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THE ASSOCIATION OF THE SOCIO-DEMOGRAPHIC AND ECONOMIC CHARACTERISTICS WITH ADVERSE PREGNANCY AND FETAL OUTCOMES AMONG HIV POSITIVE PREGNANT WOMEN RECEIVING ANTI-RETROVIRAL THERAPY IN PUBLIC HOSPITALS, NAIROBI COUNTY, KENYA

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ABSTRACT

Introduction: **Risk factors for adverse pregnancy-fetal outcomes with immune reconstitution inflammatory response syndrome (IRIS) have not been studied in Kenya among pregnant women, while focusing on the improved immunity after anti-retroviral therapy (ART) initiation. This study aimed to assess the association between the different socio-demographic and economic characteristics and adverse pregnancy-fetal outcomes among HIV positive ART naïve pregnant women**

Methodology: **We used a prospective cohort design. We used chi-square test to investigate the association between social-demographic, economic characteristics and the adverse pregnancy-fetal outcomes. The study included ART naïve pregnant women seeking maternal care services with a confirmed HIV positive status within the first trimester of the pregnancy and excluded women who were not ART naïve and had other medical conditions before hospital visitation. A p-value of < 0.05 was set as the statistical significance and we performed logistic regression analysis to show independent outcome predictors. We determined adjusted relative risk at 95% confidence interval.**

Results: **Most women aged between 30 and 39 years and most of them were women who did not have adverse pregnancy-fetal outcomes. However, this finding was not significant. The mother's status of being separated was significant for an adverse pregnancy-fetal outcome.**

Conclusions: **There was a relationship in separated women and closely, unemployment status with an experience of adverse pregnancy-fetal outcome.**

It is important that; clinical approaches should consider specific socio-demographic and economic characteristics as factors related to; HIV-immune reconstitution inflammatory response syndrome after starting ART in pregnant women, as possible causes of adverse pregnancy-fetal outcomes.

INTRODUCTION

Adverse fetal outcome is a major challenge both in low and middle-income countries. Globally, adverse birth outcomes such as preterm birth, low birth weight, stillbirth, and congenital defects are some of the common problems (1). Every year, more than 7 million perinatal deaths occur across the world and half of them are stillbirths, accounting for 3.5 million. Developed countries have an estimate of stillbirths between 4.2 and 6.8 per 1000 births, where, in low and middle-income countries, it ranges from 20 to 32 per 1000 births (2). There is about 1.4 million HIV-infected women becoming pregnant annually (3), and thus, the increased risk of adverse pregnancy-fetal outcomes has generated much concerns.

Administration of anti-retro-viral therapy (ART) during pregnancy has resulted in a remarkable shift in the pediatric human immunodeficiency virus (HIV) epidemic, opening the opportunity for global elimination of new pediatric HIV infections. In 2013, the World Health Organization (WHO) recommended all pregnant and breastfeeding women with HIV infection to start ART, and continue through mother-to-child transmission duration risk, with continuing ART lifelong option regardless of clinical or immune status in high HIV prevalence settings (4).

Anti-retro-viral therapy (ART) during pregnancy should focus on reducing prenatal transmission and treat maternal human immunodeficiency virus (HIV) disease. ART can cut perinatal transmission by several mechanisms, including lowering maternal ante-partum viral load and pre-exposure and post exposure prophylaxis of the infant. Therefore, for prevention of perinatal transmission of HIV, joined ante-partum, intra-partum, and infant anti-retro-viral prophylaxis is important (5). Initiating combination anti-retro-viral therapy (ART) can meet suppression of viral replication and an increase in CD4+ T-cell counts in most patients (6), resulting in dramatic decrease in morbidity and AIDS-related mortality (7) . However, ART initiation is not without risk of complications, particularly in the first 6 months (8).

Studies have reported an increased risk of preterm birth and low birth weight associated with initiation of highly active anti-retro-viral therapy before conception as compared with therapy initiation during pregnancy (9). Most people initiating anti-retro-viral treatment show improved immune response and experience some opportunistic infections. This process is not eventful and, some proportion of patients experience inflammatory events in response to specific opportunistic pathogens within a short period of ART initiation. This describes two specific outcomes; a partially or completely exacerbated treated opportunistic infections, paradoxical IRIS and an inflammatory response to before not diagnosed often more pronounced than the typical presentation of this opportunistic infections, the unmasking IRIS (10).

WHO & Kenya Development Health Survey, 2009 showed that, HIV-infection among women is generally higher than men .This is also associated with adverse pregnancy outcomes such as; neonatal mortality among women according to a study done in Kenya (11). In pregnant women infected with HIV, administering

ART drugs in pregnancy and/or intra-partum greatly reduce the risk of vertical HIV transmission to the unborn baby (12).

Although the benefits of anti-retro-viral (ARV) therapy for preventing mother-to-child transmission are not disputable, researchers in developed and developing nations are reporting conflicting findings on the association between ART exposure and adverse birth and related pregnancy outcomes. Directly and /or indirectly, ART has also been found to greatly contribute to adverse pregnancy and birth outcomes (13). Again, a subgroup of patients experience clinical deterioration as a result of rapid and dis-regulated restoration of antigen specific immune responses during the treatment (14).

Deaths related to IRIS are not common; however, associated high morbidity contributes to burden on the health-care system (15). This is a public health issue of concern, as increased IRIS presenting as of opportunistic infections and other non-infectious conditions are due to ART use. A few autoimmune and other non-infectious conditions may worsen or appear after initiating highly active anti-retro-viral therapy, which implies that, inflammation brought by an IRIS-like syndrome is the cause. Whether such association represents a casual or a coincidental finding, this is not yet proven (16).

There is about 30 percent of ART responding patients which present with one or more inflammatory response syndromes consistent with IRIS. This has the greatest impact in resource-poor countries especially in Africa, where patients are often very immune-deficient, including pregnancy related immune-depression and opportunistic pathogens after the start of anti-retroviral therapy (17).

Again, considering the lack of consensus over the relationship between ART during pregnancy and negative fetal outcomes and complications (18), and the greater number of HIV-positive women of reproductive age, it is of paramount importance to make clear and test the relationship of socio-demographic, economic characteristics with adverse pregnancy-fetal outcomes among ART naïve pregnant women of reproductive age(19)

MATERIALS & METHODS

Study area: This current study was conducted at two selected public hospitals in Kenya; The Kenyatta National and Mbagathi Hospitals, in Nairobi County.

Study design: This was an observational prospective cohort study. We followed the participants from the end of first trimester to two weeks post-delivery, for six and half months after confirming their HIV positive status and put-on ART treatment with a defined case of HIV-IRIS as exposed cohort and non-HIV -IRIS as the non- exposed cohort (controls).

Data Collection and analysis: We used a pre-tested data questionnaire and we performed matching by age and parity. Protocols to describe the characteristics of enrolled pregnant women, use of ART regimens, and adverse pregnancy-fetal outcomes designed. We followed the women after confirmation of IRIS exposure status, until two weeks postpartum. Pre-testing of the data collection tool for construct validity was done. The information abstraction tool was uniform for both groups with coded values, majorly focusing on the primary outcome variable with maternal HIV immune reconstitution inflammatory syndrome response status and socio-demographic, economic characteristics as the covariates. We analyzed the data using SPSS version 25.0. Chi-square test established the association between the response and predictor variables and a statistical significance of $p< 0.05$ was set. To adjust for confounding variables, we performed regression analyses. We used

adjusted odds ratio (AOR) with a corresponding 95% confidence interval to estimate the significance.

We sought ethical clearance from the Kenyatta National Hospital and University of Nairobi Ethical Review Committee, Kenya and the National Commission for Science, Technology and Innovation, Kenya provided the research permission.

Hospitals authorized through a letter, to carry on with the research, and we obtained a written informed consent from study participants.

RESULTS

Social-demographic and economic characteristics of HIV-positive ART naïve pregnant women

We gathered data from 204 HIV-positive ART naïve pregnant women. 103 (50.5%) were between the age of 20-39 years. Majority, 163 (79.9%) were from Nairobi, while the rest from other parts of the country. Most women, 131 (64.2%) were in marriage. Over 90%, 189 (92.6%) of women were Christians and only, 15 (7.4%), were Muslims. Majority, 109 (53.4%) had secondary education and 49 (24.0%), had gone up to tertiary level of education. Half of them, 101 (49.5%) were self-employed and a similar proportion, 86 (42.2%) unemployed, with 16 (7.8%) being in civil service. On income source, 46 (22.5%) were housewives, while most, 142 (69.6%) had some work to generate income. 16(7.8%) income source wasn't known. This generally shows unemployed status with self-employment engagement as shown below, in table 1.

Table 1

HIV-positive ART initiated pregnant women Social-demographic and economic characteristics

Variable	Frequency (%)
Maternal age Category in years	
20-29	73 (35.8)
30-39	103 (50.5)
40-49	28 (13.7)
Location/address	
Nairobi	163 (79.9)
Outside Nairobi	41 (20.1)
Education level	
No formal education	21 (10.3)
Primary	24 (11.8)
Secondary	109 (53.4)
Higher/university	49 (24.0)
Not recorded	1 (0.5)
Occupation	
Unemployed	86 (42.2)
Civil servant	16 (7.8)
Self-employed	101 (49.5)
Not recorded	1 (0.5)
Religion	
Christian	189 (92.6)
Muslim	15 (7.4)
Marital status	
Single	60 (29.4)
Married	131 (64.2)
Separated	9 (4.4)

Windowed	1 (0.5)
Not recorded	3 (1.5)
Income source	
Working (Self-employed or employed)	142 (69.6)
Housewife	46 (22.5)
Not recorded	16 (7.8)

Social-demographic and economic characteristics among HIV-positive ART initiated pregnant women in relation to Maternal HIV immune reconstitution inflammatory response syndrome

Occupation and income source showed a close association with developing maternal HIV immune reconstitution inflammatory response syndrome after starting anti-retro-viral therapy at p=0.036 (occupation) and p=0.042 (income source). Education level was closer to significance at p=0.056 while the other characteristics were insignificant (P=>0.05) as shown below, in table *2*

Table 2

Social-demographic characteristics of HIV positive ART initiated pregnant women in relation to maternal HIV-IRIS diagnosis status

Variable	**Maternal HIV-IRIS**		**P value**
	YES	**NO**	
Maternal age in years			
20-29	31 (30.4)	42 (41.2)	0.133
30-39	53 (52.0)	50 (49.0)	
40-49	18 (17.6)	10 (9.8)	
Location/address			
Nairobi	79 (77.5)	84 (82.4)	0.382
Outside Nairobi	23 (22.5)	18 (17.6)	
Education level			
No formal education	11 (10.8)	10 (9.8)	0.056
Primary	16 (15.7)	8 (7.8)	
Secondary	57 (55.9)	52 (51.0)	
Higher/university	17 (16.7)	32 (31.4)	
Not recorded	1 (1.0)	0	
Occupation			
Unemployed	51 (50.0)	35 (34.3)	0.036
Civil servant	9 (8.8)	7 (6.9)	
Self-employed	41 (40.2)	60 (58.8)	
Not recorded	1 (1.0)	0	
Religion			
Christian	97 (95.1)	92 (90.2)	0.180
Muslim	5 (4.9)	10 (9.8)	
Marital status			
Single	32 (31.4)	28 (27.5)	0.165
Married	60 (58.8)	71 (69.6)	
Separated	6 (5.9)	3 (2.9)	
Windowed	1 (1.0)	0	
Not recorded	3 (2.9)	0	
Income source			

Employed	7 (6.9)	5 (4.9)	0.042
Self employed	58 (56.9)	72 (70.6)	
Housewife	24 (23.5)	22 (21.6)	
Not recorded	13 (12.7)	3 (2.9)	

Social-demographic, economic characteristics of HIV positive pregnant women with adverse pregnancy-fetal outcome status

We established the relationship of the adverse pregnancy-fetal outcomes and the social-demographic and economic characteristics of HIV positive ART initiated women. Of the 204 women, 38 (18.62%) experienced at least, an adverse pregnancy-fetal outcome (of a particular nature). The common maternal age was 30-39 years with a larger proportion of this age group being in women without any adverse pregnancy-fetal experience. This observation was insignificant 19 (18.4); 84 (81.6) [OR = 0.9; 95% CI: 0.7-2.4; P= .728]. Adverse pregnancy-fetal outcomes were likely in separated women as compared to unseparated women [OR=4.2; 95%CI: 1.0-16.9; P=0.044]. Difference in proportion was there in woman's level of education among women experiencing an adverse pregnancy-fetal outcome and those who didn't, but this observation was insignificant (P>0.95). In addition, no statistically significant observation at (P>0.05) in the other socio-demographic, economic characteristics and adverse pregnancy-fetal outcome as shown below in table 3.

Table 3

Association of social-demographic, economic characteristics of HIV positive pregnant women with adverse pregnancy outcome status

Variable	**APO**		**OR (95% CI)**	**P value**
	Yes n (%)	**No n (%)**		
Maternal age in years				
20-29	15 (20.5)	58 (79.5)	1.0	
30-39	19 (18.4)	84 (81.6)	0.9 (0.4-1.7)	0.728
40-49	4 (14.3)	24 (85.7)	0.6 (0.2-2.1)	0.473
Location/address				
Nairobi	29 (17.8)	134 (82.2)	0.8 (0.3-1.8)	0.541
Outside Nairobi	9 (22.0)	32 (78.0)	1.0	
Education level				
No formal education	1 (4.8)	20 (95.2)	1.0	
Primary	4 (16.7)	20 (83.3)	4.0 (0.4-39.0)	0.233
Secondary	22 (20.2)	87 (79.8)	5.1 (0.6-39.8)	0.123
Higher/university	11 (22.4)	38 (77.6)	5.8 (0.7-48.1)	0.104
Occupation				
Unemployed	15 (17.4)	71 (82.6)	1.0	
Civil servant	4 (25.0)	12 (75.0)	1.6 (0.4-5.6)	0.479
Self-employed	18 (17.8)	83 (82.2)	1.0 (0.5-2.2)	0.946
Religion				
Christian	36 (19.0)	153 (81.0)	1.5 (0.3-7.1)	0.742
Muslim	2 (13.3)	13 (86.7)	1.0	
Marital status				
Single	11 (18.3)	49 (81.7)	1.2 (0.5-2.6)	0.693

Married	21 (16.0)	110 (84.0)	1.0	
Separated	4 (44.4)	5 (55.6)	4.2 (1.0-16.9)	0.044
Windowed	0	1 (100)	0	1.000
Income source				
Employed	3 (25.0)	9 (75.0)	1.4 (0.3-6.1)	0.680
Self employed	25 (19.2)	105 (80.8)	1.0 (0.4-2.3)	0.961
House wife	9 (19.6)	37 (80.4)	1.0	

Parity distribution among HIV positive ART naive pregnant women

47.1% of the women were of 2-3 parity followed by 43.1% with a parity of 1. Those with 4-5 parity were at 8.8% and those with 6-7 parity were only 1 % of the total, as shown below, in figure *1*

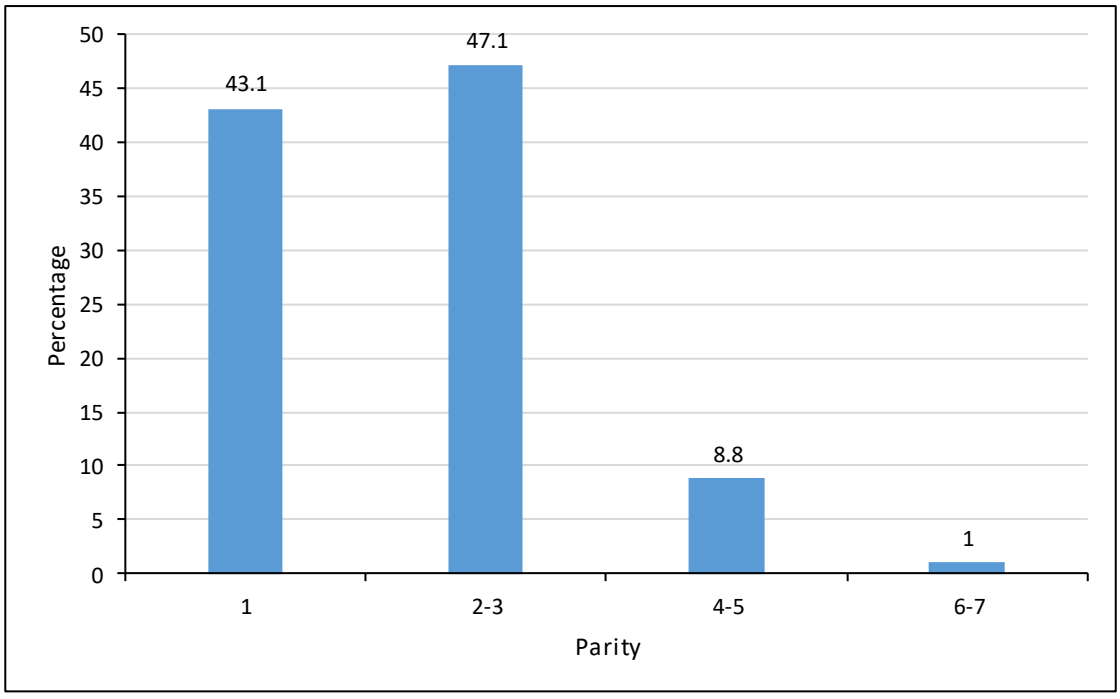

Figure 1: Parity distribution

DISCUSSION

Majority of women were between the ages of 20 to 45 years, with none being below the age of 15 years. This is consistent with KDHS, (2014) findings which show that, the reproductive age in Kenya is between 15 years to 49 years. Married women were 64.2% of the respondents and single women were 29.4%. This closely correlates with KDHS 2014 survey that; six in ten (60%) women and 5 in 10 men age 15-49 are in marriage or living together. As regards parity of a woman, those with a parity of 1 were at 43.1% and most at 47.1% with 2-3 parity. Only 1% had parity of 6 and above.

This is consistent with KDHS, 2008/2009 and 2014 survey results indicating that, more women had conceived and given birth to at least twice. The level of education among HIV positive ART initiated women was at 109 (53.4%) with secondary education and only, 49 (24.0%) with tertiary education. The rest, 11.8% had primary level education and 10 %, no basic education. This is somehow consistent with (13), findings indicating that, 7% percent of women aged 15-49 have no education and about one-quarter of women and men have completed primary school, while 16% of women and 19% of men have completed secondary school and that 88% of women age 15-49 are literate. As it regards the religion, a greater percentage of women were Christians therefore showing the religious inclination in Nairobi and Kenya at large as per Abdullah & KDHS 2008/2009 and 2014 findings which show that Christianity is at 86% and Muslims about 10%. In terms of occupation, 101 (49.5%) were self-employed and about a similar proportion, employed, 86 (42.2%), with only, 16 (7.8%) being in civil service. This finding is inclining to Kenya employment population ratio findings in 2016 that, 57.6% are in employment. On income source, 46 (22.5%) were housewives while the most, 142 (69.6%) had some work to generate income, findings which are close to those of KDHS, 2014. On parity, majority of women (47.1%) had 2-3 children followed closely by women with a parity of 1 at 43.1%. Those with 4-5 parity were at 8.8%. Women with 6-7 parity were only 1 % of the total. This is consistent with KDHS 2014 survey that most Kenya population of women has 2-3 children and among over women with over 6 children is less than 2 %. In general, there was a relationship between marital status defined by a case of woman being separated with adverse pregnancy-fetal outcome experience among HIV positive ART initiated women and, maternal HIV immune constitution inflammatory response syndrome as the exposure variable with, education level, occupation status and source of income.

CONCLUSION

The results indicated that, there was a relationship between socio-demographic, economic characteristics especially, separated marital status and an adverse pregnancy-fetal outcome, among HIV positive anti-retro-viral naïve pregnant women of reproductive age. This encounter was most significant in women diagnosed with immune reconstitution inflammatory response syndrome (IRIS) as compared to controls (non-IRIS diagnosed). Clinical approaches should consider specific socio-demographic, economic characteristics as related to; HIV immune reconstitution inflammatory response syndrome (IRIS) among ART naïve pregnant women, as adverse pregnancy-fetal outcome may occur. Integrative approach is important in diagnosing immune reconstitution inflammatory response syndrome by considering socio-demographic, economic covariates which may influence an adverse pregnancy-fetal outcome among HIV positive ART initiated pregnant women of reproductive age.

REFERENCES

1. You D, Hug L, Ejdemyr S, Idele P, Hogan D, Mathers C, et al. Global, regional, and national levels and trends in under-5 mortality between 1990 and 2015, with scenario-based projections to 2030: A systematic analysis by the un Inter-Agency Group for Child Mortality Estimation. Lancet. 2015;386(10010).

2. Silveira MF, Victora CG, Barros AJD, Santos IS, Matijasevich A, Barros FC. Determinants of preterm birth: Pelotas, Rio Grande do Sul State, Brazil, 2004 birth cohort. Cad Saude Publica. 2010;26(1).

3. WHO. Prevent HIV, test and treat all - WHO support for country impact. Who. 2016.

4. WHO. Chapter 6: Service Delivery (Consolidated Guidelines on the use of antiretroviral drugs for treating and preventing HIV infection). World Heal Organ. 2015;

5. Fowler MG, Qin M, Fiscus SA, Currier JS, Flynn PM, Chipato T, et al. Benefits and Risks of Antiretroviral Therapy for Perinatal HIV Prevention. N Engl J Med. 2016;375(18).

6. Autran B, Carcelain G, Li TS, Blanc C, Mathez D, Tubiana R, et al. Positive effects of combined antiretroviral therapy on CD4+ T cell homeostasis and function in advanced HIV disease. Science (80-). 1997;277(5322).

7. Nizami S, Morales C, Hu K, Holzman R, Rapkiewicz A. Trends in mortality from human immunodeficiency virus infection, 1984-2016: An autopsy-based study. In: Archives of Pathology and Laboratory Medicine. 2020.

8. Haddow LJ, Moosa MYS, Mosam A, Moodley P, Parboosing R, Easterbrook PJ. Incidence, Clinical Spectrum, Risk Factors and Impact of HIV-Associated Immune Reconstitution Inflammatory Syndrome in South Africa. PLoS One. 2012;7(11).

9. Abbafati C, Machado DB, Cislaghi B, Salman OM, Karanikolos M, McKee M, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258).

10. Walker NF, Scriven J, Meintjes G, Wilkinson RJ. Immune reconstitution inflammatory syndrome in HIV-infected patients. Vol. 7, HIV/AIDS - Research and Palliative Care. 2015.

11. Kaguthi G, Nduba V, Borgdorff MW, Verver S. Predictors of post neonatal mortality in Western Kenya: A cohort study. Pan Afr Med J. 2018;31.

12. Hurst SA, Appelgren KE, Kourtis AP. Prevention of mother-to-child transmission of Human Immunodeficiency Virus Type 1 (HIV): the role of neonatal and infant prophylaxis HHS Public Access. Expert Rev Anti Infect Ther. 2015;13(2).

13. Narendran G, Oliveira-De-Souza D, Vinhaes CL, Akrami K, Fukutani KF, Banu K, et al. Multifocal tuberculosis-associated immune reconstitution inflammatory syndrome - A case report of a complicated scenario. BMC Infect Dis. 2019;19(1).

14. Saag MS, Gandhi RT, Hoy JF, Landovitz RJ, Thompson MA, Sax PE, et al. Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2020 Recommendations of the International Antiviral Society-USA Panel. Vol. 324, JAMA - Journal of the American Medical Association. 2020.

15. Sereti I, Sheikh V, Shaffer D, Phanuphak N, Gabriel E, Wang J, et al. Prospective international study of incidence and predictors of immune reconstitution inflammatory syndrome and death in people living with human immunodeficiency virus and severe lymphopenia. Clin Infect Dis. 2020;71(3).

16. Sharma N, Sharma LK, Dutta D, Gadpayle AK, Anand A, Gaurav K, et al. Prevalence and predictors of thyroid dysfunction in patients with HIV infection and acquired immunodeficiency syndrome: An Indian perspective. J Thyroid Res. 2015;2015.

17. Sturt AS, Dokubo EK, Sint TT. Antiretroviral therapy (ART) for treating HIV infection in ART-eligible pregnant women. Cochrane Database Syst Rev. 2010;

18. Shelburne SA, Visnegarwala F, Darcourt J, Graviss EA, Giordano TP, White AC, et al. Incidence and risk factors for immune reconstitution inflammatory syndrome during highly active antiretroviral therapy. Vol. 19, AIDS. Lippincott Williams and Wilkins; 2005. p. 399–406.

19. Kim MK, Lee SM, Bae SH, Kim HJ, Lim NG, Yoon SJ, et al. Socioeconomic status can affect pregnancy outcomes and complications, even with a universal healthcare system. Int J Equity Health. 2018;17(1).