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Research Article

Challenges in the Management of HIV Positive Pregnant Women in a Romanian Hospital

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Abstract

Introduction: Human immunodeficiency virus (HIV) is a Lentivirus that causes AIDS (Acquired immunodeficiency syndrome). The actual incidence of HIV positive pregnant women in our country remains unknown. A HIV positive women's pregnancy represents a challenge for the obstetrician and for the infectious disease doctor.

Objective: The purpose of this study was to evaluate the incidence of HIV positive pregnant women in our hospital (Cuza Voda Iassy Maternity), the maternal and foetal complications and possible particularities that will help us have a better management regarding this pathology.

Methods: We have conducted a retrospective study from 2013 until 2018. We have studied all the medical documents of these HIV positive pregnancies both the mothers and the new-borns.

Results: The age of most cases was between 20 - 30 years and they were from Iassy county. HIV positive birth incidence was under 0.3%. 20.68% from our patients gaved birth prematurely. Impaired intrauterine foetal growth was higher in the cases with antiretroviral therapy preconceptionally. Hepatitis coinfection was frequent.

Conclusion: We have observed a low incidence of HIV positive births in our hospital, with most of the cases coming from rural areas. A high proportion of these births had complications. It becomes obvious that the severity of the infection negatively influences the evolution of the pregnancy. In cases with monitored pregnancy the evolution had less complications. To obtain a lower vertical transmission rate we need to increase patient's addressability to health care services regardless of costs and social stigma.

Keywords: *HIV; AIDS; Pregnancy; Antiretroviral Therapy*

Introduction

Human immunodeficiency virus (HIV) is a Lentivirus that causes AIDS (Acquired immunodeficiency syndrome). This retrovirus targets the immune system, specifically CD4 T cells, causing immunosuppression and the possibility for development of opportunistic infection and cancer. Because of the extremely efficient antiviral therapy this condition became a chronic illness. HIV infection evolved in time as a pandemic disease. Lifelong treatment, as OMS (World Health Organization) decided in 2013, reduced the risks and the effects of the viral infection but opened the door for the development of antiviral side effects [1-4].

Background of the Study

One of the main causes for new HIV infected patients in our days remains the vertical transmission. Even if the risk for vertical transmission dropped from 35 - 40% to under 2 - 3 by practising C-section, adequate antiviral treatment and no breastfeeding, it still remains significant. Many of HIV positive women in our country reached fertility age and their life-expectancy increased because of the efficient therapy. In Romania many of HIV positive patients are long term survivors, being infected in infancy between the end of '80 and the beginning of '90. The actual incidence of HIV positive pregnant women in our country remains unknown [5-7].

WHO (World Health Organization) classifies this disease in the following stages: stage one (asymptomatic), stage two (mild symptoms), stage three (advance symptoms) and stage four (severe symptoms). The CDC (Centers of Disease Controls and Prevention) classifies it in 3 categories according to the presences of certain infections and diseases: A category (asymptomatic HIV infection), B category (HIV infection with symptoms that are directly attributable to HIV infection) and C category (HIV infection with AIDS defining opportunistic infections). These three categories are further more divided according to the CD4 number in: categories A1, B1 and C1 having the CD4 number above 500 cells/mm^3, categories A2, B2 and C2 having a CD4 number between 200 - 499 cells/mm^3 and the last stages A3, B3 and C3 with CD4 number below 200 cells/mm^3 [8,9].

Objective of the Study

The purpose of this study was to evaluate the incidence of HIV positive pregnant women in our hospital (Cuza Voda Iassy Maternity), the maternal and foetal complications and possible particularities that will help us have a better management regarding this pathology.

Specific Aims and Hypothesis

Our hospital is the greatest maternity hospital in the region of Moldavia. Because of the implementation of a national programme for HIV prevention and treatment in our city, most of the HIV positive pregnant women were directed to give birth here. Our hospital in tight cooperation with The Infectious Disease Hospital 'Sf. Parascheva' from Iassy, ensured the treatment and the infant postexposure therapy after birth.

A HIV positive women's pregnancy represents a challenge for the obstetrician and for the infectious disease doctor. It is hard to manage these cases because of the multiple side effects of the therapy and the actual infection that will negatively influence both the mother and the unborn child.

The treatment for HIV infection has been suspected to cause a high rate of malformations, increase spontaneous abortion, SGA/FGR (small for gestational age/foetal growth restriction), preterm birth, spontaneous premature rupture of membranes. The suspected cause for malformations are the NNRTI (nonnucleoside/nucleotide reverse transcriptase inhibitors) and for premature labour, SGA and FGR the protease inhibitors in HAART (highly active antiretroviral therapy) [10-12].

Also, hepatitis B or C coinfection is another major health problem in Romania. The incidence of these coinfections, HIV and hepatitis B or HIV and hepatitis C is unknown.

Materials and Methods

We have conducted a retrospective study from 2013 until 2018. The inclusion criteria were HIV positive pregnant women with confirmed infection under infectious disease follow-up and the exclusion criteria was HIV positive unconfirmed infection. We have totalised 90 cases. We have studied all the medical documents of these HIV positive pregnancies both the mothers and the new-borns.

Study variables

The complexity of disease staging and the low incidence makes it very difficult to obtain a homogeneous lot of patients.

Statistical analysis

The data obtained were processed using SPSS.

Ethical approval

We have obtained informed consent from these patients to review their medical documents.

Results

Sociodemographic characteristics

The incidence of HIV positive pregnant women births was low, as shown in table 1.

The distribution of cases, depending on the city of provenance from the region of Moldavia is illustrated in figure 1.

Year	Total number of births in Cuza Voda	Number of HIV positive births in Cuza Voda	Percent
2013	5770	17	0.29
2014	5643	11	0.19
2015	5946	91	0.15
2016	6352	5	0.23
2017	6169	16	0.25
2018	6373	17	0.23

Table 1: *Incidence of HIV positive patient births.*

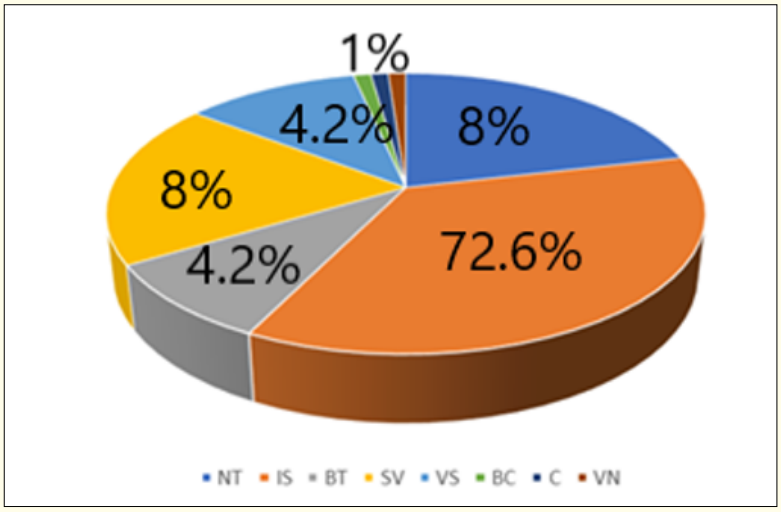

Figure 1: *HIV positive pregnant women distribution in the region of Moldavia.*

Most of the cases were form rural environment, form around Iassy city 72.6%. The majority consists in patients from 20 - 25 years and 25 - 30 years category, as shown in figure 2. They are called long term survivors, being infected in childhood, at the end of 1980 and the beginning of 1990. This was the period in which the first HIV positive child cases appeared. Under adequate antiretroviral therapy these patients have reached fertile age and managed to obtain a pregnancy.

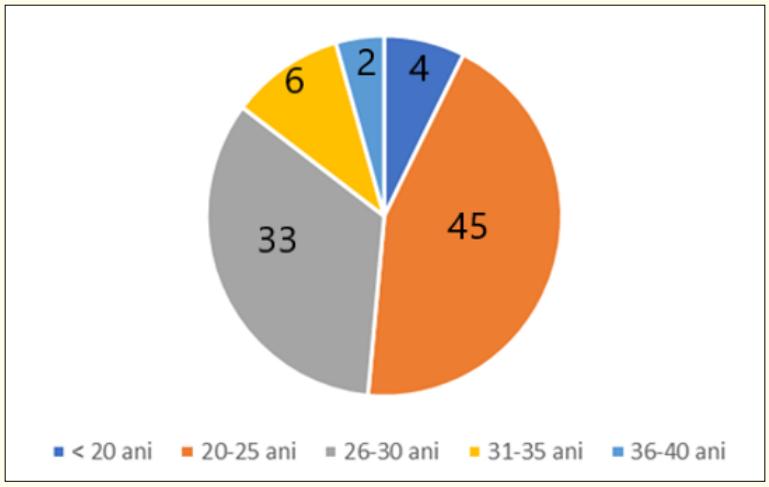

Figure 2: *Age distribution of HIV positive pregnant women.*

Disease stage distribution of cases is represented in figure 3. From our 90 HIV positive patients, 26 of them had an unmonitored pregnancy and 10 of them had their pregnancy partially monitored by an obstetrician.

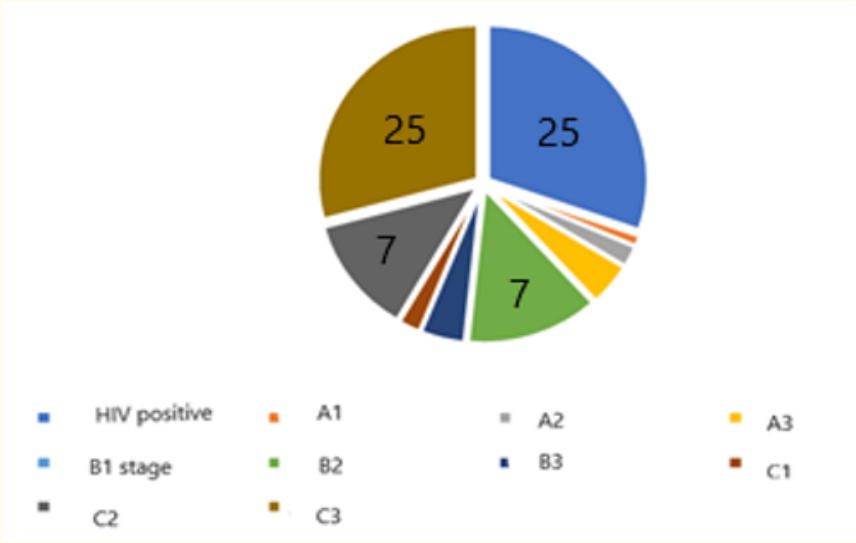

Figure 3: *Disease stage distribution.*

18.8% of cases had hepatitis B coinfection, 1.1% of cases had hepatitis C coinfection and 1.1% both hepatitis and HIV infection simultaneously.

Main variable results

Premature birth is defined as the birth under 37 weeks of gestation. It can be either spontaneous or iatrogenic induced premature birth. A premature birth represents a health care major problem being responsible for almost 70% of perinatal mortality in developed countries. The incidence varies between 7.6 - 12% in these countries, whereas in less developed countries the incidence rises over 15% from total births [10,13]. 20.68% from our patients gaved birth prematurely, most of them at 36 weeks of gestation, only 4 cases with extreme prematurity under 32 weeks of gestation. 4.59% of our cases were iatrogenic premature births: 2 cases because of placenta praevia, one case having a praevia myoma and in the last one the mother had a brain tumour that needed the evacuation of pregnancy and after that therapy for the mother was initiated. The rest of premature births were spontaneous, 22.98% having preterm rupture of membranes caused by untreated vaginal infection.

43.67% of cases had Apgar scores below 9, from these 13.79% having IUGR and a similar percent having acute sufferance with foetal cardiac rhythm pattern modifications.

The incidence of spontaneous abortion was 2.22% in these cases. Studies report a rate of spontaneous abortion in pregnant women without this pathology varying between 10 to 20%. This variation is consecutively to the ability of recognizing the existence of a pregnancy before the abortion [14]. In our case, in which concerns the 90 HIV positive patients from this study, 70% of them being treated with ART (antiretroviral therapy) preconceptionally, we have observed a lower rate of spontaneous abortion then described in literature.

The information about foetal malformation rate in HIV positive pregnant patients under ART are inconclusive, some studies showing a higher rate and some stipulating that the therapy doesn't increase the risk of malformations. Our evaluation established a 3.33% rate of foetal malformations: one of them being major - holoprosencephaly, the rest being minor malformations - cleft palate and congenital strabismus. The rate of congenital anomalies in general population, depending of the region, is between 2 to 3% [15]. In conclusion our study did not detect a higher rate of foetal anomalies in these cases even if 70% of them had ART long time before conceiving. 3.33% of the pregnancies had oligoamnios without foetal sufferance, one case polyhydramnios. 3.33% of the women had uterine malformations detected by ultrasound previous giving birth and confirmed during C-section (bicornuate uterus and unicornuate uterus with rudimentary horn), an incidence not higher than in general population 5.5 - 6.7% [16]. In 4.59% of cases the foetus was in breech presentation, similar with the incidence in general population.

The most frequent pathology associated with HIV infection in our study was HPV (Human papillomavirus) external lesions, genital warts.

The difference between FGR and SGA is quite difficult. We have considered having SGA or FGR a foetus under the 10^{th} percentile of weight or under 2,500 grams. For a higher accuracy we have studied the new-borns medical charts to see if this diagnosis is correct. The new-born's evaluation consists in the Ballard score and the ponderal index calculation. So, 14.94% of the babies were SGA/FGR. The incidence in our hospital of these two pathologies in general pregnant population was between 2.61 and 3.73% in these 6 years as shown in figure 4 and 5.

The rate of FGR/SGA in studies vary between 3 and 7% in general population, in our case the rate in HIV positive pregnant women was increased because of the chronic viral infection itself and secondly because of the treatment. From the group of patients with ART initiated during pregnancy, from the HIV positive category only, we have registered no case with SGA/FGR. These patients represent 26.83% from the total HIV positive pregnancies. In our study the SGA/FGR pathology was present only in HIV positive pregnant women under HAART long time before conceiving. The mean foetal weight in the cases with ART long time before conception was 2930g, in contrast the mean foetal weight in cases with ART started during pregnancy was 2737g, being 6.59% difference between the two groups.

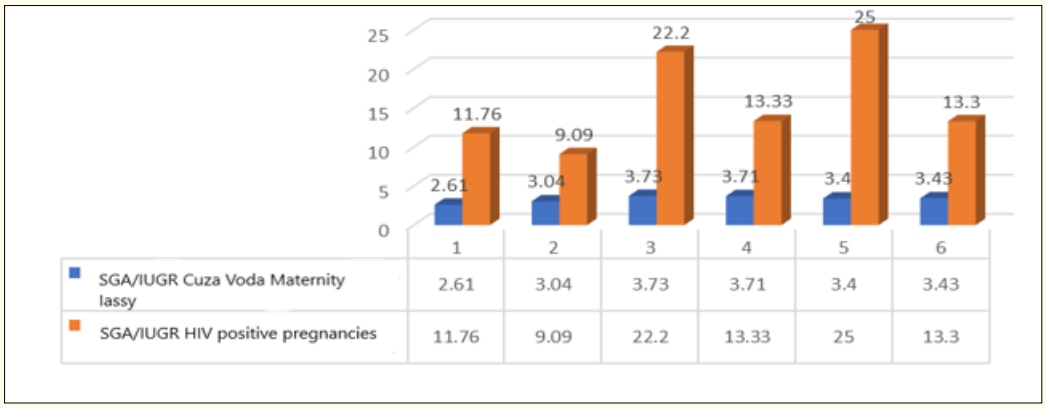

Figure 4: *FGR/SGA percentage in general pregnant population in our hospital and in HIV pregnancies.*

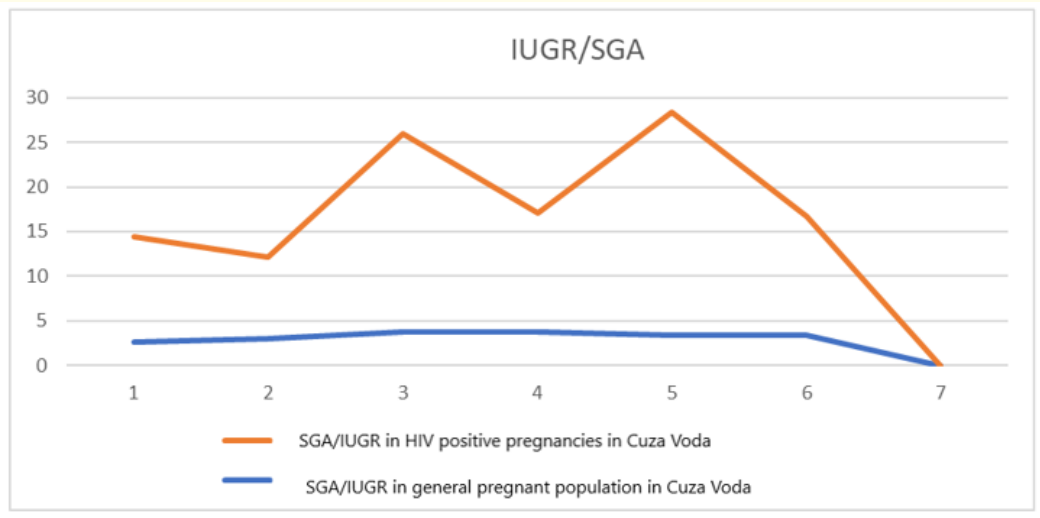

Figure 5: *FGR/SGA percentage in general pregnant population in our Hospital and in HIV pregnancies.*

We have also observed an increased rate of higher prematurity in cases with ART preconceptionally, with an increase rate of preterm rupture of membranes (60%). Only 40% of the cases with ART during pregnancy had preterm rupture of membranes. The rate of premature birth and premature rupture of membranes was also higher in cases with unmonitored pregnancies. Also, the lack of pregnancy monitoring led more frequently to acute foetal sufferance at the time of admission in the hospital and to a higher rate of vaginal birth past term. In our country, and in our hospital also, internal protocol establishes that all HIV positive pregnancies must be evacuated by C-section electively, at 38 weeks of gestation, to drop the rate of vertical transmission. To afford a vaginal HIV positive birth the hospital needs to procure Zidovudine to assure HIV vertical transmission protection. If the vaginal birth was not expected, there is no ART that will help prevent transmission. So, a vaginal unplanned birth, without ART protection, will increase the vertical transmission rate.

Discussion

We have observed a low incidence of HIV positive births in our hospital, with most of the cases coming from rural areas. A high proportion of these births had complications. It becomes obvious that the severity of the infection negatively influences the evolution of the pregnancy. In cases with monitored pregnancy the evolution had less complications. To obtain a lower vertical transmission rate we need to increase patient's addressability to health care services regardless of costs and social stigma.

Coinfection with hepatitis viruses increase the risk of complications, premature birth also adds more negative impact on new-borns evolution. The socioeconomical burden of HIV positive pregnancy with premature birth is higher. A better monitoring of the pregnancy will assure a lower rate of premature iatrogenic birth caused by SGA/FGR. The percentage of FGR/SGA was higher in our study than in general population, accordingly with the results presented in other studies, in literature.

We didn't observe an increase in spontaneous abortion rate or in congenital malformation rate. As the major associated pathology remains HPV infection it becomes obvious that these patients need periodic cervical cancer testing.

Limitations of the Study

The complexity of disease staging and the low incidence makes it very difficult to obtain a homogeneous lot of patients from the same disease category. So, our study will have the rate of errors that result from this aspect. Many of the patients refuse to address to medical services being afraid of social stigma and because of the costs. We still have a high rate of patients that are unemployed and without any financial means.

Recommendation for Further Studies

The benefits of ART are beyond doubt, but we need to evaluate the possible side effects and negative aspects and to find ways to reduce and prevent them, for assuring a better adherence to treatment. Many women discontinue treatment because they worry about the side effects on their baby. If we succeed in showing them that ART has more benefits than side effects and negative aspects, we will be one step closer in lowering the disease's incidence.

Conclusion

To reduce the costs and assure a lower rate of transmission, pregnancies need obstetrical monitoring in close collaboration with an infectious disease doctor. The medical decisions need to be adjusted to each case's particularity.

Prematurity remains the main cause for mortality, morbidity and high costs being a health care major problem in our country. Means to reduce it becomes one of our goals. Also, another cause of mortality, morbidity and increase costs is represented by FGR pathology. Any information and any medical action that will help us reduce these pathologies becomes very valuable.

Key Messages

- Vertical transmission of HIV represents one of the main sources for new seropositive patients.
- Antiretroviral therapy made AIDS a chronic condition with increase life spam.
- The need to find means to reduce antiretroviral therapy's side effects.

Conflicts of Interest

There were no conflicts of interest.

Ethics Approval

Informed consent was approved by the Ethical Commission of Research from The University of Medicine and Pharmacy "Gr. T. Popa" Iassi (no. 24411).

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