Rapid testing at labor and delivery to prevent mother-to-child HIV transmission in developing settings: issues and challenges

Nitika Pant Pai† & Marina B Klein

Worldwide, approximately 2.5 million children (95% CI: 2.2–2.6) are living with HIV infection. In 2007 alone, approximately 420,000 children (95%CI: 350,000–540,000) were newly infected with HIV – a vast majority of these infections were acquired through maternal–fetal transmission. Many of these infections could have been reduced by timely diagnosis and the delivery of interventions aimed at preventing mother-to-child HIV transmission. This perspective examines the attitudes preventing women from accessing HIV testing early on during pregnancy and the issues and challenges that remain in the institutionalization of interventions to prevent mother-to-child HIV transmission at labor and delivery. Socio–cultural and economic factors prevent women from accessing testing at an opportune time during pregnancy. In addition, a lack of adequate infrastructure often prevents timely delivery of interventions to those who access testing at the last minute (i.e., during labor and delivery). In the wake of a pediatric HIV epidemic and the need for lifelong provision of antiretroviral therapy to infected children, a simple strategy for provision of round-the-clock rapid testing and counseling services in the labor rooms may be cost saving to the healthcare systems worldwide.

Globally, the prevention of mother-to-child HIV transmission (PMTCT) during labor, delivery and during breastfeeding are key to averting a pediatric HIV epidemic [1,2]. According to the modeling estimates from Kourtis et al., approximately 80% of HIV transmission occurs during the late stages of pregnancy, including the labor and delivery period [3]. In 2007 worldwide, approximately 2.5 million children (95% CI: 2.2–2.6) were living with HIV, of which approximately 420,000 children were newly infected with HIV [101]. A vast majority (85–90%) of these infections were acquired through mother–child transmission.

With the aim of reducing HIV transmission, the WHO recommends provision of PMTCT services to pregnant women worldwide. Although the WHO draws up expert guidelines and provides support to countries for achieving targets and implementing guidelines, various national governmental organizations and/or international donor organizations provide services (or in some cases the women may pay for these services themselves). The PMTCT services include elective cesarean sections, provision of antiretroviral therapy during pregnancy, labor and postpartum, CD4 testing and infant prophylaxis [102]. In women who do not breast feed, the combination of such interventions is known to reduce HIV transmission to 1.4–10% [102]. However, in order to maximize the benefits, timely administration of these interventions is essential. Often, despite availability, women fail to receive these interventions [3]. A vast majority of HIV+ women live in sub-Saharan Africa, where antenatal coverage levels are relatively low. In some rural settings, women prefer home delivery and only present to hospital at the last minute for difficult labor. Anecdotal reports from India suggest that these ‘unregistered’ women constitute a large proportion delivering women [4]. In addition, factors such as failure to ascertain serostatus during early pregnancy or even during labor [5], presentation with emergent obstetric/maternal complications [4], and lack of infrastructure for testing and counseling services in the labor room are further barriers in service delivery [4]. Not surprisingly, therefore, only 8–10% of women worldwide (primarily from developing settings) report having received PMTCT interventions [4,6,7].

This perspective examines barriers preventing women from accessing testing early during pregnancy and evaluates the challenges in accepting and receiving testing, and in the provision of round-the-clock rapid HIV testing.
and counseling services. Although much of the focus in this perspective is on women in under-resourced settings in the developing world, many of the issues may also be directly relevant to antenatal settings in the developed world. In addition, this review will not apply to the large numbers of women in low-income settings who do not deliver in public healthcare facilities.

**Barriers to seeking testing & counseling services in pregnancy (including intrapartum period)**
Factors that prevent women from seeking HIV testing during pregnancy may be classified into three broad categories: socio–cultural, economic and infrastructural.

**Socio–cultural factors**
Socio–cultural factors that deter women from accessing HIV testing during pregnancy include:

- Fear of social ostracization
- Fear of partner notification [8]
- Risk of domestic violence including intimate partner violence [8–11]
- Lack of social support at home, from spouses and partners [12]
- Lack of knowledge on benefits of timely HIV testing and of delivery of interventions
- High preference for home delivery, for example, as seen in rural Indian and African women [4]
- Lack of trust in the HIV test result [8]

This lack of trust is related to the occurrence of falsely reactive rapid HIV tests [13–15].

**Economic factors**
Economic factors can be classified into macro- and micro-level factors. Macro-level factors include a lack of public health infrastructure in which HIV testing would be provided. Micro-level factors include lack of transportation to a test center, loss of daily wages, lack of money and childcare services.

**Infrastructural factors**
Availability of rapid tests & personnel in the labor room
An irregular supply of rapid test kits, use of old technology-based tests requiring lab technicians at odd hours, the absence of a dedicated team to deliver interventions and overall poor quality care in the hospitals are barriers in the provision of HIV testing [4,16].

**Availability of round-the-clock counseling in the labor room**
Although counseling is a challenging endeavor in the labor room [17,18], provision of the two-stage counseling sessions, in other words, short prepartum and extended postpartum counseling sessions tailored to the needs of the women in labor have been met with success [4,19]. Informed consent for HIV testing is difficult to obtain in an overburdened and overcrowded labor room [17]. However, patient-tailored approaches geared at maintaining privacy and confidentiality increase the number of women who choose to be tested for HIV [4].

**Presence of an adequate time window to deliver interventions in the labor room**
It is often the case that owing to a lack of an adequate ‘time window’ to deliver PMTCT interventions, and in the event that a patient presents with emergent and life threatening obstetric indications, HIV testing in the labor room is not prioritized and interventions not delivered [16].

**Identifying pregnant women in need of testing**
It is important to identify women who often do not seek antenatal services on time. These women include: those who decline prior HIV testing, those who suspect exposure to HIV at a later stage in pregnancy, those who seroconvert during pregnancy or those who have a high-risk behavioral profile and may require repeat testing for HIV earlier than labor and delivery. Early and timely identification of these women could be made possible by offering routine testing at their second visits unless they refuse or show documentation of prior testing results. Such strategies may mitigate the burden of undiagnosed HIV infection in women who present for testing only at labor and delivery.

**Example of round-the-clock labor room testing & counseling program from rural India**
In a recent study, we investigated the impact and feasibility of providing round-the-clock, rapid, point-of-care HIV testing and introducing two-stage counseling services (i.e., short prepartum and an extended postpartum counseling session) to pregnant women in labor [4]. We successfully tested 1222 out of 1252 women (98%) with rapid oral HIV and finger stick tests. Of the 1222 women that were tested, 54% presented with no history of a previous HIV test and 82% of women were not confident of their test
results prior to the study. As a result of the study, 15 women were diagnosed with HIV infection and received interventions, including 11 newly detected infections at delivery. The total time from enrolment to provision of interventions was 40–60 min. In a resource-constrained setting we demonstrated the feasibility of round-the-clock testing and counseling to women in labor [4]. A substantial number of women availing testing and received PMTCT interventions as a result of this program.

To date, numerous research studies conducted in developed (i.e., USA and Canada) and developing (i.e., Brazil, Mexico, Cameroon, Russia, Rwanda, Nigeria, Uganda, Zambia, Peru and India) settings have demonstrated successful implementation of a rapid HIV testing program in labor and delivery [19–28].

Challenges in the implementation of interventions
In an editorial, Celentano et al. discusses the institutionalization of these interventions in countries where public health resources are limited [29]. In US and African settings, the use of rapid tests compared with conventional tests were found to be time and cost effective in labor and delivery settings [28,30–33]. However, in an overburdened public healthcare system with limited resources, additional infrastructural resources (i.e., round-the-clock availability of counselors and user friendly, accurate rapid tests) are needed to offer these interventions on a regular basis. In addition, team preparedness, protocols for patient management and procedures for referral and on-site confirmatory testing services have to be in place. Arguments against the provision of such a strategy fall short, if we keep the following issues in mind: lifelong treatment for pediatric HIV infection [29]; risk of undiagnosed HIV infection in women of child-bearing potential; management of advanced HIV infection in women, infants and their partners; the likelihood of HIV transmission to their regular and casual partners, and among their sexual network within their communities [29].

Issues to consider with rapid point-of-care tests
The Mother-to-Infant Rapid Intervention at Delivery (MIRIAD) study in the USA was the first large study to successfully demonstrate that the implementation of a rapid testing strategy was a possibility in labor rooms across the USA [23]. Following its success, the CDC recommended diagnosing women with unknown serostatus with the fastest method available for labor and the delivery room [34–37]. To do so, rapid point-of-care tests are now being used in the USA. Although most rapid point-of-care tests, (i.e., oral fluid-based and blood-based) have high diagnostic accuracies, (99.5–99.9% sensitivity and 99.5–100% specificity), it is possible, sometimes, to obtain false-positive and false-negative results with them [34,38].

Recently, false-positive test results were reported with oral fluid-based tests in New York, USA [14]. False-positive test results depend on the prevalence of disease and the level of risk of HIV in the population tested and the predictive values of the test [39]. False positive results may occur in a population with low prevalence of HIV, and with a low-risk profile. Conversely, false-negative results may occur when a patient is in the window period and is seroconverting. Some false-positive and false-negatives results are inevitable, and these possibilities are to be communicated to the patients prior to testing.

In order to reduce the likelihood of the occurrence of false-positives and false-negative results, it may be advantageous to test patients using dual tests in a parallel testing strategy, even in resource-constrained settings [39]. This strategy, albeit costly, is more accurate in comparison with the use of single tests or a serial testing strategy [39,40], but ensures a certain level of safeguard towards occurrence of false test results. With either strategy, the test results are to be considered preliminary positive and confirmatory testing with reference standards (i.e., dual ELISA, or dual ELISA and western blot or ELISA and western blot) is necessary.

It is also important while conducting rapid tests to have the necessary protocols in order to obtain confirmatory test results in a short time (<1 day). It is pertinent to have ELISA (with p24 antigens) tests available on site, especially for women who miss the intervention owing to a false-negative rapid test result. Testing with either another rapid test or an ELISA may discover this. In instances where indeterminate western blot results are obtained, HIV/RNA testing should be considered [14,41]. HIV/RNA testing is expensive for developing settings; in this instance dual ELISA is sufficient for confirmatory tests. However, in resource-constrained settings, a result of high costs of confirmatory tests, it is better to err on the side of treating the patient than miss delivering the intervention. These possibilities (i.e., test limitations, delivery of interventions and treatment) have to be communicated to the patient and their family members during labor.
A recent meta-analysis has discussed the implications of these rapid test results on diagnostic accuracy [39]. Furthermore, the type of algorithm, reference standards and rapid tests impact on the diagnostic accuracy of a rapid test [38,39]. Appropriate education, awareness, explanation of consequences of test errors and patient management by the counselors is essential in order to increase trust and confidence in the test result. As well as educating patients, counselors and health professionals require training and information on handling these occurrences in field settings. Rapid tests are convenient testing platforms, but if quality assurance and quality control procedures are not in place, then invalid, indeterminate, false-negative/positive test outcomes are more likely to occur. The specificities and sensitivities of rapid tests are fairly high (i.e., Determine® rapid HIV test [Inverness Medical Innovations, USA] has a sensitivity of 100% and specificity of 100% and Oraquick® ADVANCE HIV1/2 rapid test [OraSure Technologies Inc., PA, USA] has a sensitivity of 99.6% [95% CI: 98.9–99.8] and specificity of 99.9% [95% CI: 99.6–99.9]). The CDC have detailed procedures for ensuring quality assurance and quality control procedures on site, and wherever possible, training health professionals with these guidelines should be emphasized.

**Issues with patient management**

Patients should be informed of the possibility of inadvertent delivery of interventions (i.e., cesarean section) in false positives, and the possibility of missing delivery of interventions (i.e., antiretroviral therapy administration) in false negatives [38]. In women presenting with ruptured membranes, or in those in active labor, there is clear evidence that an emergent cesarean section is not beneficial for HIV prevention [42,43]. In such cases, individual patient management should be optimized depending on local resources and local management protocols. A recent paper by Rahangdale et al. adequately describes this need for optimization of services in the context of resource rich settings [34]. In resource-constrained settings, hospital-specific, site-specific and country-specific protocols must be aimed at optimizing benefit.

**Issues with partner notification**

Most women fear facing the social consequences of a positive HIV test result [17]. To overcome this issue, partner education, awareness of the spread and management of disease, along with notification, may help reduce the risk of domestic violence. A few studies from India and Africa have also demonstrated that provision of social support, primarily by husbands or partners has led to an improved uptake of testing during pregnancy [9,17,44]. Although, a recent paper by Homsey et al. reports that partner testing and support was high in the intrapartum setting in Uganda [45], in another paper, the same author argues the need for partner consent as the main reason for opting out of routine testing for PMTCT in HIV in Uganda [46]. To summarize, partner consent, partner support and involvement for testing are key to sustainable and successful implementation of PMTCT programs, and should be tried wherever feasible.

**Issues with stigma & discrimination**

HIV testing is highly stigmatized, and discrimination in rural areas has been documented worldwide [9,12,16,47]. Despite this stigma and discrimination, a certain proportion of the population do seek HIV testing. Such differences in health-seeking behaviors require further investigation. There may be rural–urban differences in the perception women have towards HIV testing and seeking interventions [17]. Factors preventing women from asking for an HIV test from the health professionals during labor have not been explored in the rural context. These differences in health-seeking behavior may not only be related to fear of reprisal and violence in rural settings, but also a genuine lack of awareness concerning HIV treatment, knowledge about prevention of transmission to their babies and lesser power in marital relationships to seek such interventions. Similarly, factors deterring educated, informed urban women from getting tested also require further study.

It is also important to reiterate and replay messages tailored to increasing the general awareness of PMTCT. Raising the bar for knowledge requires effective mobilization of local television and media resources. Messages endorsing seeking treatment and testing by movie celebrities and television personalities are effective in this regard. Messages that insist on asking for an HIV test even in labor, and requesting women preferring home delivery to seek HIV testing, may help change attitudes with respect to testing per se in seeking interventions.

**Using locally available resources to optimize delivery of interventions**

Ideally, we should expect every pregnant woman to receive care during the first trimester to avail the entire range of services offered by an
interventions for PMTCT and over 82% women and children were delivered by traditional birth attendants. This was demonstrated successfully in an innovative program using traditional birth attendants to provide PMTCT services in rural Cameroon [24]. This program involved providing training to birth attendants to perform HIV testing using Oraquick and provide nevirapine for PMTCT in positive women. A total of 30 traditional birth attendants tested and counseled over 2300 women in 20 villages [24]. Of 82 women found to be HIV positive, 42 women were delivered by traditional birth attendants and over 82% women and children received interventions for PMTCT [24]. The program provides an excellent example of using locally available manpower and resources to provide sustainable health interventions. In other countries with high rates of HIV infections, innovative research programs are needed to engage midwives or other paramedic health professionals in the provision of antenatal HIV testing and PMTCT. This may also include raising their salaries and providing additional training, which has been as successfully carried out in Uganda and Tanzania [24]. However, offering monetary incentives to midwives, could potentially lead to inadvertent promotion of HIV testing without consent or testing under coercion. In addition, there is a need for qualitative studies with in-depth interviews, as well as focus group discussions for pregnant women who prefer home delivery in order to advance the understanding of their health needs, and set priorities and barriers towards designing services tailored to their needs and circumstances.

Cost–effectiveness of rapid point of testing in labor initiatives

Although it has been demonstrated that rapid testing in labor is cost effective [28,30], the evaluation of novel innovative programs in country-specific contexts has not yet been done. Future models for cost–effectiveness may factor in variables such as the use of midwives, trained birth attendants, paramedical health professionals for creating a sustainable model of health delivery, and comparison of early testing in pregnancy with delayed testing in pregnancy. Dynamic cost–effectiveness models are needed to help justify economic arguments for including the best strategy for a given setting [48]. Context-specific, country-specific, culturally sensitive interventions tailored to the needs of the

Executive summary

Background

- Approximately 80% of HIV transmission occurs during the late stages of pregnancy, labor and at the delivery period. Pregnant women often present with undiagnosed serostatus at labor in both developed and developing countries. In order to prevent mother-to-child HIV transmission (PMTCT), interventions recommended by the WHO are made available in many resource-constrained settings. As yet, their delivery has been suboptimal; to date, only 8–10% of women report having received these interventions on time.

Issues & challenges

- Aside from socio–cultural factors such as stigma and discrimination, a fear of partner violence, economic factors at macro- and micro-levels, and infrastructural factors deter women from accessing HIV testing early on in their pregnancy. Owing to a shortage of adequate personnel on site, lack of an adequate time window, and the limited availability of counselors and paramedic staff who can deliver rapid HIV tests, women during labor and the delivery period are prevented from using PMTCT interventions. To institutionalize labor room testing, the infrastructural resources listed above, as well as protocols for patient management, team preparedness and an adequate time window (2–4 h) to deliver interventions are necessary prerequisites. The strategy of provision of labor room testing may be cost effective compared with the costs involved in managing and treating life-long HIV–infected children and undetected untreated HIV in women.

Conclusion

- Besides infrastructural resources needed to deliver testing and counseling in the labor ward, four recommendations have been proposed to facilitate the delivery of care for women in labor. First, an enhanced use of media to raise the knowledge levels and request women who prefer home delivery to seek PMTCT interventions. Second, the use of traditional birth attendants and local paramedical professionals. Third, the involvement of male partners in expanding the provision of testing and counseling. Fourth, the support of innovative research programs to enhance the delivery of service. Evidence from several resource-constrained settings seems to suggest that rapid testing during labor and delivery is a possibility; what is needed is the political will to implement it in local settings. If prevention of pediatric HIV is to be prioritized, then, in the long run, this simple cost-saving strategy may be beneficial to many healthcare systems worldwide.
population provided for by a given care facility will ensure sustainable and effective delivery of the optimized interventions.

Future perspective

Although routine opt-out testing and labor room testing initiatives have been attempted in some countries [3,4,7,20,40,45,49], the overall coverage of testing services in the labor rooms is quite unsatisfactory [27]. To encourage women to access testing early on and in labor, some of our recommendations may be considered by policy experts. These may help raise the current level of awareness and education, especially in rural women who may always prefer to deliver at home and do not consider getting tested at the hospital. These recommendations are:

- Enhanced use of media (i.e., campaigns, local TV and newspapers) to raise the bar of knowledge of these interventions;
- Offering monetary incentives to midwives and traditional birth attendants (i.e., raising their salaries for each additional case notified) for service delivery [24];
- Greater partner involvement: spouses, partners and significant others must be asked to get involved and to participate and enhance HIV testing;
- Innovative research programs: locally tailored and culturally sensitive to enhance service delivery – in other words, training locally available man power, using minimal resources geared towards sustained delivery of available interventions with minimal increment in costs.

Furthermore, increasing testing of women as early as possible in pregnancy would be ideal and desirable. Intrapartum testing should be the strategy on reserve, aimed at groups of women who do not access antenatal testing early on in the course of pregnancy. Finally, evidence from several resource-constrained settings suggests that rapid testing during labor and delivery is a possibility, but a political will to implement it in local settings is necessary.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties. No writing assistance was utilized in the production of this manuscript.

Bibliography

Papers of special note have been highlighted as:

• of interest
•• of considerable interest

2. Comprehensive review summarizing the literature in the prevention of mother-to-child HIV transmission (PMTCT) that includes a figure modeling the probability of HIV transmission throughout pregnancy and the postpartum period.
•• Large study from India evaluating an innovative 24/7 oral rapid HIV testing and counseling program for women in labor.
• Provides an overview and a sound critique of issues and challenges in PMTCT worldwide.
• Provides a Ugandan perspective of challenges in PMTCT based on study experiences.

**Provides an Asian perspective on barriers in accessing HIV testing and challenges in improving the uptake of PMTCT interventions.**


**Landmark study from the USA, the largest rapid testing in labor to date.**

A Ugandan experience in PMTCT utilizing available resources for the delivery of interventions – example of innovative research.


A Ugandan experience in PMTCT utilizing available resources for the delivery of interventions – example of innovative research.


Websites


Affiliations

• Nitika Pant Pai
Immunodeficiency Service, Montreal Chest Institute, McGill University Health Center, Montreal, Canada
Tel.: +1 514 934 1934 ext. 32146
Fax: +1 514 843 2092
nitika.pai@mail.mcgill.ca

• Marina B Klein
Immunodeficiency Service, Montreal Chest Institute, McGill University Health Center, Montreal, Canada
Tel.: +1 514 934 1934 ext. 32306
Fax: +1 514 843 2092
marina.klein@mcgill.ca