified factors) **ART**: Antiretroviral therapy, **AFID**: Adherence from initiated date.

Table 4, description of (Table 5) also at statistically significant level (P =0.004) that demonstrated: Out of the overall 14 found affected by MOF, the 7 (50.0%) found without accessed to ART initiations, together with the 1(7.1%) out of 25 found ≥ 6 months on ART adherence as described in table 3 and 4 were found death (n=7+1= 8 (100.0%) as described in table 5), while the survival status of the others (6) were unknown; out of the overall 7 found affected by HSF, the 6 (85.7%) found not initiated on ART as described in table 4, only 1 (50.0%) was found death and the survival status of rest (5) were unknown, while the 1 (14.3%) found paused/discharged on ART adherence while infected was found alive 1 (50.0%); out of the overall 10 found affected by IF, the 3 found death in defaults previously as described in table 3 were among the 5 (100.0%) defaults in table 4, together with the 2 (20.0%) found not initiated on ART as described in 4 were found death (n= 3+2= 5 (100.0%) as described in table 5), while survival status of the rest (5) were unknown; all the 3 found affected by NF (2 (66.7%) defaulters and 1 loss to followed-up), together with the 2(100.0) defaults found affected by SDF were found alive but not in care and treatment (NF 3 (100.0%) and SDF 2 (100.0%) as described in table 5).

Table 5: Associated contributing factors in respect to survival status.

Variable	**Survival status**		P value
	Alive	Death	
Associated reasons: n (%)			0.004
HF	1 (50.0)	1 (50.0)	
IF	0 (0.0)	5 (100.0)	

MOF	0 (0.0)	8 (100.0)
NF	3 (100.0)	0 (0.0)
SDF	2 (100.0)	0 (0.0)
UF	1 (25.0)	4 (75.0)

NB: **HF** (health services factors), **IF** (immigration factors), **MOF** (miss-opportunity factors), **NF** (natural factors), **SDF** (stigma and discrimination factors), and **UF** (unidentified factors)

IV. Discussion:

Our study found 6.7% (95/1420) proxy prevalence of HIV-1 infection among HIV exposed infants who had their samples collected from 2015 to 2019 and were tested for EID of HIV-1 infection. This is similar to the findings of the only study report in the Gambia that revealed May-June 2016 MTCT of HIV-1 infection prevalence of 6.4% (7/109). Although, this may require further studies however, the similarity together with reference to the objective of the national HIV/AIDS strategic plan 2014-2020 (reducing MTCT at six weeks from 10 % to 3 % in 2020 [17]), could be interpreted that the established major risk factors found to be significantly associated with MTCT of HIV-1 infection in the Gambia (late initiation of ART for HIV infected mothers and default during pregnancy through breastfeeding) [5], are anticipated to be still in conflict with national PMTCT responses mechanisms. These risk factors to MTCT in the Gambia located within Sub-Saharan Africa were also observed significantly reported across several studies in the same region [4, 11, 12]. Therefore, more attention is required to control or reduce these major challenging risk factors in the region especially, in the Gambia where it could be anticipated may significantly influence the attainment of targeted 2014-2020 HIV/AIDS strategy plan objective discussed above. Nonetheless, if failing to ensure EID of HIV infection among exposed infants and immediate ART initiation for infected ones can significantly increase their chances of mortality risk [6, 7, 13, 14], then lack of access or default from ART would be more fetal. This is observed significantly (P = <0.001) being symbolized by our finding with 14 deaths without accessed to ART initiations and 3 during their default periods, when compared to only 1 death during on complete ART adherence as described in table 3. Therefore, logistics in ensuring complete implementation and enforcement PMTCT-EID services as described above could be emphasized requires attention in the Gambia. Underscoring HIV infected mothers with similar characteristic(s) of risk factor(s) to MTCT in the region as discussed above, are significantly found either associated with delayed in bringing their high risk exposed infants for EID of HIV infection; or default of both mother-infant pairs from ART adherence; or miss opportune access to universal ART initiation for their infected infants despite, with their receipt of infants test results [6, 15]. Combination of which ultimately, increases their infant's chances of HIV related mortality risk and loss to followed-up of both mother-infant pairs [6]. This could be understood supportive to the finding of our study with miss opportunity factors (MOF) referred to in this study (PCR DNA-HIV-1 infected infants born to HIV infected mothers who either have not taken any form of ART or only received shortcut of ART during pregnancy to post-delivery; or had denied initiation of ART for their infected infants despite their receipt of infants test results) was found significantly associated to the lack of access to ART by 7 infected infants and the stop of ART by 1 as described in table 4, resulting to their death (n =8) as described in (Table 5), together with high loss to followed-up (n =6) also as described in table 4) resulting to 3 found alive but not in care and treatment also as in (Table 5).

Immigration Factors (IF) referred to in the study (PCR DNA-HIV-1 infected infants whose mother-infant pair traveled out of the area/country where they were enrolled in care and treatment beyond their clinic appointment dates) was found significantly associated to death of 5 out of the 10 affected as described in table 5. However, considering its associated impact found as described in table 4 and 5, together with associated impact of MOF discussed above ultimately, demonstrated almost all the casualties/deaths either without access to ART initiations or default from ART adherence was found primarily, embedded in MOF followed

by IF as described in (table 5). Nonetheless, underscoring failing to ensure EID of HIV infection among exposed infants and immediate ART initiation for infected ones, together with their retention in care and treatment can significantly increase their chances of mortality risk as discussed above, then lack of access to ART initiation and default from ART adherence could be more fetal. Therefore, it could be anticipated that more than the 8 and 5 affected by MOF and IF respectively may have died, considering 6/14 and 5/10 affected by MOF and IF respectively survival status were unknown as described in table 5. Thus, mother-infants pair affected by either IF or MOF or both requires high attention to mitigate or reduce HIV related infancy death in the Gambia.

Surprisingly, 1 out of the overall 7 HIV-1 infected infants affected by health service factors (HSF) as described in (Table 4) was found death without accessed to ART initiation as described in (Table 5), together with paused/discharged of another 1 infected infant from ART adherence as described in (Table 5). However, regardless to the 7.4% (7/95) PCR DNA HIV-1 infected infants who had their test results only available at the testing laboratory records as described in (Table 1), but with lack of accessed to by 5 whose survival status were also unknown, together with the death of 1 without accessed to ART initiation and the paused/discharged of the 1 discussed above found associated with the overall 7 affected by HSF ultimately, demonstrated the need of trainings on and enforcement of national PMTCT-EID standard operating procedures (SOPs), together with effective monitoring and supervision in place in the Gambia. If prioritize and enforce effectively, could ultimately mitigate health service factor contributions to negative outcome of HIV-1 infected infants in the Gambia. This could be emphasized requires urgent attention underscoring the 1 who was discharged from ART adherence was corrected by the study through facilitating confirmatory test for the infant and resumption on ART during the study. Therefore, it could be anticipated that if there was an effective monitoring and supervision in place to ensure the effective implementation and enforcement of PMTCT-EID standards, together with provision of frequent refresher trainings as discussed above, then it would have be detected for appropriated actions or in fact prevented. Furthermore, underscoring high chances of HIV related mortality attributed to lack of access to ART, default and loss to follow-up of infected infants inconveniently, natural factors (NF) referred to in this study (PCR DNA-HIV-1 infected infants whose mother died either before or after initiation of ART for their infants; or divorce of parents resulting in the lack of accessed to their infected infants), was found associated to the defaulted of 2 and the loss to followed-up 1 found alive but not in care and treatment. In addition, stigma and discrimination factors (SDF) referred to in this study (PCR DNA-HIV-1 infected infants whose mothers-infants pair stop ART as a result in fear of possible discloser of status to husband), was found significantly associated to the defaulted of 2 also found alive but not in care and treatment. This ultimately calls for effective enforcement of national HIV/AIDS Act, to ensure the survival rights of infected infants with such characteristics. As such issues could ultimately set-back national responses to HIV/AIDS prevention and control services, considering labor and cost of resources utilized to diagnosed and initiated ART for even one person

V. Conclusion

Despite with implementation and massive scaled-up of PMTCT services in the Gambia, 2015- 2019 proxy national prevalence of 6.7% (95/1420) was found among HIV exposed infants in the Gambia. Therefore, a few chances of attaining the national targeted 3% by 2020 as discussed above could be anticipated considering their difference. Nonetheless, underscoring majority of these infants found death were not initiated on universal ART found Primarily, associated with MOF followed by IF. Therefore, the needs to focus on HIV infected mother-infant pairs with either IF or MOF characteristic is highly required in the Gambia. This could be anticipated through intensifying counseling and HIV exposure screening detection among all infants with unknown status during immunization visits, together with follow-up mechanisms to ensure their increase up-take and adherence to universal ART if confirm infected. Furthermore, the surprising contribution of HSF in the negative outcome of HIV-1 infected infants as discussed above ultimately requires trainings on and enforcement of national PMTCT-EID SOPs, together with effective monitoring and supervision in place also as discussed above. Whereas NF and SDF found associated to defaults and loss to followed-up of both mother-infant pairs despite, they could be seen at their respective PMTCT or ART health facilities/clinics for anticipated frequent HIV related morbidities issues. This ultimately requires sustainable sensitizations on national HIV/AIDS Act for its effective enforcement particularly, to ensure the survival rights of infected infants born to mother with these unfortunate factors.

VI. Study Limitations:

Since the molecular platforms used in the Gambia for EID testing can only detected HIV-1 DNA/RNA, the study is limited to the inclusion of HIV-2 infants. Furthermore since

the study was done through retrospective data collection, consent was not obtained to directly involve mothers of infected infants for their direct response on reasons particularly, on default and denial of ART for their infected infants thus, a limitation of the study. The study is also limited to without determining the outcome of negatively test HIV exposed infants, because the study is an extract from the researcher's main thesis project. In addition, the study is limited to without findings on turnaround time involve in EID to initiation of ART for infected infants, because the study is purposely aimed to determine the outcome of PCR DNA-HIV-1 infected infants in respect to death, loss to follow-up and default. However, we recommend for study on turnaround involve in EID of HIV infection among exposed infants to ART for infected ones in the Gambia. This is lacking despite, it is generally known of its potentiality in identifying the level of contribution of both maternal and health services factors in delay in EID to ART initiation for infected ones. Most importantly, it can determine if HIV exposed infants are being diagnosed and ART is initiated for infected ones within WHO/national recommended timeframe. Therefore, we emphasize the need of an urgent study on turnaround time described above.

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Table 6: Contacts details of study collaborators at the respective 15 study sites.

No.	Study sites center names	Names of lab staff collaborators	Names of PMTC services providers collaborators	Names of ART service providers collaborators	Names of social workers collaborators
1	SOS clinic	Adama Bah	Marohey Ceesay	Marohey Ceesay	Angelic Mendy
2	Sibanor clinic	Nfamara BadjieBadjie	Sainabou Drammeh	Hulaymatou Badjie	Mama Susso
3	Banjulinding major health center	Fatou Badjie	Burrey Joof	Tida Sanneh	
4	Bajakunda major health	Dawda Colley	Buba Makalo	Sulayman Sarr	
5	Serrekunda health center	Lamin M.M Jallow	Fatou Joof	Lissa Marong	
6	Janjangbureh major health center	NA	Anna P Bojang	Elizabeth Mendy	
7	Brikama/Hands-On-Care district hospital	Alhagie Komma	Fatoubinou gibba and Kaddy jaiteh	Saikou Sabally and Benerad Gomez	Seedy Jarjue
8	Soma district hospital	Tijan Janneh	Binta Manneh	Sheriff Ceesay	Bakary Conta
9	Basse district hospital	Tumbul Samateh	Mariama Joof	Hamidou Nyassi	
10	Essau district hospital	Dembo Jammeh	Fatou Camara	Nyima Badjie	Vincent Silver
11	Bansang general hospital	Kebba Saidy	Abdoulie Jallow	Muhammed Jatta	Sulayman Jallow
12	Farafeni general hospital	Nfamara Manjang	Haddy Sarr and Fatou Badjie	Ebrima dibba	Musa Gindo

13	Serrekunda general hospital	Isha Leigh	Yvonne Sarr	Fatou Saho	Salifu M. Bah
14	Bwiam general hospital	Musa Badjie	Ebrima Fatty	Ebrima Fatty	Demba Jammeh
15	Edward Fransis Small Teaching hospital	Mustapha M. Ceesay	Abdoulie Jallow	Abdoulie Jallow	Abdul Aziz Bangura

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IX. Declaration of conflict of interest:

No conflict of interest is required by the researcher in respect to universal access for future study but must be citied accordingly as indicate in the journal.

X. Authors' contributions:

MC conceived the research idea, designed the study, data collection, data analysis, interpretation of data and led the writing of the manuscript. AHA and BS, assisted in the conceiving the research idea, designed the study, designing, analysis and interpretation of data and supported the writing of the zero draft manuscript and final edition. NN made intellectual contribution to revising of the manuscript. All authors read and approve the final manuscript, together with all collaborators accepted inclusion of their names as described above.

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