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CLINICAL RESEARCH / KLİNİK ARAŞTIRMA

Pregnancy and Neonatal Outcomes Among Women Living with HIV: A Multi-center, Descriptive Study in Turkey

HIV ile Yaşayan Kadınlarda Gebelik ve Yenidoğan Sonuçları: Türkiye'de Çok Merkezli, Tanımlayıcı Bir Çalışma

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Abstract

Objective: Most new confirmed cases in our country consist of young people in the 20-35 age group, which corresponds to the reproductive age in women. This study evaluated the impact of diagnosing and treating human immunodeficiency virus (HIV) during pregnancy on vertical transmission and birth outcomes.

Methods: This multicentred descriptive study assessed the pregnancy and delivery process, prevention and treatment practices, breastfeeding and perinatal transmission rate.

Results: Of the 55 pregnancies in women living with HIV, only 58.2% had HIV status, 81.2% were under antiretroviral therapy, and 46.2% needed treatment change. Lamivudine/zidovudine + lopinavir/ritonavir (32.7%) and tenofovir/emtricitabine + lopinavir/ritonavir (24.5%) were the two most used regiments. The mean duration of treatment in women starting the treatment during pregnancy was 19.5±7.9 weeks. Viral suppression at the delivery was similar among women who initiated treatment before and during pregnancy (p=0.659). Additionally, 89.1% of women were undetectable status (<50 copies/mL); however, 2% of them had >400 copies/mL at the delivery, and three newborns (5.5%) had HIV infections. None of the newborns had congenital anomalies.

Conclusion: Our study findings revealed that addressing HIV status within routine pregnancy follow-ups and providing effective treatment before or starting from the early stage of the pregnancy have a crucial effect on protecting from the vertical transmission.

Keywords: HIV, acquired immunodeficiency syndrome, pregnancy, women, viral load

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Öz

Amaç: Ülkemizde teyit edilen yeni vakaların çoğunluğu kadınlarda üreme çağına denk gelen 20-35 yaş grubundaki gençlerden oluşmaktadır. Bu çalışma, hamilelik sırasında insan bağışıklık yetmezlik virüsü (HIV) teşhisi ve tedavisinin dikey geçiş ve doğum sonuçları üzerine etkisini değerlendirmeyi amaçladı.

Yöntem: Çok merkezli tanımlayıcı çalışma plandı. Gebelik ve doğum sürecini, önleme ve tedavi uygulamalarını, emzirmeyi ve perinatal bulaşma oranını değerlendirdi.

Bulgular: HIV ile yaşayan 55 gebenin sadece %58,2'si HIV durumunu biliyordu, %81,2'si antiretroviral tedavi kullanıyordu ve %46,2'si tedavi değişikliğine ihtiyaç duyuyordu. Lamivudin/zidovudin + lopinavir/ritonavir (%32,7) ve tenofovir/emtrisitabin + lopinavir/ritonavir (%24,5) en çok kullanılan iki rejimdi. Tedaviye gebelik döneminde başlayan kadınlarda ortalama tedavi süresi 19,5±7,9 hafta idi. Doğumda viral baskılanma, gebelik öncesi ve gebelik sırasında tedaviye başlayan kadınlarda benzerdi (p=0,659). Ayrıca, kadınların %89,1'i saptanamayan HIV RNA durumuna sahipti (<50 kopya/mL); ancak %2'sinde doğumda >400 kopya/mL ve üç yenidoğanda (%5,5) HIV enfeksiyonu vardı. Yenidoğanların hiçbirinde konjenital anomali yoktu.

Sonuç: Çalışma bulgularımız, rutin gebelik takiplerinde HIV durumunun ele alınmasının ve gebeliğin erken döneminde veya erken dönemden itibaren etkin tedavinin sağlanmasının vertikal bulaştan korunmada önemli bir etkiye sahip olduğunu ortaya koymuştur.

Anahtar Kelimeler: HIV, edinilmiş immün yetmezlik sendromu, gebelik, kadın, viral yük

Introduction

As part of the continuing global human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) epidemic, approximately 38 million people are thought to live with HIV by 2022. Women and girls comprise nearly half of all these cases, and children between 0 and 14 years comprise 1.7 million cases[1]. Women have a special place in HIV epidemics because they may transmit the disease to their children. Among children under 15 years of age, the main cause of infection is the transmission from mother to child[2]. The more widespread availability of antiretroviral treatments and measures aimed at reducing the vertical transmission has resulted in a 31% decrease in newly diagnosed cases of HIV infection and a 53% decrease in newly diagnosed pediatric cases with HIV infection since 2010. In 2020, 84% of individuals living with HIV knew their HIV status, 79% of women aged 15 and 85% of pregnant women could access antiretroviral treatment[1]. Nevertheless, a total of 160,000 children under five years were newly diagnosed with HIV, the most common source of infection being women who did not receive antiretroviral therapy (ART) during pregnancy or women who were infected recently or during the breastfeeding period[3]. In Turkey, an HIV screening test is a part of the routine pregnancy follow-up. It is recommended to perform the test in the early stages of pregnancy and repeat it in the last trimester in high-risk pregnant women. Measures and treatments to prevent perinatal transmission are accessible and free to all pregnant women. In the first available national guidelines published in 2013, the first line recommended regimen was zidovudine (ZDV)/lamivudine (3TC) plus nevirapine or lopinavir/ritonavir (LPV/r). While in the latter guideline, which was available since 2019, treatment options were changed; ZDV/3TC and nevirapine were removed, tenofovir/emtricitabine (FTC) and abacavir/3TC plus darunavir/ritonavir or raltegravir (RAL) was recommended[4,5]. Although our country represents a low-endemic area, a notable increase in the number of individuals living with HIV has occurred recently. Twenty seven thousand seven hundred and sixty five cases were reported in 1985 and November 30, 2020, and 19% of the cases in women. Although the reported cases of vertical transmission is very low (191 patients, 0.69%), 10 new cases between 0 and 14 were detected in 2020[6].

The main causes for the increase in HIV, AIDS, and other sexually transmitted diseases in Turkey is the lack of sexual education in schools and scientific information on safe sex outside school, sex tourism originating from eastern Europe and the awareness of HIV. Additionally, multiple sex partners, poor condom use, finding HIV-positive partners from internet-based applications and drugs that increase sexual performance may also play a role among MSM's[7-9]. Prevention of perinatal HIV transmission is based on the use of ART during pregnancy, suppression of viral load before labor, administration of intravenous (IV) ZDV during labor if necessary, performing a cesarean section if indicated according to the maternal plasma viral load, and antiretroviral prophylaxis of the newborn[5]. Complete suppression of the viral load at delivery reduces the perinatal transmission rates by 0-0.5%[10].

More women with HIV positivity want to have a baby because of the availability of effective ART options and increased life expectancy. However, more than half of these cases do not receive adequate consultancy before pregnancy[11-13]. Due to

the recent increase in the number of cases living with HIV, including women in our country, pregnant women with HIV have also increased. However, the outcomes of HIV infection in mothers and their children are very limited in Turkey[14-16]. This study was undertaken to evaluate the course of pregnancy, prophylactic measures in mothers and children, and perinatal transmission rates using clinical and laboratory assessments among women diagnosed with HIV infection or during pregnancy.

Materials and Methods

This descriptive study was conducted at seven academic centres and research hospitals in Turkey. Women attending HIV outpatient units between January 1990 and December 2019 who were diagnosed with HIV infection before or during pregnancy or at the time of labor and live births were included. Except for the first date of inclusion, no other exclusion criteria were applied. The following descriptive variables were examined: nationality, age, planned versus unplanned pregnancy, method of conception, ART usage and regimen, CD4 + T lymphocyte counts at the time of diagnosis and birth, HIV RNA count, route of delivery, use of prophylaxis by the mother and child, breastfeeding status, and HIV-infection status of the child. A standardized form for collecting these variables was sent to all participating centres. The study data were retrieved from patient files and a digital hospital database. The study was approved by the University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital Training and Research Hospital Ethics Committee (decision no: 2021/05-41, date: 17.05.2021).

Statistical Analysis

Descriptive statistics were expressed as number and percentage for categorical variables, as the mean and standard deviation for continuous variables with a normal distribution, and as median and 25th and 75th quartiles for continuous variables without normal distribution. Pearson's chi-square or Fisher's exact test compared categorical data. Continuous variables without normal distribution were compared with the Mann-Whitney U test. Analyses were carried out using Statistical Package for the Social Sciences 22.0 software pack (IBM Corporation, Armonk, New York, United States), and a p level of <0.05 was considered statistically significant for a two-sided p-value.

Results

This study examined 55 pregnancies in 48 women living with HIV. The diagnosis was made before pregnancy in 58.2% (n=32), during pregnancy in 36.4% (n=20), and at the time of labor in 5.5% (n=3). In one case, an anti-HIV test was negative at the beginning of pregnancy, followed by an acute HIV infection during the following course of pregnancy. Only 32.8% of pregnancies were planned. The most common method of conception was unprotected sexual intercourse in 96.4% (n=53). Two pregnancies occurred after sperm wash and in vitro fertilization.

Sociodemographic Characteristics of Pregnant Women

The mean age was 29.42±6.31 years (range: 14-41 y), and 36 cases (%75) had Turkish citizenship.

Basal Viral Load, CD4 + T Lymphocyte Count, and Treatment Status

In 32 of the 48 pregnant women who had complete data at the time of initial diagnosis, the basal median HIV-RNA was 69.850 copies/mL (25-75%=11.639-117.500; min=3.168-max=20,924,956 copies/mL); 34 patients had data for basal CD4 + T lymphocyte count, and median was 305.5 cells/mm^3 (25-25%=225-468.7; min=8-max=1,394 cells/mm^3). CD4 + T lymphocyte count was <200 cells/mm^3 in 7 women, who were considered to have AIDS. Of the 32 women diagnosed before pregnancy, 26 (81.2%) received ART, while the corresponding figure for all pregnancies was 47.2%. Treatment regimens are presented in Table 1. The proportion of women receiving ART before pregnancy was 15.4% (n=2/13) among non-Turkish citizens, while it was 57.1% (n=24/42) among Turkish citizens (p=0.008). All the 20 women who were diagnosed during pregnancy started ART. Women who received an integrase inhibitor [dolutegravir (DTG) or RAL] for the first time during pregnancy were diagnosed in the third trimester (n=3).

HIV Viral Load, CD4 + T Lymphocyte Count, and Treatment Status During Pregnancy

At the time pregnancy was diagnosed, 45 of 55 women whose medical records were available, 22 (48.9%), had a negative viral load (<50 copies/mL) and were all receiving ART. In the remaining 23 pregnant women with detectable viral load (range=51-20,924,956 copies/mL), 3 were diagnosed with HIV at delivery, 15 were diagnosed during pregnancy, and 5 were diagnosed before pregnancy. The mean CD4 + 4 lymphocyte count at the time of pregnancy test was 427 cells/mm^3 (25-75%=298.7-598; min=139-max=1245 cells/mm^3) for 40 women with available medical records. Except for 3 patients whose seropositivity was first detected during delivery and 3 patients (2 non-Turkish citizens) diagnosed

before pregnancy, all patients (n=49.89%) were found to receive treatment. The mean time of ART initiation during pregnancy was 18 weeks (6-32). ART was initiated in the first, second, and third trimesters in 6, 12, and 5 cases, respectively. The mean duration of ART was 19.5±7.9 weeks. Of the 26 women who started treatment before pregnancy, 14 (53.8%) continued their existing ART regimen, whereas 12 (46.2%) had a treatment switch. The most common treatment switch was from FTC/tenofovir disoproxil fumarate (TDF) + efavirenz (EFV) (n=6) to ZDV/3TC + LPV/r (n=3) or TDF/FTC + LPV/r (n=2). In one patient receiving DTG, a switch to raltegravir was made. A total of 4 received EFV (1 throughout pregnancy, 3 at the end of the first trimester), and 7 received DTG (4 throughout pregnancy, 3 in the last trimester).

HIV RNA and CD4 + T Lymphocyte Count at the Closest Time to Delivery and Obstetric Follow-Up

Of the 46 of the 49 women whose medical records were available, 89.1% (n=41) had a viral load of <50 copies/mL, 8.7% (n=4) had a viral load of 51 to 400 copies/mL, and 2.2% (n=1) had a viral load >400 copies/mL. The viral suppression (viral load <50 copies/mL) proportion before delivery in women who initiated ART prior to and during pregnancy was similar (p=0.659). In 46 women whose data were available, median CD4 + T-cell count just before delivery was 455 cells/mm^3 (25-75%=322-652,7; min=158-max=1,016 cells/mm^3). CD4 + T-cell counts before delivery did not show a significant difference among women who did and did not receive ART before pregnancy (p=0.434). In one woman with a twin pregnancy who started ART at 14 weeks of gestation, intrauterine death occurred in one of the fetuses. Additionally, two women who did not receive ART experienced premature delivery, while another case with a pre-delivery HIV-RNA of 100 copies/mL and CD4 + T lymphocyte count of 180 cells/mm^3 had ophthalmic herpes infection.

Delivery, Prophylaxis, and Treatment Status

Only three women had a vaginal delivery, while the remaining (94.5%) had a cesarean section. All three women with vaginal delivery had ART during pregnancy, whereas none received IV ZDV at the time of delivery. Of the 2 pregnant women with medical records, one had a negative viral load, while the other had a viral load of 51 copies/mL. Prophylactic ZDV was given to all newborns born with vaginal delivery, and HIV infection was not detected. At the time of delivery, 52.7% of pregnant women (n=29) received IV ZDV, while 53.7% of the pregnant women with a viral load of < 50 copies/ml received ZDV. Of the newborns, 56.4% (n=31) received ZDV for 6 weeks, 36.4% (n=20) for 4 weeks, 1.8% (n=1) ZDV for 6 weeks and 3 doses of NVP, while 1.8% (n=1) received 5 weeks of ZDV after a one-week interval. However, combined antiretroviral prophylaxis was administered to only one of the 8 newborns with a higher risk (mothers not having ART, detectable HIV RNA at the time of delivery, acute HIV infection) of perinatal transmission. Only 2 babies received prophylaxis, and one of these babies died 12h after delivery. Only 1 mother breastfed her baby, who was consequently to have HIV positivity. Of the 49 women with available data, all received ART after delivery. Among 26 women who received treatment before pregnancy, 12 continued their existing treatment after pregnancy and delivery, while a treatment change was made in 7 during pregnancy, although these women re-initiated the pre-pregnancy regimen following delivery. Among 23 women who started ART during pregnancy, 10 (43.4%) continued their existing treatment following the delivery. The detailed distribution of treatments is shown in the Graphic 1.

Health Outcomes in Newborns

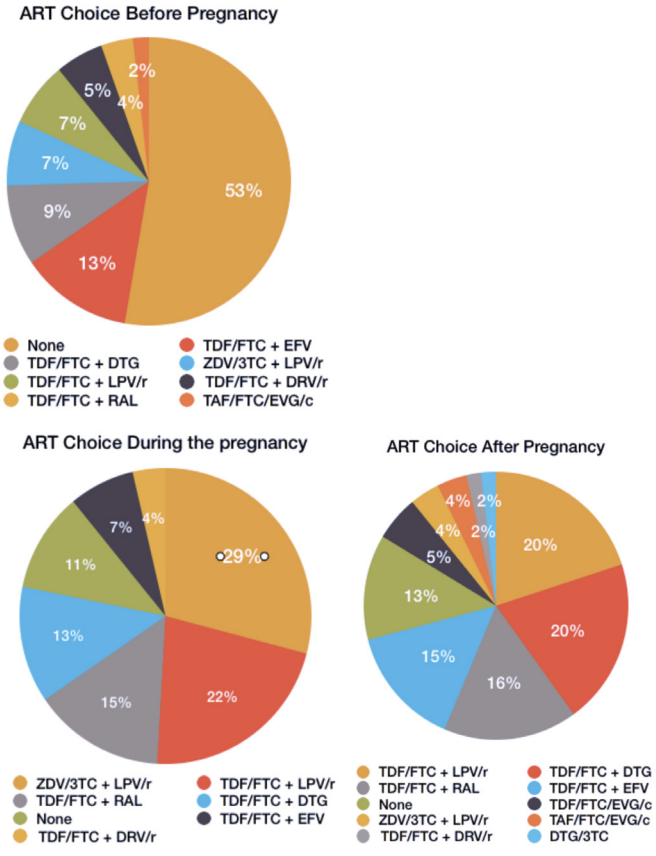
There were 3 newborns (5.5%) with HIV infection in 55 pregnancies. Additionally, the mother of one of these newborns was diagnosed with "acute HIV infection" at delivery time. Table 1 shows the characteristics of newborns and mothers. In one newborn whose mother had an ophthalmic herpes infection during pregnancy, cytomegalovirus retinitis and pneumonia were detected in addition to HIV infection. None of these newborns had neural tube defects or other congenital anomaly types. Unfortunately, one newborn died 12h after delivery. No perinatal transmission occurred in pregnant women who started ART in the 1st or 2nd trimester.

The main characteristics of pregnant women living with HIV and their newborns are presented in Table 1.

Discussion

This study provides crucial data on the course of pregnancy in women living with HIV and the outcomes of newborns in our country and contributes to the limited data pool. The study covers a long time, during which changes in the practice of follow-up, treatment, and prophylaxis approaches occurred in line with the emergence of new scientific data and recommendations. HIV infection is now considered a chronic manageable condition with the introduction of effective ART, which increases the quality and duration of life. This has provoked a more pronounced desire to become pregnant among women living with HIV. Furthermore, recently introduced first-line treatment regimens based on integrase

inhibitors can rapidly reduce viral load, leading to significant changes in approaches toward conception, pregnancy and delivery among women living with HIV, facilitating childbirth in this patient group[17]. In a meta-analysis, 42% of individuals living with HIV reported their desire to have a child, with reported rates as high as 68.9% in some communities[18,19]. Therefore, it is of utmost importance to have planned pregnancies in these women to allow discussions regarding family planning, the desire to become pregnant, risks, gender-specific treatments, pre-intercourse prophylaxis in serodiscordant couples, and to implement best practices possible. In our study, although the pregnancy was planned in more than half of the women diagnosed with HIV before pregnancy, approximately 40% had an unplanned pregnancy, indicating the lack of adequate awareness regarding contraception and the lack of proper medical consultation. In a previous study, 57% of the 159



Graphic 1. The detailed distribution of treatment

ART: Antiretroviral therapy, TDF: Tenofovir disoproxil fumarate, FTC: Emtricitabine, DTG: Dolutegravir, LPV/r: Lopinavir/ritonavir, RAL: Raltegravir, EFV: Efavirenz, ZDV: Zidovudine, 3TC: Lamivudine, DRV/r: Darunavir/ritonavir, TAF: Tenofovir alafenamide, EVG/c: Elvitegravir/cobicistat

Table 1. Main characteristics of pregnant women living with HIV and their newborns

Age of pregnant women (mean)	**29.42±6.31 (14-41) years**
Nationality	n (%)
Turkish	36 (75%)
Non-Turkish	12 (25%)
Diagnosis of HIV infection	n (%)
Before pregnancy	32 (58.2%)
During pregnancy	20 (36.4%)
In time of delivery	3 (5.5%)
Mode of conception	n (%)
Unprotected sexual intercourse	53 (96.4%)
Sperm washing and in vitro fertilization	2 (3.6%)
Started ART before pregnancy	n (%)
Yes	26 (47.3%)
No	29 (52.7%)
HIV RNA	Median (copies/mL)
At the time of HIV/AIDS diagnosis (32 patients)	69.850 (IQR 11.639-117.500)
At the time of pregnancy diagnosis (45 patients)	n (%)
Negative (<50)	A total of 22 (48.9%)
Positive	A total of 23 (51.1%)
Around the time of delivery (46 patients)	n (%)
Negative (<50)	A total of 41 (89.1%)
Positive (51-400)	A total of 4 (98.7%)
Positive (>400)	1 patient (2.2%)
CD4+ T cells	mm^3 (median)
At the time of HIV/AIDS diagnosis (34 patients)	305.5 (IQR 225 - 468.7)
At the time of pregnancy diagnosis (40 patients)	427 (IQR 298.7 - 598)
Around the time of delivery (46 patients)	455 (IQR 322 - 652.7)
Mode of delivery	n (%)
Vaginal delivery	3 (5.5%)
C/S	52 (94.5%)
IV zidovudine prophylaxis	n (%)
Yes	29 (52.7%)
No	26 (47.3%)
Prophylaxis for newborn	n (%)
Yes	53 (96.3%)
No	2 (3.7%)
Breast-feeding	n (%)
Yes	1 (1.8%)
No	54 (98.2%)
HIV status of the baby	n (%)
Positive	3 (5.5%)
Negative	52 (94.5%)

HIV: Human immunodeficiency virus, ART: Antiretroviral therapy, AIDS: Acquired immunodeficiency syndrome, IV: Intravenous, IQR: Interquartile range

pregnant women had no prior discussion with healthcare providers on treatment regimens[12]. The most important determinant of perinatal transmission is the maternal HIV RNA during the antenatal period and delivery. The HIV RNA level should be reduced to an undetectable level before planning a pregnancy or as rapidly as possible after confirmation of pregnancy[10,20]. In a large cohort study, the reported perinatal transmission rates were 0.3%, 1.5%, and 2.8% for viral load levels of <50 copies/mL, 50-399 copies/mL, and >400 copies/mL, respectively[21]. However, although the viral load is a strong predictor of transmission, this is not an absolute risk, with some HIV-negative newborns despite high-maternal HIV RNA levels[22]. Several conditions apart from the plasma viral load may increase the risk of infection, including the presence of HIV-1 DNA in the cervix/vagina, cervical/vaginal ulcers, and prematurity[23]. Although only half of the pregnant women in our study had negative HIV RNA at the time of the diagnosis of pregnancy, in total, the risk of transmission was found to be almost non-existent in more than 90% of the cases owing to ART during pregnancy. A woman with a very high viral load due to acute HIV infection and another woman with an initial HIV RNA=100 copies/mL who had a possible increase in viral load at delivery due to a secondary viral infection close to delivery had babies infected with HIV. However, no perinatal transmission was observed in two other women diagnosed at the time of delivery with viral loads of 21,000 copies/mL and 52,800 copies/mL, respectively. Among three women with a pre-delivery CD4 + T lymphocyte count of <200 cells/mm^3, one had HIV transmission to the newborn. However, whether a low CD4 + T lymphocyte count is a risk factor for perinatal transmission remains controversial. In comparison, one study reported no significantly increased risk of a CD4 + T lymphocyte count of <200 cells/mm^3 measured at 32 weeks of gestation[23,24], another group of investigators reported a 5.4-fold increased risk at a CD4 + T lymphocyte count of <200 cells/mm^3 measured intrapartum[25]. Early control of viral load is one of the most important preventive measures against in utero and intrapartum HIV transmission[24]. In a study, ART initiated during pregnancy was found to reduce the risk of transmission by 8% for each additional week of treatment[26] and in another study, the failure to reach viral suppression at delivery was linked with a shorter duration of treatment[27]. In our study, the viral suppression proportions at the closest time to delivery did not differ significantly between women who started ART or during pregnancy. The possibility of transmission was minimized in approximately 90% of the cases. These findings reveal the importance of early screening in pregnancy and, therefore, early initiation of treatment.

One of the most notable findings of our study was that more than half of our cases used a treatment regimen that included LPV/r. A significant decrease in the number of pregnant women receiving this treatment after pregnancy suggests that this treatment was specifically used during the pregnancy. In most recent treatment guidelines, LPV/r is recommended only for particular circumstances due to difficulties associated with its use, poor pharmacokinetics, association with premature delivery, and the presence of safer alternatives[28-31]. A similar observation was also made for ZDV, which poses practical challenges due to a twice-daily dosing regimen and is also associated with significant side effects. In some patients, with confirmation of pregnancy, a switch was made from TDF to ZDV, although TDF is easier to use and has lesser side effects. One potential explanation may be related to the fact that these medicines remained among first or second-line treatment options in the treatment guidelines issued in 2013 by the Turkish Ministry of Health[4]. Additionally, the retrospective nature of our study with the inclusion of patients who had been followed up in previous years may be another reason for the use of these medicines. During pregnancy, an antiretroviral regimen should ideally exhibit high efficacy with low toxicity, high-transplacental passage, ease of use, and favorable pharmacokinetic properties[28]. Furthermore, due of the rapid reduction of viral load by integrase strand transfer inhibitor in the treatment naive pregnant women, these agents are recommended as a first-line option, especially in the presence of acute HIV infection or in women presenting late during pregnancy[17]. Another crucial consideration during pregnancy relates to the safety of the drug for the baby. In almost half of the women receiving treatment ART before pregnancy, a treatment switch was made in our study. Although viral suppression was achieved in almost all of these cases, treatment was switched, indicating potential teratogenicity concerns. The most frequently switched drug at the pregnancy diagnosis was EFV, which may be related to excluding this agent in previous guidelines issued after reports of congenital defects caused by EFV in primates. However, after it was evident that EFV was not associated with such effects in humans, this agent was re-included in the guidelines.

Similarly, in a study by Zash et al.[32] from Botswana, neural tube defects were more commonly observed in women who became pregnant while receiving DTG, leading to the

rapid inclusion of recommendations against the use of DTG in guidelines. However, during the later courses of the Botswana study, the rate of neural tube defects was reduced significantly, resulting in this re-inclusion[33]; however, it is still not recommended during the conception period. No neural tube defects or other congenital abnormalities were found in babies of all pregnant women in our study, including the 11 patients who received DTG or EFV. Undoubtedly, this number is too small to reach conclusions or provide firm interpretations. Although variable threshold levels have been adopted in different guidelines, HIV RNA of <50 to <100 copies/mL 4-6 weeks before delivery is thought to negate the need for IV intrapartum ZDV. Similarly, HIV RNA of <50 to <1000 copies/mL is generally believed to allow for vaginal delivery despite some variation. EACS guidelines recommend elective cesarean section and IV ZDV treatment at an HIV RNA of > 50 copies. In contrast, British HIV Association guidelines recommend elective vaginal delivery in the absence of obstetric contraindications if HIV RNA is <50 copies/mL at the 36th week of pregnancy[28,31,34]. Physicians should follow the latest guidelines to maintain the best practices.

Previous studies from our country reported a cesarean section rate of 84.4-92.3% among pregnant women living with HIV, while intrapartum ZDV prophylaxis was administered to 73.3-78.1%[14-16]. In our study, in approximately half of the pregnant women with viral suppression, IV ZDV was administered at delivery, and except for three cases, all women underwent cesarean section. Both elective cesarean section and IV ZDV administration rates are higher than expected. This is thought to be due to doctors' legal and medical concerns.

It is encouraging to observe that nearly all babies in our study received prophylaxis. Three babies in our study had HIV infection, with a perinatal transmission rate of 5.5%. Despite the limited number of previous studies, these figures in our country ranged between 6.2% and 8.3%[14-16]. In China, a transmission rate of 0.3% was achieved with prenatal ART use, administration of prophylaxis to the infant, and abstinence from breastfeeding had increased to 36.4% when no preventive measures were taken[25]. In Thailand, the vertical transmission rate was 1% when >95% of pregnant women received treatment during breastfeeding. A transmission rate of 41% was reported in Afghanistan when only 11% of pregnant women could receive ART[35]. Based on WHO data, the perinatal transmission rate is above 10% in many countries[36].

Study Limitations

The most important limitation of our study relates to missing patient data resulting from the retrospective design and the lack of an algorithmic approach to laboratory tests. Another limitation concerns the that the study involved only seven centres from 3 provinces, with a small sample size that interrupts the generalizability of the results. The fact that the centres participating in the study were tertiary level hospitals that follow up and treat patients with HIV may have caused selection bias. However, we think that the effect of this situation is low because HIV tests are carried out in all health institutions in our country, and patients are referred to higher-level centres when positivity is detected. Additionally, there may be observational bias because different nucleic acid amplification tests can be used at different centres. We believe that it does not affect the main findings of our study, as it will not change the treatment indication and prophylaxis practices. This study included patients who were followed up for nearly 30 years. During this time, there have been significant changes in the management of HIV during pregnancy, limiting the interpretability of the results. However, we believe that this study contributes to the limited data on pregnant women with HIV in a real-life setting in Turkey.

Conclusion

As a result, the desire of women living with HIV to have children in our country increases. For this reason, all women, including those who do not plan to become pregnant, should be informed about contraception methods, pregnancy requests and processes, antiretroviral treatment plans and teratogenicity. The treatment regimens recommended as the first choice in the guidelines are available in our country. According to our study results, the main problem is the lack of awareness of the HIV screening test in sexually active women and physicians. The perinatal transmission was not detected in women diagnosed with early pregnancy and who started ART. For this reason, studies should be conducted to raise awareness among women in society, and training should be carried out in hospitals so that physicians do not miss HIV infection during pregnancy follow-up.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital Training and Research Hospital Ethics Committee (decision no: 2021/05-41, date: 17.05.2021).

Informed Consent: Retrospective study.

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Authorship Contributions

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