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Dysregulation of Th1/Th2 Cytokines in Conjoint Cases of Human Immunodeficiency Virus and Pregnancy: A cohort Study in Western Kenya.

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Introduction

- Pregnancy and early HIV infection present diverse cytokine responses.
- A successful pregnancy present with an increase of Th2 and suppression of Th1type of cytokines[1].
- Early HIV infection on the contrary is characterized by an increase of Th1 cytokines[2].
- Despite of these, the delicate balance of Th1/Th2 in conjoint cases of HIV and pregnancy remain unknown.
- Academic Model for providing access to Health care (AMPATH) Centre at Moi Teaching and Referral Hospital (MTRH) is the largest HIV/AIDS care program in Kenya.
- AMPATH has a mean of 25,000 HIV-positive pregnant women under care annually[3].
- Despite of this , trends, changes and differences of Th1 and Th2 cytokines among the HIV-infected pregnant women remains unknown.

Objective

- To determine the trends, changes and differences ofTh1(IL-2, IFN-γ, TNF) and Th2 (IL-10, IL-6, IL-4) blood cytokines in advancing pregnancy among HIV-infected and HIV-non-infected women.

Methods

- Ethical approval was obtained from MTRH Ethical Review Committee.
- HIV-infected (asymptomatic, antiretroviral-naïve) and healthy HIV-non-infected pregnant women were targeted for the study.
- Forty four participants in each group were consecutively recruited at AMPATH/MTRH in Western Kenya.
- Study participants were matched by age, parity and gestational age.
- In a prospective cohort study design, blood cytokines were measured by trimester in each participant.
- The cytokines were analysed using BD™Cytometric Bead Array Technology and FACSCalibur™ flow cytometer.
- Data analysis was performed using STATA version 13 special edition.
- Significance levels were tested at $P \leq 0.05$.

Results

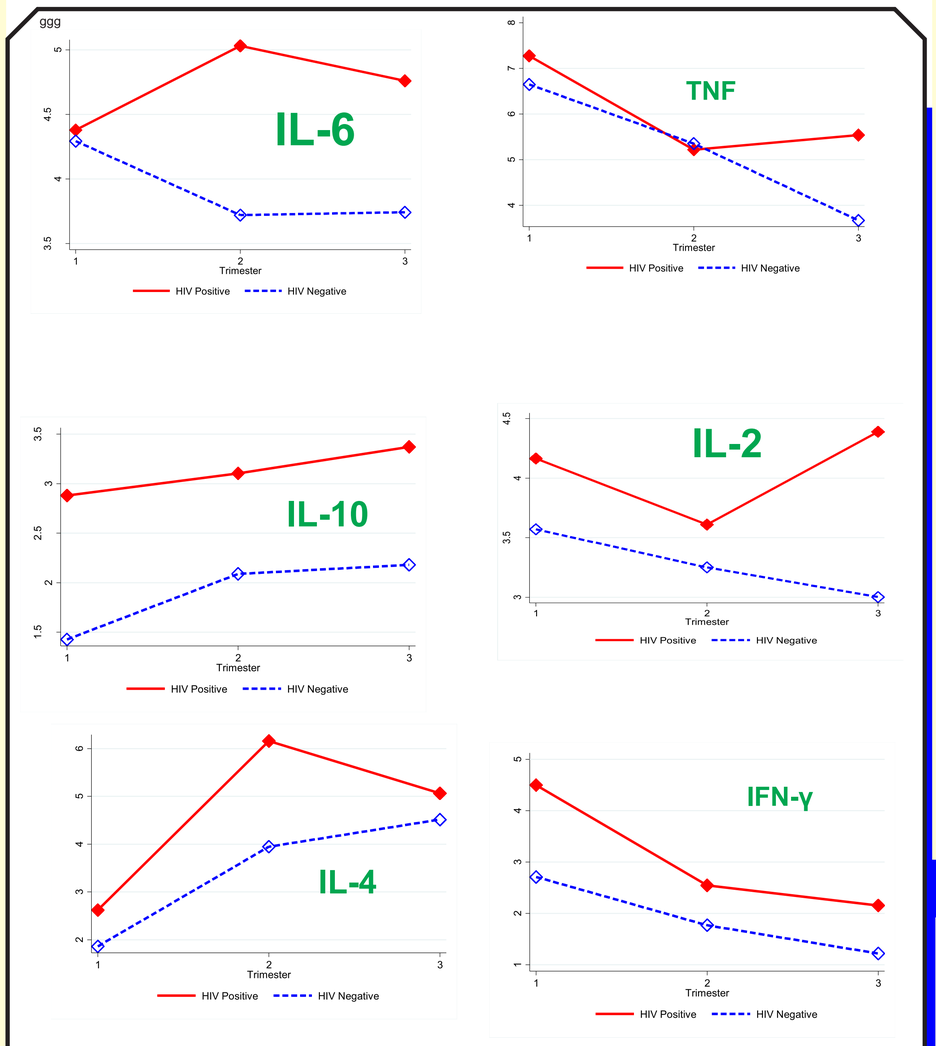

Figure 1-6: Trendsof Th_1/Th_2 cytokinesfrom the first trimester to the third trimester stratified by HIV status

Figure Legend: The trends of TNF and IFN- decreased while those of IL-10 and IL-4 increased as pregnancy advanced in both groups.

Changes of Th1/Th2 Cytokines in Advancing Pregnancy among HIV-Infected and HIV-non-Infected Pregnant Women.

Table 1: Changes of Th_1/Th_2 cytokines levelsby trimester of pregnancyin both groups.

		HIV -Positive		HIV -negative	
		Mean Change(95% CI)		Mean Change(95% CI)	
Cytokine	Trimester	1	2	1	2
IL -2	2	-0.6(-1.1,-0.03) ***P*=0.036**	N/A	-0.3(-0.8, 0.2) *P*=0.226	N/A
	3	0.2(-0.3, 0.7) *P*=0.399	0.8(0.3, 1.3) ***P*=0.003**	-0.6(-1.1,-0.1) ***P*=0.032**	-0.2(-0.8, 0.3) *P*=0.348
IFN -γ	2	-2.0(-2.7,-1.2) ***P*<0.0001**	N/A	-0.9(-1.7,-0.2) ***P*=0.015**	N/A
	3	-2.3(-3.1,-1.6) ***P*<0.0001**	-0.4(-1.2, 0.4) *P*=0.313	-1.5(-2.3,-0.7) ***P*<0.0001**	-0.6(-1.3, 0.2) *P*=0.156
TNF	2	-2.1(-3.1,-1.0) ***P*<0.0001**	N/A	-1.3(-2.4,-0.2) ***P*=0.016**	N/A
	3	-1.7(-2.8,-0.7) ***P*=0.001**	0.3(-0.7, 1.4) *P*=0.551	-3.0(-4.0,-1.9) ***P*<0.0001**	-1.7(-2.7,-0.6) ***P*=0.002**
IL -10	2	0.2(-0.4, 0.7) *P*=0.554	N/A	0.7(0.1, 1.2) *P*=0.019	N/A
	3	0.5(-0.1, 1.0) *P*=0.082	0.3(-0.2, 0.9) *P*=0.258	0.8(0.2,1.3) ***P*=0.008**	0.1(-0.5, 0.6) *P*=0.745
IL -6	2	0.7 (0.1, 1.2) ***P*=0.029**	N/A	-0.6 (-1.2, 0.01) *P*=0.056	N/A
	3	0.4 (-0.2, 1.0) *P*=0.202	-0.3 (-0.9, 0.3) *P*=0.367	-0.6 (-1.2, 0.01) *P*=0.066	0.02 (-0.6, 0.6) *P*=0.941
IL -4	2	3.5(2.6, 4.5) ***P*<0.0001**	N/A	2.1(1.1, 3.0) ***P*<0.0001**	N/A
	3	2.4(1.5, 3.4) ***P*<0.0001**	-1.1(-2.0,-0.2) ***P*=0.022**	2.7(1.7, 3.6) ***P*<0.0001**	0.6(-0.4, 1.5) *P*=0.234

Table legend: Significant changes of IL-2 [in the 2nd trimester, (*P*=0.003) and in the third trimester,(*P*=0.003) compared to 2nd], IL-6 (in the second trimester, P=0.029)and IL-4 (in the 3rd trimester, (*P*=0.022) compared to 2nd) were observed among the HIV-infected different from what was observed among HIV-non-infected. Significant changes of IL-10 were observed among the HIV-non-infected in the third trimester (*P*=0.008) compared to those of HIV-infected women.

Differences of Th1/Th2 Cytokines in Advancing Pregnancy between HIV-positive and HIV-negative Pregnant Women.

Table 2: Differences of Th_1/Th_2 cytokine levels between HIV-positive and HIV-negative participants by trimester of pregnancy

Variable		HIV -positive	HIV -negative	Difference (95% CL)	
	Trimester	Mean (SD)	Mean (SD)	(Mean HIV+) - (Mean HIV-)	*P*
IFN-γ	1	4.5(4.3)	2.7(1.6)	1.8(0.4, 3.2)	**0.013**
	3	2.2(2.2)	1.2(1.4)	1(0.1, 1.7)	**0.021**
IL-4	2	6.2(4.7)	3.9(3.8)	2.3(0.4, 4.0)	**0.017**
IL-10	1	2.9(3.3)	1.4(1.2)	1.5(0.4, 2.5)	**0.008**
	2	3.1(2.3)	2.1(1.5)	1.0(0.2, 1.9)	**0.019**
	3	3.4(2.5)	2.2(1.6)	1.2(0.3, 2.1)	**0.009**

Table legend: Significant differences of IFN-γ, IL-4 and IL-10 levels in different trimesters of pregnancy were observed indicating higher cytokine levels among the HIV-infected compared to HIV-non-infected.
NB: Other cytokine not presented in this table did not show any significant difference between the two groups.

Conclusions

- A decrease trend of Th1(TNF, **IFN-γ)** and increase trend of Th2 (IL-10, IL-4) cytokines was demonstrated in both groups as pregnancy advanced.
- HIV-infected women demonstrated significant changes of IL-2, IL-6 & IL-4 and non-significant change of IL-10 different to those of HIV- non-infected.
- The difference of Th1/Th2 between HIV-infected and HIV-non-infected women demonstrated significant higher levels of IFN-γ, IL-10 and IL-4 cytokines compared to HIV-non-infected women during pregnancy.

Recommendation

- Th1(IL-2, IFN-γ) and Th2(IL-6, 1L-10, IL-4) cytokines should also be considered in routine monitoring of the HIV-infected pregnant women.

Future research

- An all-inclusive cytokines research to provide an insight of the trends, changes and differences of other cytokines not considered in the present study.

References

1. Piccinni MP, Scaletti C, Maggi E, Romagnani S. Role of hormone-controlled Th1- and Th2-type cytokines in successful pregnancy. J Neuroimmunol. 2000;109:30-33. doi:10.1016/S0165-5728(00)00299-X.
2. Nixon DE, Landay AL. Biomarkers of immune dysfunction in HIV. Curr Opin HIV AIDS. 2010;5(6):498-503. doi: 10.1097/COH.0b013e32833ed6f4
3. Einterz RM, Kimaiyo S, Mengech HNK, et al. Responding to the HIV pandemic: the power of an academic medical partnership. Acad Med. 2007; 82:812-818. doi:10.1097/ ACM.0b013e3180cc29f1.