Bottlenecks and opportunities for delivering integrated pediatric HIV services in Nepal

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Background
In children, integration of HIV in MNCH services has been shown to increase uptake of early infant diagnosis. This article examines bottlenecks and opportunities for scaling up integrated pediatric HIV services in Nepal.

Methods
This is a descriptive study using both mixed qualitative and quantitative methods, conducted in January 2015 in 19 facilities in five regions of Nepal most affected by HIV epidemic. The qualitative methods comprised in-depth structured interviews with key informants (leadership of The National Center for AIDS and STD Control and National Public Health Laboratory, district management teams, medical officers in charge of health facilities and HIV clinics, frontline staff at antenatal care and HIV clinics and laboratory). The quantitative methods were used to abstract data of HIV-infected pregnant women seen between January and December 2014, HIV-exposed infants aged less than 12 months, and HIV infected children aged less than 15 years who were initiated HIV treatment from 2010 to 2014. Structured tools were used to collect data which were analysed using IBM SPSS.

Results
Of the 19 facilities assessed, 18(98%), 18(98%), 14(75%), and 11(58%) provided prevention of mother-to-child transmission (PMTCT), Expanded Program on Immunization (EPI), pediatric ART and nutrition rehabilitation services, respectively. However, only 1(5%) facility collected onsite dried blood spots (DBS) for PCR HIV testing and 6(32%) facilities provided counselling and referral for DBS. In 2014, of the 121 HIV-exposed infants recorded, only 21(17%) received PCR test. The median turnaround time of the PCR test results was 54 days. Of the 21 records with PCR test, 11(52.5%) were from PMTCT clinics, 7(33%) from Nutritional rehabilitation clinics, and 3(14.5%) from pediatric outpatient clinic.

Conversely, 934 children were initiated ART between 2010 and 2014, of which 5% were infants and 29% aged between 1 and 5 years. 298 (32%) had comorbidities of which 64% had malnutrition. A total of 534 (57%) had tuberculosis (TB) status assessed of which 58 (11%) had active TB. Infants had lowest retention (63%), high mortality (17.4%), and loss to follow-up (10.9%).

Conclusion
Few facilities collect DBS and few children receive PCR tests with limited linkage to ART. This has led to late ART initiation, comorbidities, including TB coinfections and poor outcomes. The results indicate that there are opportunities for improving HIV case finding among HIV-exposed infants in PMTCT, EPI, TB, and nutrition services if provider initiated testing and counselling at the point of service delivery is institutionalized in these settings.

Keywords
dried blood spots, nutrition, pediatric ART, prevention of mother-to-child transmission
INTRODUCTION

There has been 2.3 (1.9–2.7) million new HIV infections globally, showing a 33% decline in the number of new infections from 3.4 (3.1–3.7) million in 2001 [1]. Some of the greatest reductions seen in new infections have been among newborns, declining from 530,000 in 2000 to 260,000 in 2013, as a result of national and global efforts invested in prevention of mother-to-child transmission (PMTCT) programs [2].

Nepal had a HIV prevalence rate 0.2% (0.2–0.3%) among adults of 15–49 years of age; with 1900 (1500–2500) of children 0–14 years of age living with HIV in 2013. According to Nepal National Center for AIDS and STD Control (NCASC), Nepal’s HIV epidemic is largely concentrated among most at risk populations and some migrants. HIV prevalence rates among intravenous drug users (IDUs) in 2011 in Kathmandu was 6.3% and there were between 24,649 and 28,359 female sex workers in Nepal with an estimated HIV prevalence rates of 1.7%. HIV infection rate among street-based sex workers in the Kathmandu Valley is 4.2%. Nationally, clients of female sex workers accounted for 4.4% of total estimated HIV infections [3]. In addition, high number of sex workers who migrated or were trafficked to Mumbai, India to work, increase HIV prevalence rates in the sex workers’ network in Nepal, [3]. Children born from these groups of populations were the most at high risk of contracting HIV mainly during perinatal period.

Recently, the NCASC developed a new National HIV/AIDS Strategy 2011–2016, which highlights prevention, including prevention PMTCT as a key strategic direction. National Public Health Laboratory (NPHL) has been equipped to perform early infant diagnosis (EID); and the linkages among health facilities and referral system put in place. However, the coverage of pediatric HIV care remains unacceptably low [4–6]. Limited follow-up with mother–child pairs up to 18 months postpartum and EID, were still critical gaps in the current pediatric HIV care programs [7]. Other missed opportunities in these settings included the systemic screening, prevention, and treatment of tuberculosis (TB) and viral hepatitis.

The study aim is to describe the delivery of pediatric HIV care and treatment program setup with regard to the comprehensiveness of EID services for HIV-exposed and ART services for HIV-infected children. The clinical profile and retention in care, and HIV managers’ and healthcare providers’ perspectives toward pediatric HIV program have also been investigated.

METHODS

Population

This was a retrospective review of routinely recorded data for EID and pediatric ART program, retrieved at selected health facilities in Nepal between January and February 2015. No children neither women/mothers were interviewed.

The selection of sites was based on the regions that are most affected by HIV epidemic according to the National surveillance report of the country. The criteria for selection included the following: having introduced HIV services, geographical locations (urban/rural), level (primary to secondary), ownership (public/private), and having high patients’ load (more than 10 cases of HIV infection in 2014). Thus, 19 Health facilities were selected and are shown in Table 1.

The abstraction of data was done from HIV clinics, antenatal care clinics and maternity wards. Interviews were conducted with Key informants (KI) from all these 19 health facilities. Only laboratories with complete and up-to-date data for HIV infection up to the month preceding the study were considered. Thus, only nine laboratory registers were analysed. Among these nine laboratories one was private, which was supported by Family Health International (FHI).

Study design

This was a descriptive cross-sectional study. We collected data between January and February, 2015 for quantitative analysis and conducted interviews for qualitative study of the pediatric program. The interview was conducted with the leadership of NCASC and NPHL at the central level, district management teams, medical officers in charge of health facilities and HIV clinics, frontline staff at antenatal care and HIV clinics and laboratory. The assessment used questions that have been utilized in similar efforts in other countries in similar efforts. Thus, it was not necessary to pilot testing them. The interview lasted approximately 15–20 min. It covered the following four sets of questions that were designed to identify downstream, midstream, and upstream of pediatric HIV care and treatment, among which included: aspects related to the policy framework, national guidelines, strategy on HIV/AIDS, and service delivery for prevention mother-to-child transmission of HIV (PMTCT), HIV-exposed, and infected children. The elements in policy framework that were looked at included the coordination and decentralization of pediatric HIV services, data-informed planning and budgeting.
plan, organizational and delivery model of HIV testing services for pregnant women and HIV-exposed children, community engagement and participation, supply chain management, overarchings services design, EID and antiretroviral treatment (ART). Questions for KI at national level also looked at the legal environment such monitoring, and task shifting/sharing for HIV treatment and care for children. For the district health management, the questions were related to the supervision and local coordination of interventions. The questions related to operations of activities and service provisions were asked to the health facility in-charge and frontline staff (physicians, nurses, and counselors) at HIV clinics.

The collection of medical recorded data was conducted following the PMTCT cascade between January to December 2014 for all HIV-exposed children aged between 1 and 12 months; and HIV-infected children below 15 years who were treated from 2010 to 2014 at selected sites. Registers at HIV clinics, antenatal care, and maternity wards were the primary source of these data. Registers for PMTCT, HIV-exposed children and pediatric HIV care from visited facilities were used to estimate the coverage of services and median value of HIV rapid test for pregnant women and children above 12 months of age, EID, cotrimoxazole prophylaxis (CPT), clinical profile, regimen of ART, CD4 trend, lost to follow up (LTFU), and outcomes. Data identifying women and children in this study were not collected.

**Data analysis**

Data were recorded in excel sheet and imported into IBM Statistical Package for the Social Sciences 23 software for analysis. We used descriptive statistics to assess our results. Quantitative indicators were measured for initiation of antiretroviral (ARV) prophylaxis for the newborn; EID, initiation of CPT and ART for children. The retention in care was measured by the rates of continuation of follow-ups. The additional variables included the clinical profile, WHO clinical staging, the HIV treatment regimens, and rates of TB/HIV coinfections. Transfer-outs and stopped treatment were excluded as outcomes from the analysis.

For qualitative analysis, we transcribed each open question of the interview and enter it into Quality System Regulation (QSR) Nvivo10. This software allowed us to utilize the data for the creation of concepts, categories, and themes, as opposed to relying on predetermined analysis items. Once the codebook was developed, two of our collaborators independently coded the interviews. Thus, QSR Nvivo10 supported the data analysis and identified trends in the data. The analysis itself was an inductive process, which allowed themes to emerge from the data. The themes were coded into categories which were continuously refined throughout the analysis. Finally, relationships between categories were created and inferences were made. The analysis and its process were discussed among the team members.

| Region     | Health facility                          | Geographic location |
|------------|------------------------------------------|---------------------|
| Eastern    | 1. Mechi Zonal Hospital, Bhadrapur        | Urban               |
|            | 2. Kosi Zonal hospital, Biratnagar        | Urban               |
|            | 3. BPKIHS, Dharan                        | Urban               |
|            | 4. Itahari PHC                           | Rural               |
|            | 5. Sonapur subhealth post                | Rural               |
| Central    | 1. Sukra Raj Tropical and Infectious Disease Hospital, Kathmandu | Urban               |
|            | 2. Kanti Children’s Hospital, Kathmandu   | Urban               |
|            | 3. TU Teaching Hospital, Kathmandu        | Urban               |
|            | 4. Bharatpur Hospital, Chitwan           | Urban               |
|            | 5. Khaireni PHC, Chitwan                 | Rural               |
| Western    | 1. Western Regional Hospital, Pokhara     | Urban               |
| Mid-western| 1. Bheri Zonal Hospital, Nepalgunj        | Urban               |
|            | 2. Mid-western Regional Hospital, Surkhet | Urban               |
|            | 3. Mehal Kuna PHC, Surkhet                | Rural               |
| Far-west   | 1. Mahakali Zonal Hospital, Mahendranagar | Urban               |
|            | 2. Sub-Regional Hospital, Dadeldhura      | Urban               |
|            | 3. Doli Hospital, Doli                    | Rural               |
|            | 4. Seti Zonal Hospital, Dhangadi          | Urban               |
Ethical considerations
Personal identifying data were all removed to ensure confidentiality and privacy of patient information and cleared by relevant authorities. The National Health Research Council has approved the study protocol for ethical clearance.

RESULTS
Profile of health facilities and key informants
A total of 67 staff (KI) at different levels of HIV program management and implementation from all five regions and the 19 selected health facilities were interviewed. Fifty seven percentage were men and 43% women; and 53% of them have been working for more than 10 years. There were 41% health-care providers, 28% district health management staff, 28% hospital managers, and 3% national HIV management staff. 52% respondents were aged between 41 and 50; and 27% were 31–40 years old. The mean of age was (mean = 45 ± 6; minimum = 25; maximum = 60 years).

Quantitative data
Knowledge of policy, guidelines, and organization of HIV programs
Just over three out of 10 KI knew Nepal HIV policy, guidelines, Annual plan to scale up EID, Annual plan to scale up Initiation of HIV treatment in children, Annual plan to scale up retention of HIV-infected children task shifting policy for pediatric HIV treatment and care.

Availability of pediatric HIV care at health facilities
Out of 19 facilities surveyed, only 31% offered counseling and referrals for EID services to either to Kathmandu or to project run by FHI360. Stock-out for HIV kits and cotrimoxazole for the last 3 months have been reported, respectively in 3% and 18% of health facilities, respectively. Prescriptions for HIV treatment were dispensed by lay counsellors and nurses in 16% and 84% health facilities, respectively. Eighty percentage and 20% of pediatric ART were initiated by pediatricians and medical officers, respectively. Only one percentage of facilities had trained nurses on the collection of DBS and 10% of them had trained laboratory staff on DBS collection.

Early infant diagnosis tests
Only 17% of health facilities offered EID services. The prescription of HIV DNA/PCR tests varied between health facilities. Facilities in Mid-West, Western and Central regions prescribed EID tests more than Eastern region. Most of EID tests were prescribed from Far-West and Central regions, except for BPKIHS in Dharan. These all tests were done through FHI 360 program. Only 27% (21/78) of HIV-exposed infants were tested for HIV using DNA/PCR technology as seen in Fig. 2. Approximately, 43% (9/21) of infants had the first PCR test between 11 and 16 weeks, and the remaining 29% (7/21) children were tested between 17 and 20 weeks of age. The mean overall turnaround time for PCR tests was 54 days. Of the 21 records with PCR test results abstracted, 52.5% (11/21) were from PMTCT settings, 33% (7/21) from Nutritional rehabilitation clinics, and 14.5% (3/21) from pediatric outpatient clinic. There were no DBS from EPI clinics despite their high coverage in the country. The HIV prevalence rates among the 21 infants varied from 6 to 20 weeks. These HIV prevalence rates were 5% at 6–10 weeks, 7% at 11–19 weeks, and 6% at 17–20 weeks of age.

Cotrimoxazole prophylaxis
About 78% of infants received cotrimoxazole prophylaxis treatment (CPT) at 6 weeks of age, this proportion increased to 88% at 10 weeks, at 95% by the age of 12 weeks, and all infants were on CPT by the age of 16 weeks of age. Twenty two percentage (16/78) infants did not receive CPT at 6 weeks of age because it was out of stock. Cotrimoxazole was dispensed by ART clinic nurses and/or counsellors.

Services provided to HIV-infected children
Just 934 children have treated with ART between 2010 and 2014. Malnutrition (64%), gingivitis (63%), respiratory infections (45%), and mucocutaneous diseases (34%) were the most common clinical presentations. Twenty two (13.1%) of children were asymptomatic.
About ART regimen pattern for children, the most commonly used ART regimen was AZT + 3TC + NVP with 57% among all records for children aged between 1 and 4 years, followed by d4T + 3TC + NVP in 29%, d4T + 3TC + EFV in 9% of children, and TDF + 3TC + LPV/r in 5% of children. The majorities of children on ART were aged between 5 and 15 years, and represented 66% of the overall data abstracted from all 19 health facilities.

ART outcomes
The outcomes of ART were well documented in 836 records out of a total of 934 data after 12 months of initiation of ART. Of 836 children on ART, 65% of children were aged between 5 and 15 years and 95% among them had cumulative death rates of 5.5%. Infants (<1 year) were the most vulnerable and represented 4.9% of the cohort with the lowest ART initiation (63%) and the highest death rates of 17.4%, most probably because of low EID uptake. The children aged between 1 and 4 years were the second least enrolled children on ART in comparison to other age groups. LTFU levels were at 11% for infants and between 7 and 9% for the remaining of the age groups. There has been no difference between urban and urban facilities. The registers do not have data related to the outcomes of those who were lost to follow-up, as seen in Table 2.

ART adherence and retention in care
This variable was poorly provided in all records for children. We have used refills of prescriptions as proxy to adherence. Considering this approach, there were 356 records that provided adequate information on refills. Out of these 356 records, only 15% (53/356) records did not show regular collection of refills.

Qualitative analysis

Bottlenecks and causes
The key bottlenecks and related causes on the above findings are summarized in Table 3. This includes enabling environment, supply, and demand of services. Twenty four percent of pregnant women have delivered without knowing their HIV status.
**DISCUSSION**

This study describes the implementation of pediatric HIV care and treatment program in some regions of Nepal, with emphasis on the HIV program staff’s perspectives and pediatric HIV care cascades. There are eleven main findings. First, there is no clear understanding of policies on EID services and task shifting. Study observed that few HIV program staff were still not sure whether EID services can be provided in the all country or not and that task shifting can help to increase DBS collection and initiation of ART. This situation can be improved with staff orientation and dissemination of all national documents, training, and closed supervision as found by previous investigators [8,9].

Second, the lack of money to pay for other blood tests, husband permission before testing, stigma [10], and out-stock of testing kits were the main reasons for pregnant women giving birth without knowing their HIV status. Because, HIV tests were performed with blood drawn for other tests which are charged for at laboratory, if women did not pay for these other blood tests, HIV tests will also be deferred until such time the payment is made.

Third, the study showed that the prescription of HIV DNA/PCR tests varied between health facilities, with Mid-West, Western, and Central regions prescribing more than Eastern region. Very few HIV-exposed infants were offered EID services because of low-skilled staff, operational challenges, organizational model, and socio-economic situations of parents [11–13]. The mean overall turnaround time for all PCR tests was 54 days. This long turnaround time was mainly due to the lack of money for parents to bring the children for blood collection facilities, at FHI360 site or NLHP in Kathmandu, the only sites where DBS could be collected. Most of DBS were from PMTCT, Nutritional rehabilitation clinics, and pediatric outpatient clinic; and no DBS from EPI clinics despite their high coverage in the country. The study underlined the need of integrating EID with other MNCH services, as shown in other studies [14].

Forth, the supply of commodities was a serious challenge in some settings. Twenty two percentage of HIV-exposed infants did not receive CPT at 6 weeks of age because it was out of stock, as found. by many investigators [15–18].

Fifth, HIV-infected children were treated very late and limited numbers of them were screening for TB and viral hepatitis. Like previous investigators, we found a high prevalence rate of TB/HIV coinfections [19–20] and the prevalence rates of viral hepatitis coinfections were also high in children living with HIV [21–23].

Sixth, the study observed a low rate of retention in care and a very high LTFU rate; as shown by previous studies [24–30]. Caregivers and healthcare
providers’ behaviors and attitudes impact on the retention in care. These characteristics included low socio-economic status and level of household support and issues such as lack of food, time constraints to bring the child to the health facilities, perceptions that the child is healthy in the absence of symptoms, stigma, religious beliefs, and male partner support [31].

Seventh, the knowledge of professionals in charge of HIV programs on policies, strategies, guidelines, and priority of pediatric HIV program is critical to delivery services [32]. This was weak in this study. This situation can be improved with training and closed supervision [33]. PMTCT has shown to be cost-effective intervention that leads to the uptake of EID and pediatric HIV care and treatment. However, the identification of pregnant women living with HIV and follow-up of pair mother–child remain a challenge in many settings [34–37] like in this study.

Eighth, this study found that the long-standing health-systems issues were the most common reason for the long turnaround time, including cost of transportation for the collection of DBS and referral of children to the laboratory instead of blood samples at the two sites of collection for DBS in all country, which was due to limited skilled staff and service accessibility, and community-level factors (particularly stigma, fear of disclosure and lack of partner support) [38,39], and weak integration [40].

Ninth, study observed that the delay in initiation CPT was delayed because of unavailability of cotrimoxazole at HIV clinics rather than failure for prescriptions.

Tenth, study observed that 42% of HIV infected children were at WHO stage II; 38% at stage III; 17%

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**Table 4.** Key bottlenecks and related causes for enabling environment and supply of services (continue)

| Area of intervention | Domain of intervention | Key bottlenecks | Causes |
|----------------------|------------------------|-----------------|--------|
| Coordination         | Regular supervision is limited | Irregular support from the supervisors |
|                      | HIV program is vertical within health facilities | Weak integration of HIV with other health services program |
| Management and planning | District annual plans fall short on addressing the bottlenecks | No bottlenecks analysis conducted to inform planning |
| Budget/financing     | District budget and HIV budget are not known | Lack of detailed budget for many activities under pediatric HIV and |
| Ensuring quality     | Not much is done to ensure quality | No quality improvement plan |
| Supply factors       | Accessibility of early infant diagnosis services | early infant diagnosis is limited to few sites | No decentralization of services |
|                      | Skilled staff to perform specific tasks (dried blood spots ...) | Only laboratory staff are allowed to collect blood samples | Limited trained staff |
|                      | Operations system in place to transfer specimen to lab and reception of results | Sending parents and children to another city and town just for collection blood samples | Poor system for collection and transfer of blood samples to the lab |
|                      | Ensuring quality of services through quality improvement efforts | No priority on quality improvement planning | No quality improvement framework activities |

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**Table 5.** Key bottlenecks and related causes for demand of services

| Area of intervention | Domain of intervention | Key bottlenecks | Causes |
|----------------------|------------------------|-----------------|--------|
| Demand factors       | Access to early infant diagnosis | Limited sites provide these services | Initiation of ART only done at hospitals despite that PHCs having medical officers onsite who can be trained |
|                      | Poverty for population who are affected by HIV | Limited uptake of services | High cost of transportation and living conditions to travel to early infant diagnosis collection sites and ART clinics |
|                      | Stigma and discrimination | Cultural and religious beliefs | Some hospitals refer HIV-infected pregnant women even for normal delivery because of HIV status |
at stage IV, and the remaining 3% at stage I [41]. Sixty six percentage of children were 5–14 years old, 29% were 1–4 years old; and only 5% of children were less than 12 months old. The study observed that TB screening were conducted only in 11% of HIV-infected children.

Eleventh, adherence to ART and retention in care are still a big challenge as shown by previous study [42]. We observed that adherence to ART was poorly provided in all records for children. Using prescription refills as proxy, 15% records did not show regular adherence; and this can be improved by engaging with parents, strengthening community support, and usage of mHealth technologies, as evidenced by others [43–44].

**LIMITATIONS OF THE STUDY**

This study did not look at quality of care. Although the quality of care can be assessed using the quality of pediatric ART services using 2010 WHO guidelines, this approach has limitation on its own. For example, the timing that laps between the diagnosis and the initiation of ART does not provide the quality of services per se. Thus, assessment of quality should look at processes that have been applied to meet a set of criteria which ensure that the services have achieved the acceptable level as set by guidelines and standards. Unfortunately, there were no data in any register at health facilities that recorded quality events, quality materials, and quality metrics which can be linked to the measurement of quality of services. This is an area that needs more attention.

Nepal has adapted all recommended registers from WHO. These registers include all variables and interventions related to good pediatric HIV care and treatment; and are available at all selected facilities. However, these tools are not filled in regularly with complete data. Only one facility was moving to electronic system.

The fact that the government wished that the assessment be limited to the health facilities that had big number of people living with HIV, could limit the real picture of overall regions, because data from these facilities excluded data from other health facilities in the study. However, as the excluded data represented not more 10% than of the total number of PLHIV seen during this period of the study, we estimated that the impact of this bias was minimal.

**CONCLUSION**

Few facilities collect DBS and few children receive PCR tests with limited linkage to ART. This has led to late ART initiation, comorbidities, including TB coinfections, and poor outcomes. The results indicate that there are opportunities for improving HIV case finding among HIV-exposed infants in PMTCT, EPI, TB, and nutrition services if provider initiated testing and counselling at the point of service delivery are institutionalized in these settings (Tables 4 and 5).

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**Conflicts of interest**

There are no conflicts of interest.

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