Helminth-induced changes in cytokine profile of pregnant women with co-infections of helminthes and *Plasmodium* or HIV

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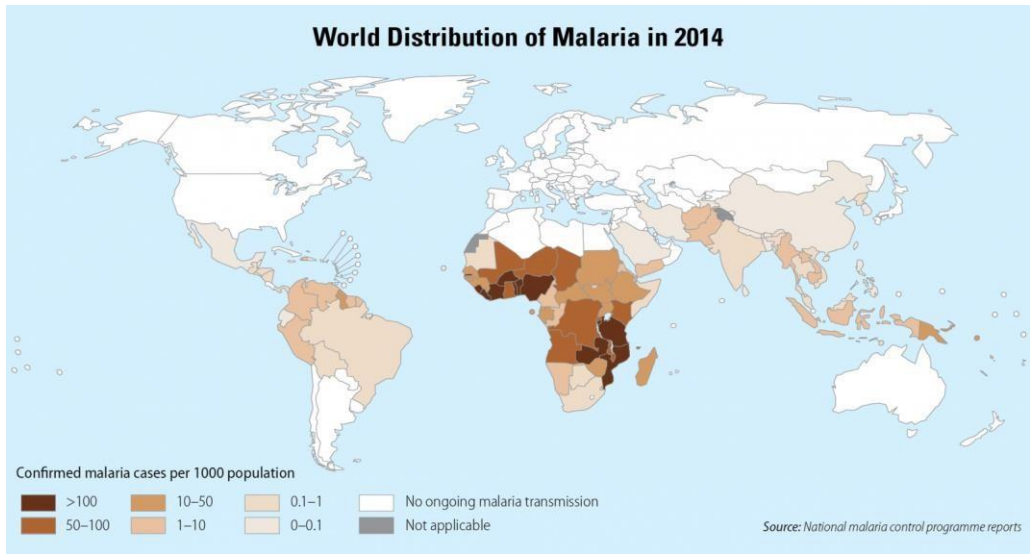
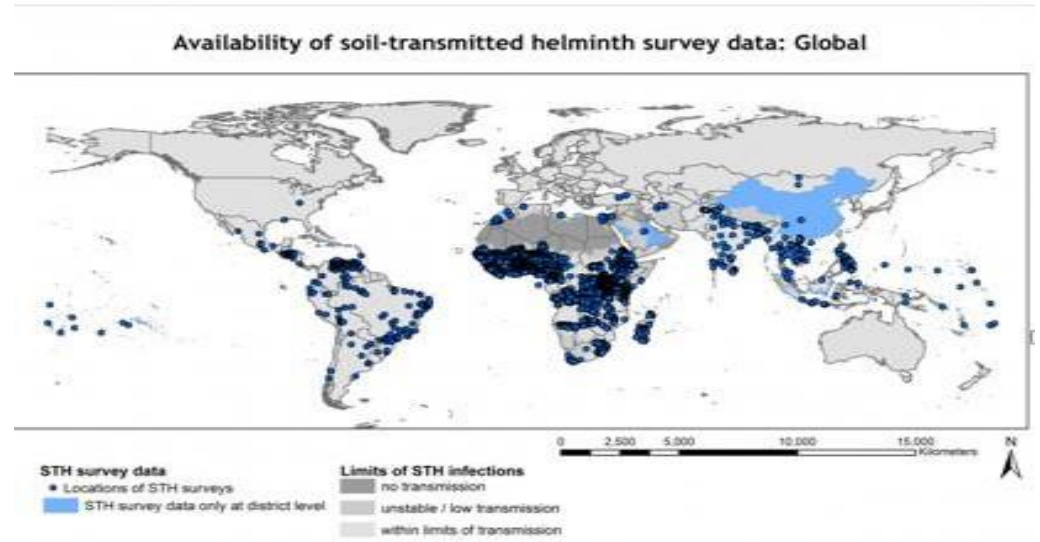
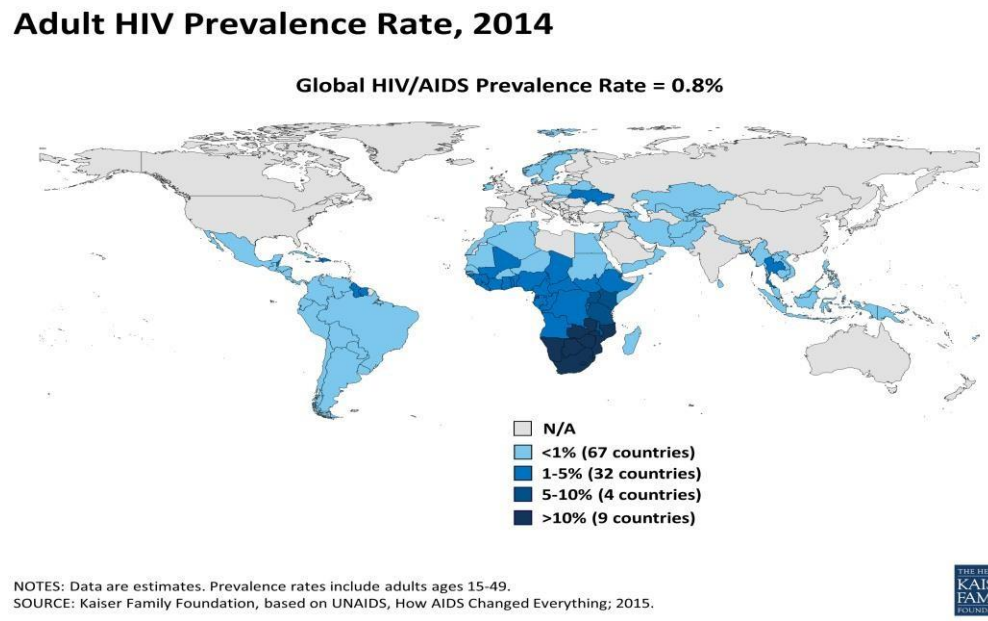
Background







UNAIDS, 2014; WHO, 2014, Pullan *et al.*, 2014

Background

- Cytokines (Th 2 cytokines) are involved in initiation and maintenance of pregnancy (Desai *et al*., 2007).

- Pregnancy-induced immune responses affected by inflammation or infectious diseases (Marzi *et al.,* 1996).

- Dominance of Th 1 cytokines is associated with IUGR, spontaneous abortion and PTD (Moormann *et al*, 1999; Sykes *et al*, 2012).

- *Plasmodium* infection caused a Th 1 biased response associated with increased parasite density (Achidi *et al* 2007; Nmorsi *et al* 2010).

- Helminth infections display a strong polarization towards a Th 2 response (Anthony *et al* 2007, Abdoli and Pirestani 2014).

Background

- Helminthic infection influenced susceptibility and severity of *Plasmodium* and HIV infections in pregnancy (Egwunyenga *et al.*, 2001; Ndibazza *et al.*, 2013).

- Some studies evaluated the systemic cytokine concentrations in co-infection of these diseases among pregnant women (Adeoti et al, 2015; Nmorsi et al, 2010).

- However, there is still a dearth of information on the immunological interplay of these infectious diseases.

- We investigated the modulatory effect of helminth in co-infections of the infective agents among pregnant women.

Research questions

1. What changes occur in the immune responses to single and co-infections?

2. Is helminth playing a modulatory role in co-infection with either malaria or HIV?

Study sites and population

- Antenatal clinics of two healthcare facilities in Ibadan metropolis and PEPFAR clinic.

- Pregnant women 18-45 years old.

  - ***Inclusion criteria*** - Screening for both malaria and helminth parasites.
  - ***Exclusion criteria*** - Subjects with obvious complications in pregnancy.
    - Confirmed HIV infected pregnant women were excluded in ANCs.

Study procedures

Baseline screening

Malaria parasites

Helminthes ova

Ethical approval

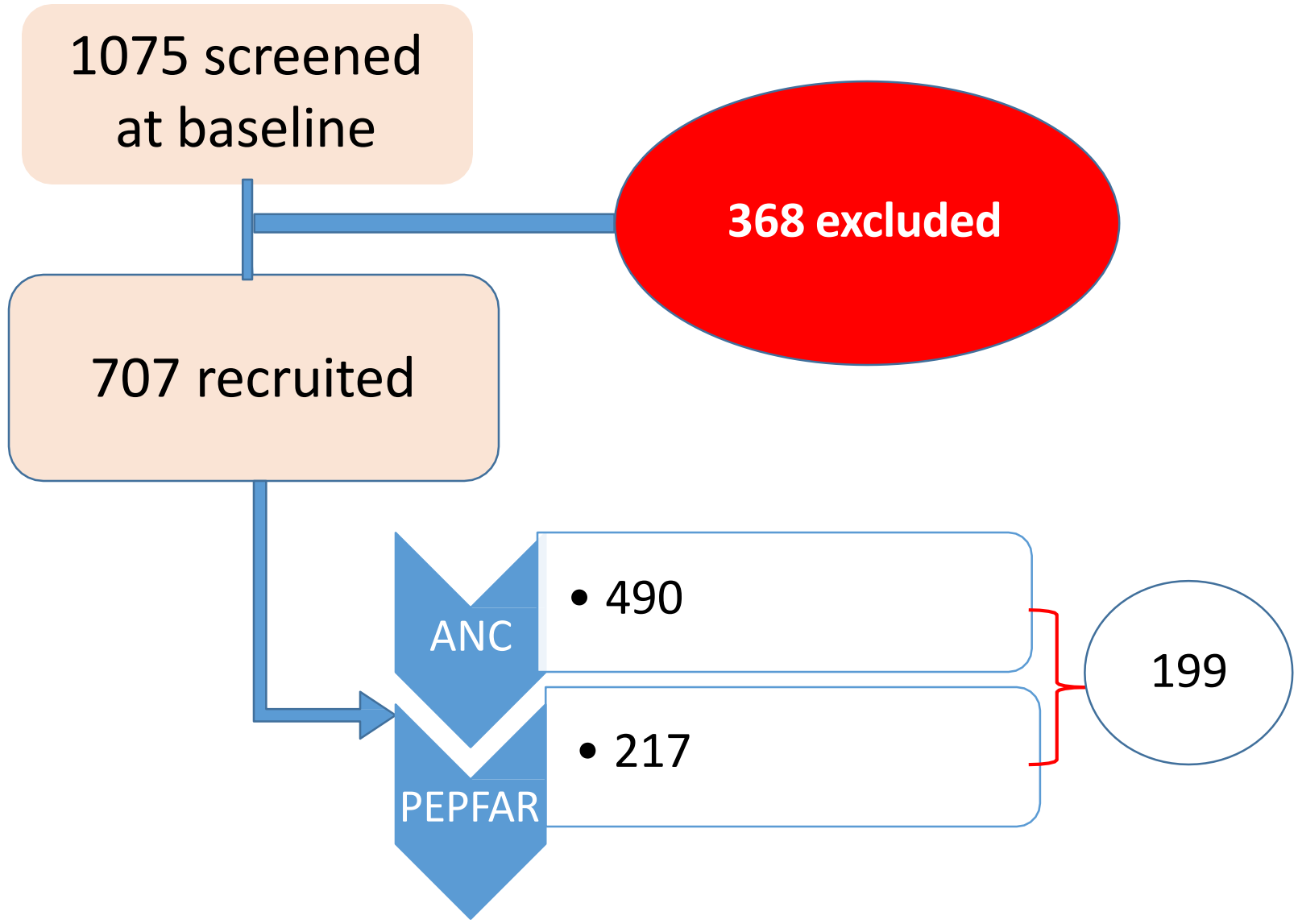
Questionnaire administration

Venous blood collection

Serum stored at -20°C for cytokine analysis

Th 1 cytokines - TNF-α, IFN-γ, IL-1α, IL-2, IL-12p70, IL-17
Th 2 cytokines - IL-4, IL-6, IL-10, IL-13

RECRUITMENT CHART

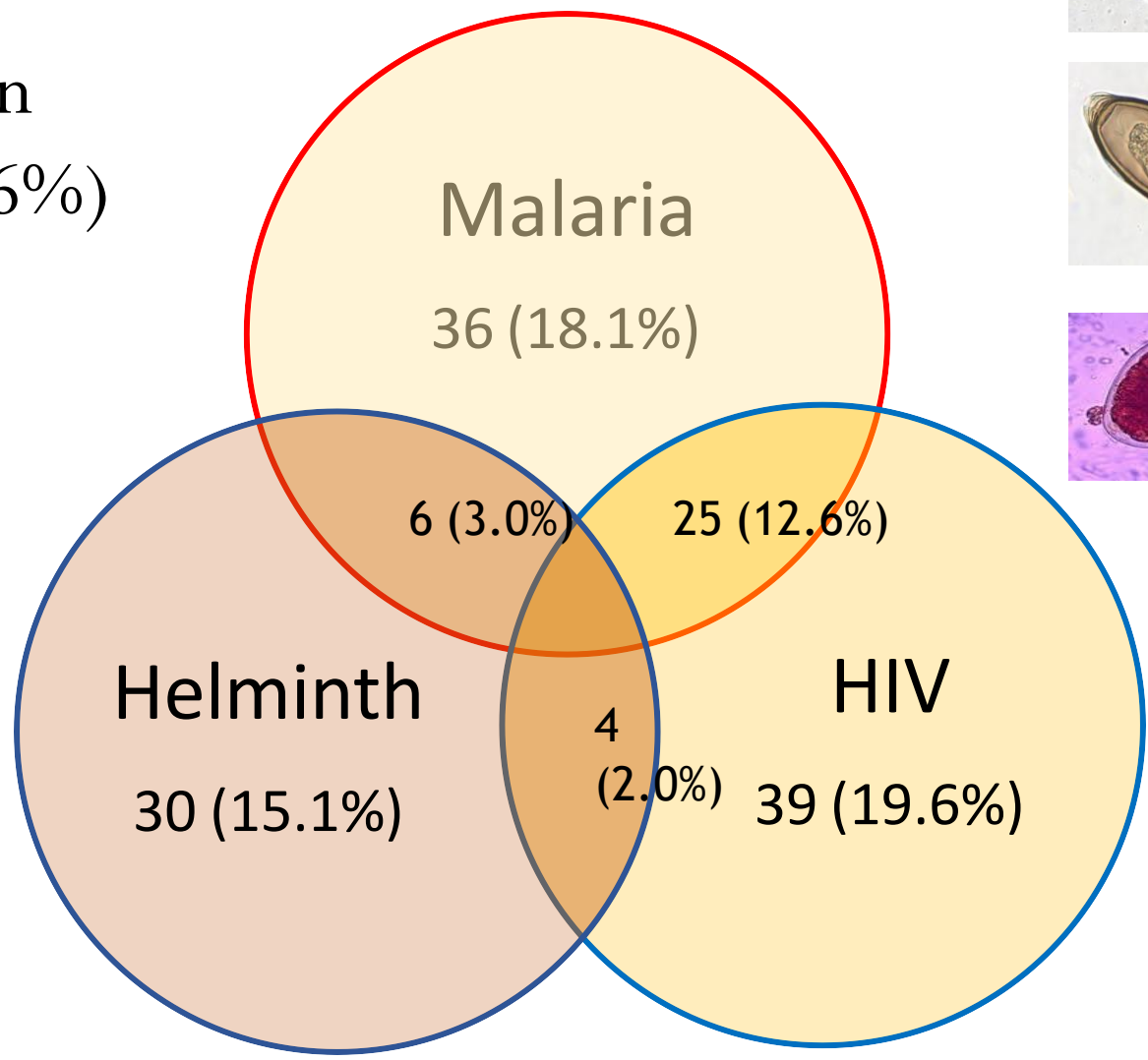


Data analysis

- Frequencies were analysed using descriptive statistics.
- Mann-Whitney U test was used to determine significant differences in median values at $p<0.05$.
- All statistical test was done using SPSS software 22.0 while Graph Pad Prism software 6.0 was used in plotting graphs.

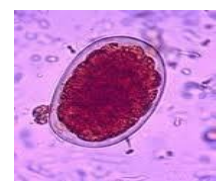
Results and Discussion

No infection
59 (29.6%)



- 19.6%

- 2.5%



- 0.5%

Helminth in *Plasmodium* infection

The cytokine profile of those infected with *Plasmodium* only was not significantly altered relative to those uninfected.

Increase in IFN-γ, IL-2 etc. associated with increase in malaria severity (Prakash *et al.*, 2006; Nmorsi *et al.*, 2010; Nasr *et al.*, 2014;).

Co-infection with helminthes increased IL-2 and decreased IFN-γ relative to those infected with *Plasmodium* only.

Acute malaria cases in Brazil found no difference (Sánchez-arcila et al, 2014).

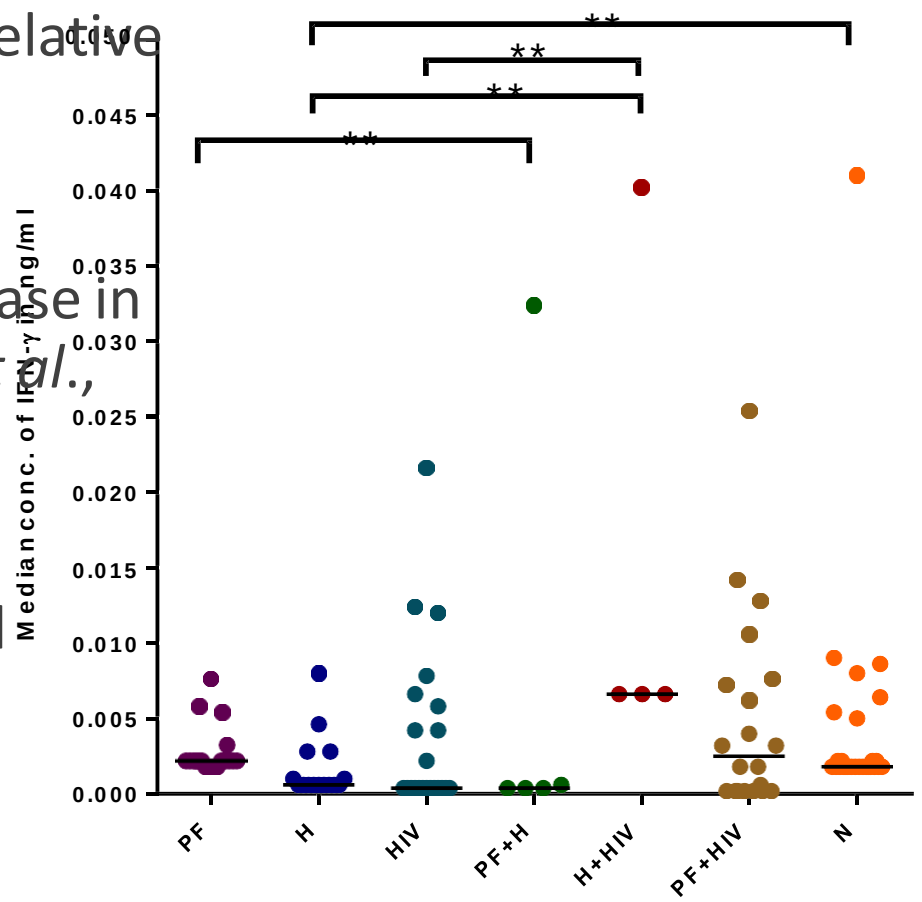


Figure 1: Median concentrations of IFN-γ among the infected and uninfected groups
Key: PF - *P. falciparum*, H - Helminth, N -Uninfected
****p<0.05**

Helminth in HIV infection

- Increase in TNF-α, IL-4, IL-6 and IL-17 and decrease in IL-1α, IL-10 and IL-12p70.
- TNF-α and IL-6 increased among HIV infected individuals (Tudela *et al.*, 2014), HIV infected pregnant women (Sachdeva *et al*., 2008, Richardson & Weinberg, 2011).
- Increased TNF-α suppressed HIV-1 replication in peripheral blood monocytes and alveolar macrophages (Lane et al, 1999, Breen, 2002).
- IL-10 production was higher in cells derived from HIV-uninfected pregnant women similar to the IL-10 production in peripheral blood obtained in this study (Hygino et al, 2012).

Helminth in HIV infection

- Increased concentrations of IFN-γ and IL-10 relative to those infected with HIV only.

- Increased IFN-γ inhibit HIV-1 replication (Alfano & Poli, 2005).

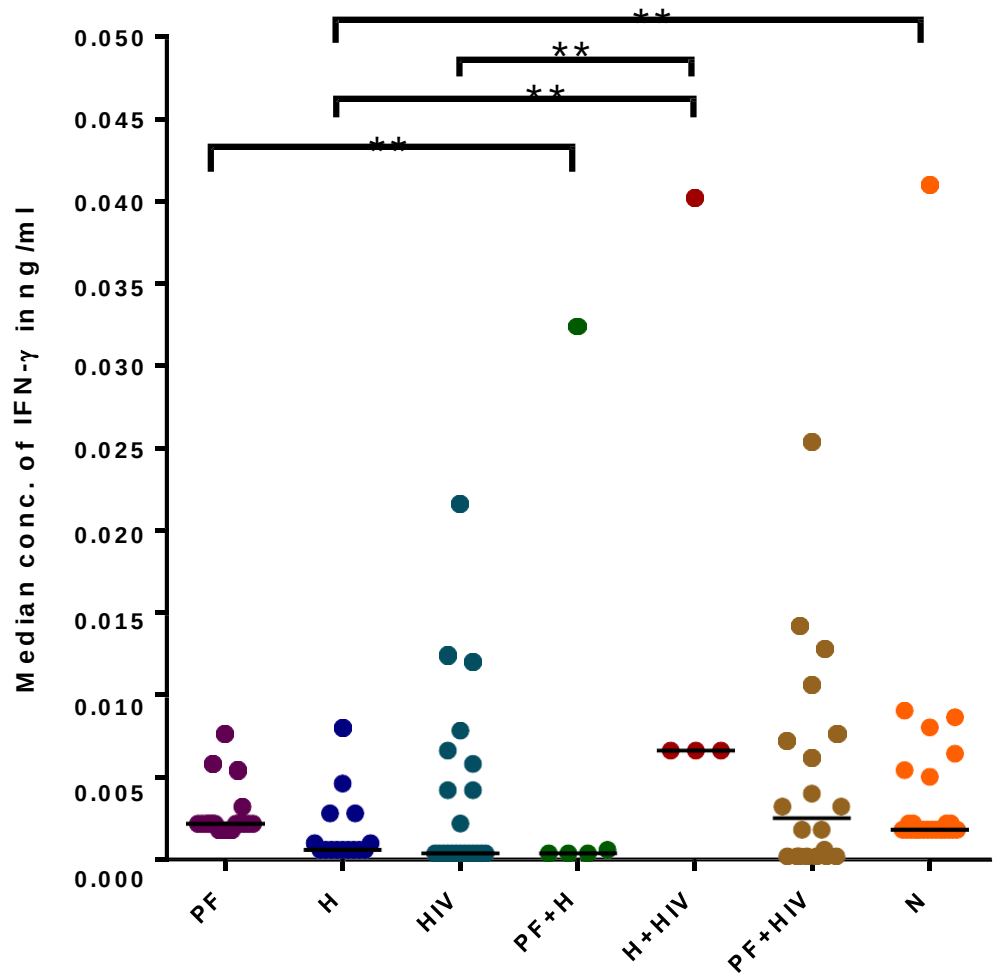


Figure 1: Median concentrations of IFN-γ among the infected and uninfected groups

Key: PF - *P. falciparum*, H - Helminth, N - Uninfected
****p<0.05**

Helminth in HIV infection

- Increased IL-10 involved in impaired innate immune responses in AIDS patients (Ma and Montaner, 2000).

- Impairment of HIV immune profile by helminth infection occurs particularly in those who excrete worm eggs (Mkhize-Kwitshana *et al.,* 2011).

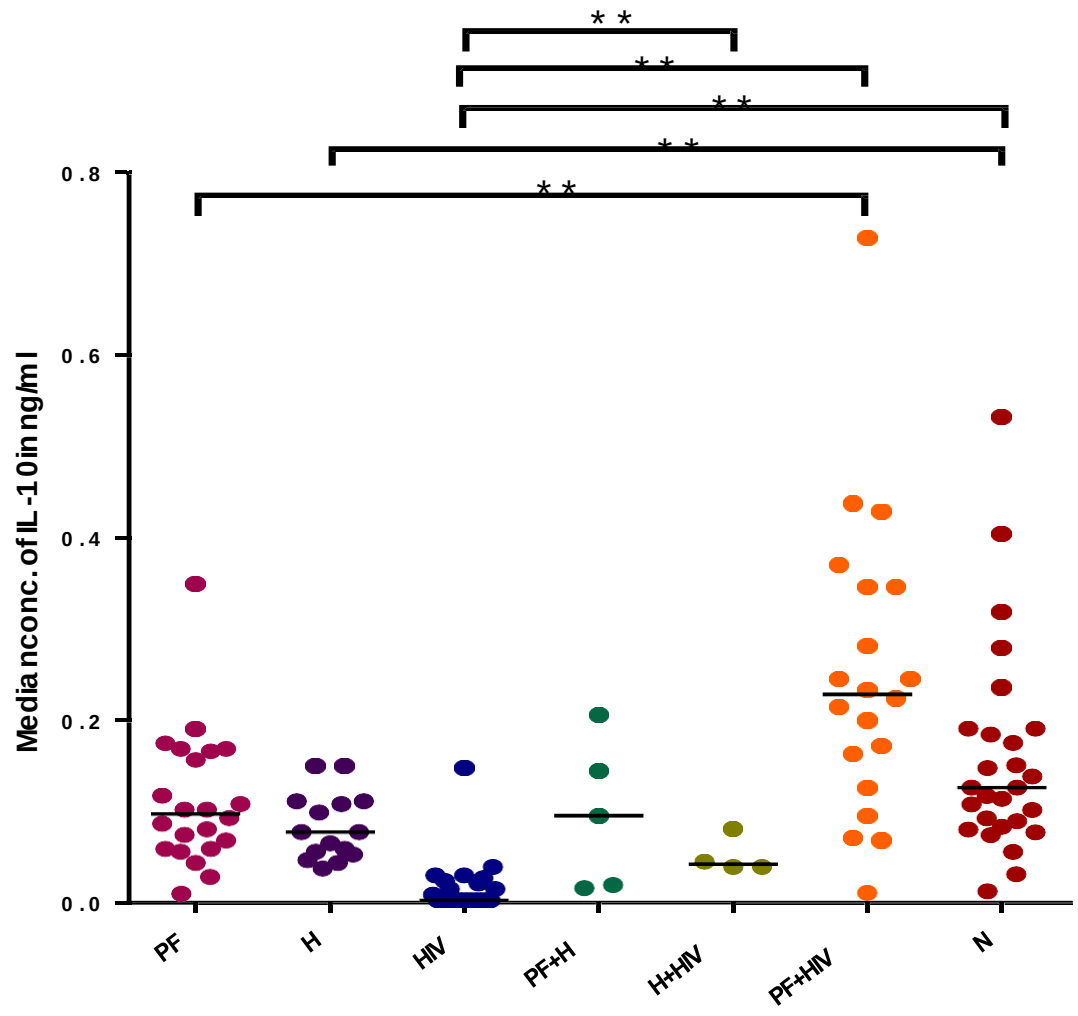


Figure 2: Median concentrations of IL-10 among the infected and uninfected groups

Key: PF - *P. falciparum*, H - Helminth, N - Uninfected ****p<0.05**

Th 1:Th 2 Ratio

	PF	HIV	PF + H	HIV + H	N
IFN-γ:IL-4	0.0002	0.000019	0.00004	0.00047	
IFN-γ:IL-10	0.0226	0.1333	0.0042	0.1571	
TNF-α:IL-4		0.009			0.0008
TNF-α:IL-10		62.87			0.0571
IL-17:IL-10		20111.33			154.96

Plasmodium - Helminth reduced Th 1:Th 2 ratio

Protective role in asymptomatic cases.

HIV - Helminth increased Th 1: Th 2 ratio

Inhibit HIV replication.

Acknowledgement

Supervisors:

- *Prof. George Ademowo*
- *Prof. Alexander Odaibo*

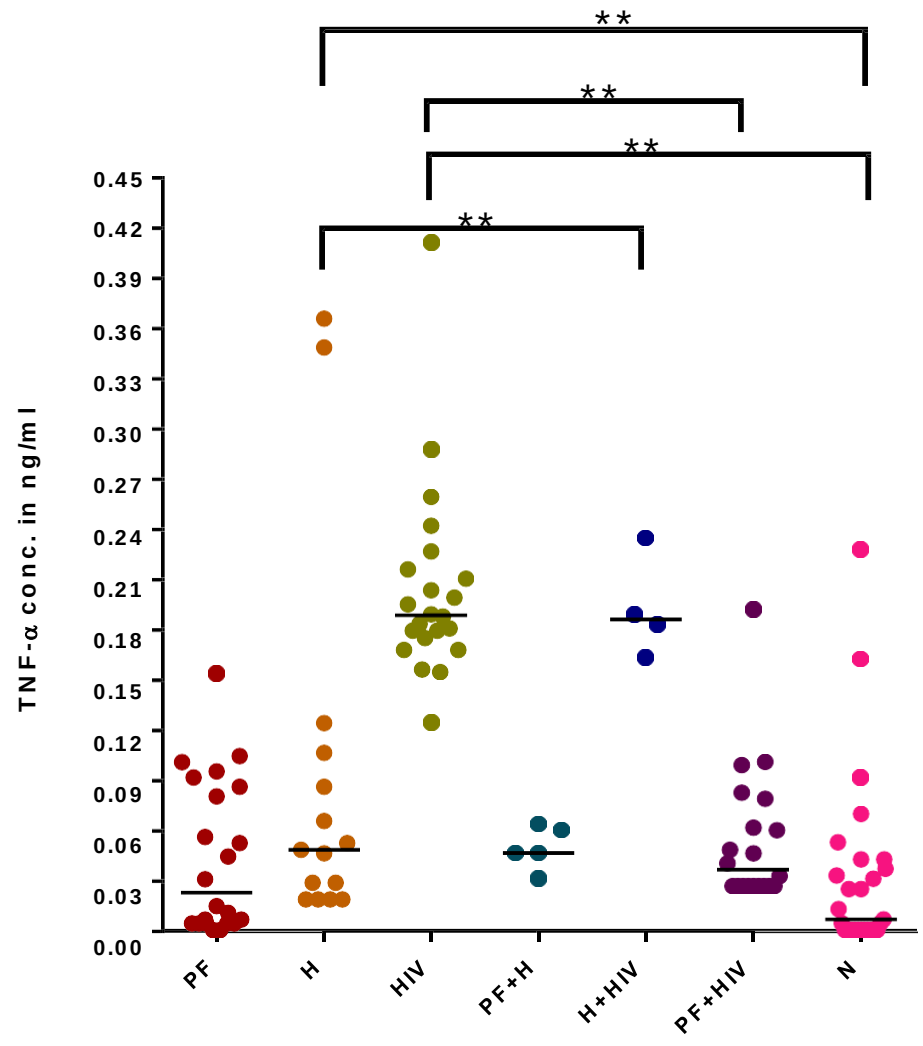
Study participants

Field support workers

Lab. technologists

IDEA

IIDP
Institute of Infectious Diseases of Poverty
IRMP Institut de Recherche sur les Maladies de la Pauvreté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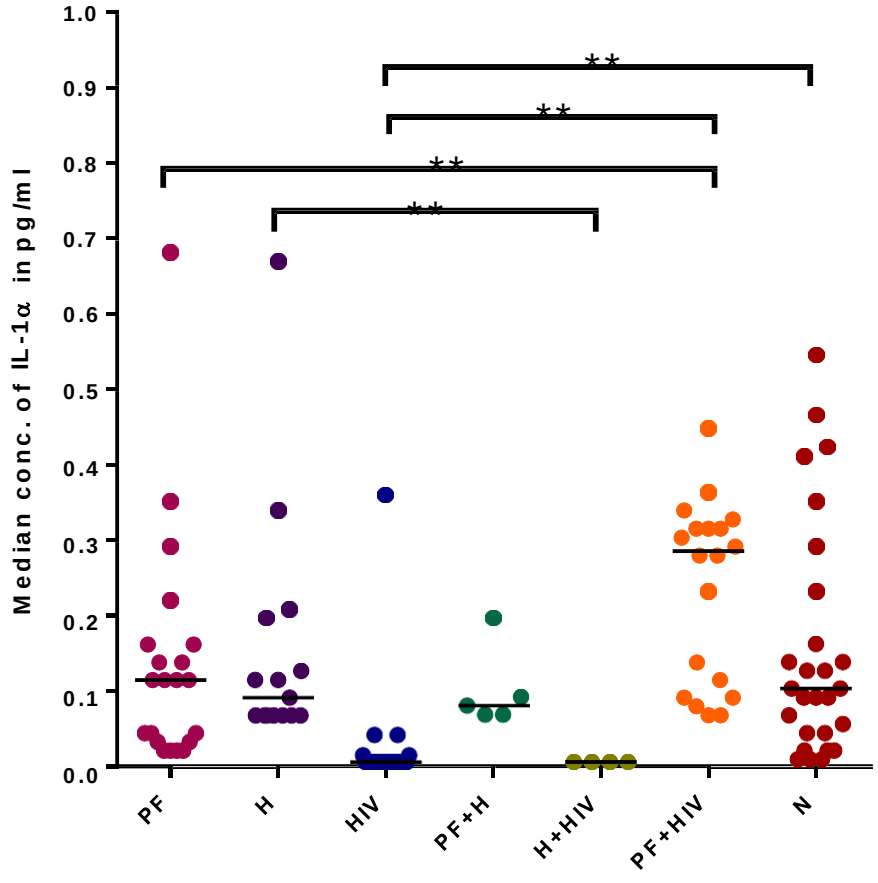
0.45
0.42
0.39
0.36
0.33
0.30
0.27
0.24
0.21
0.18
0.15
0.12
0.09
0.06
0.03
0.00
TNF-α conc. in ng/ml
PF
H
HIV
PF+H
H+HIV
PF+HIV
N


Median conc. of IL-1α in pg/ml
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
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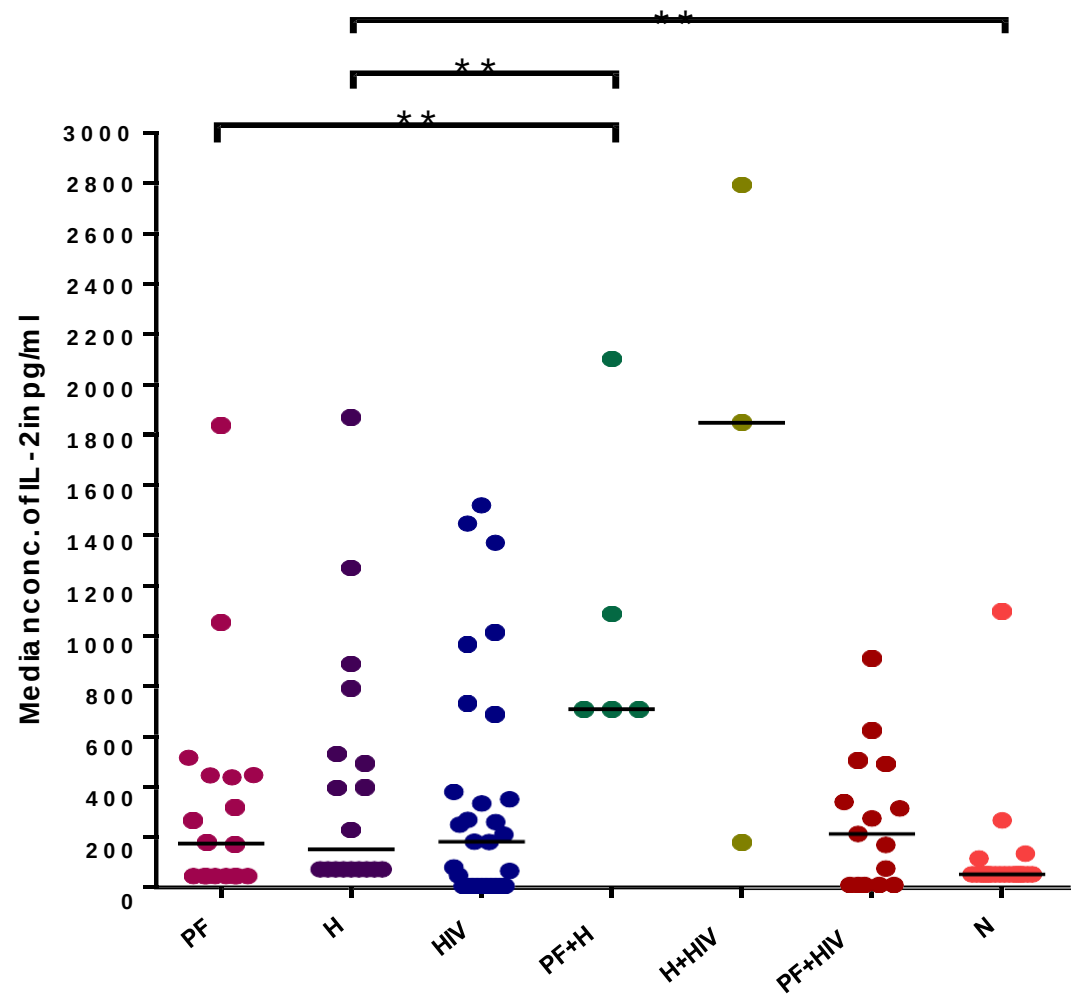
**
**
**
PF
H
HIV
PF+H
H+HIV
PF+HIV
N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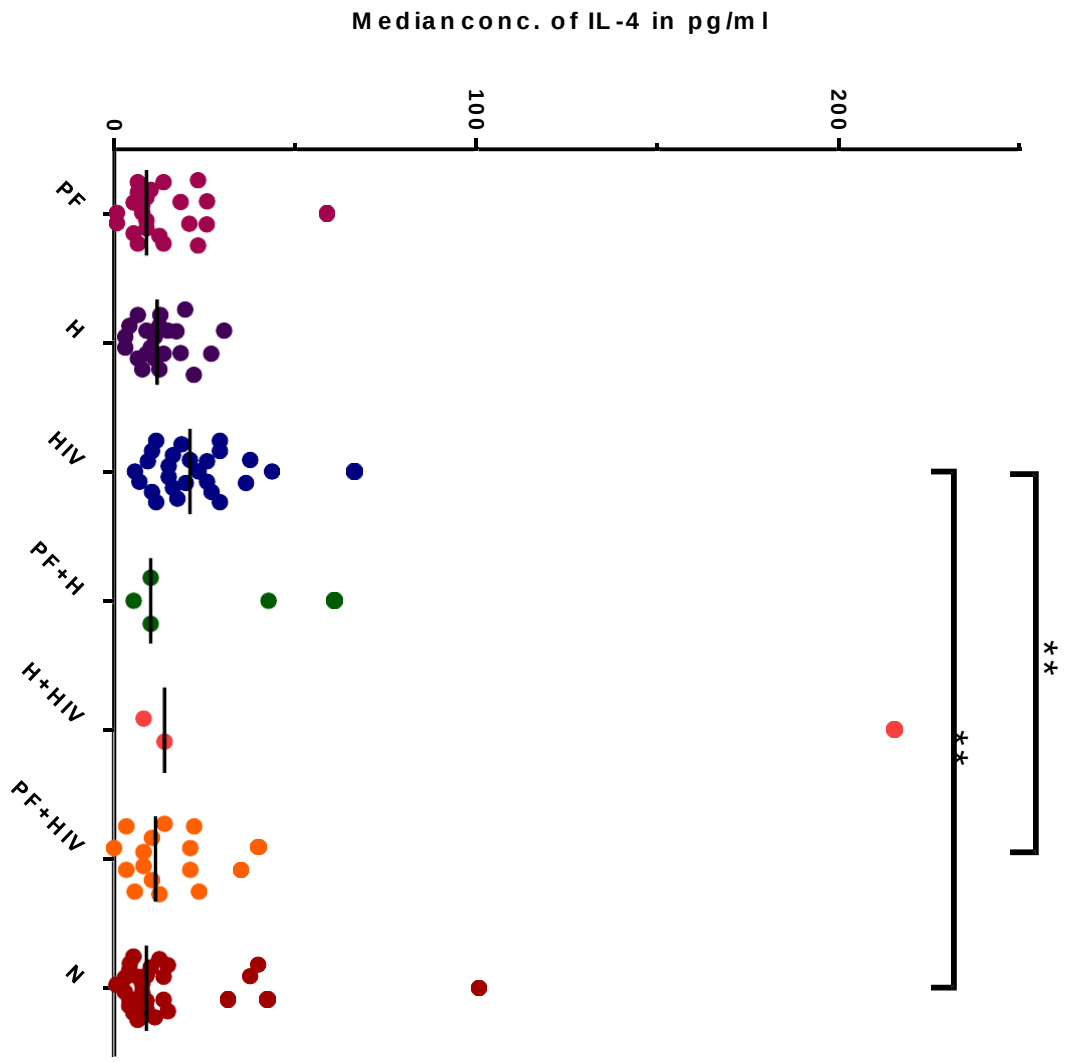
**
**
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Median conc. of IL-2 in pg/ml
PF
H
HIV
PF+H
H+HIV
PF+HIV
N


Median conc. of IL-4 in pg/ml
0
100
200
PF
H
HIV
PF+H
H+HIV
PF+HIV
N
**
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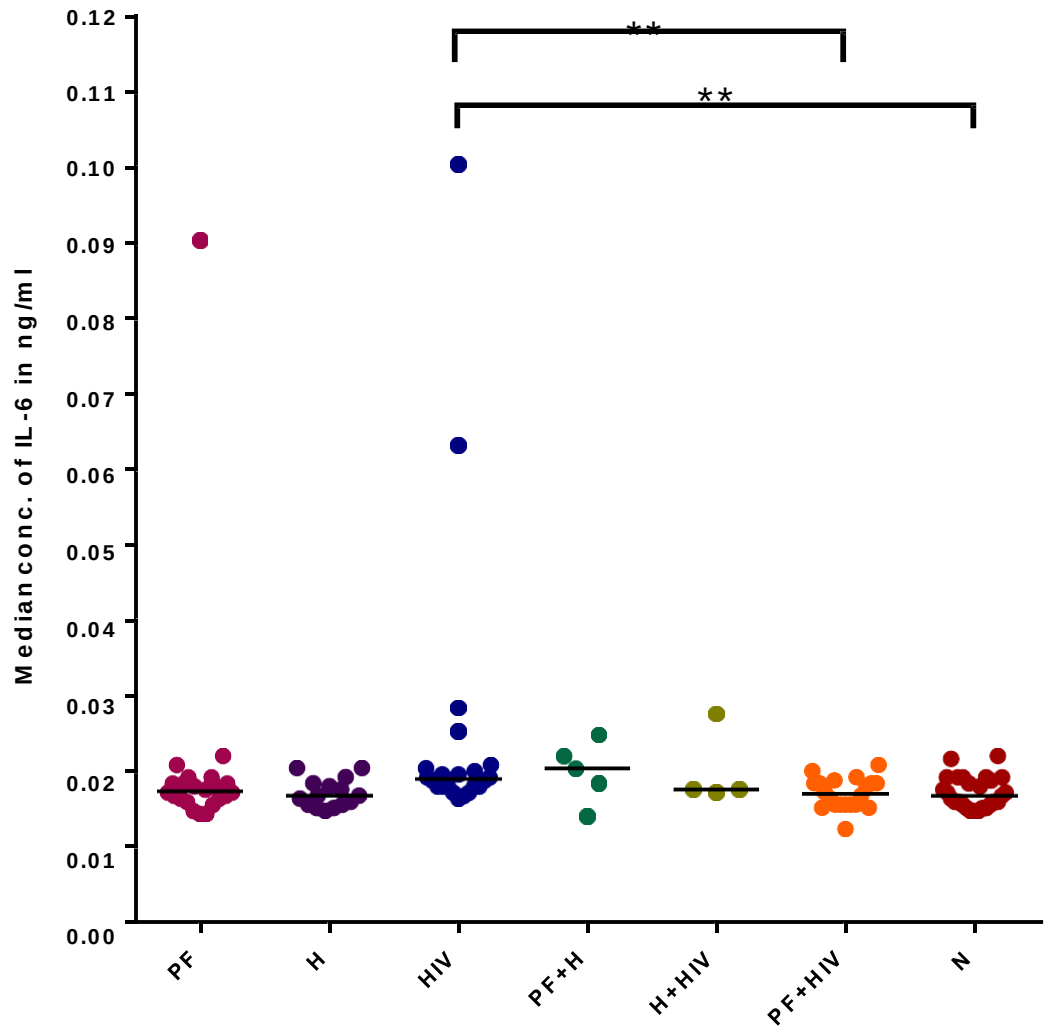
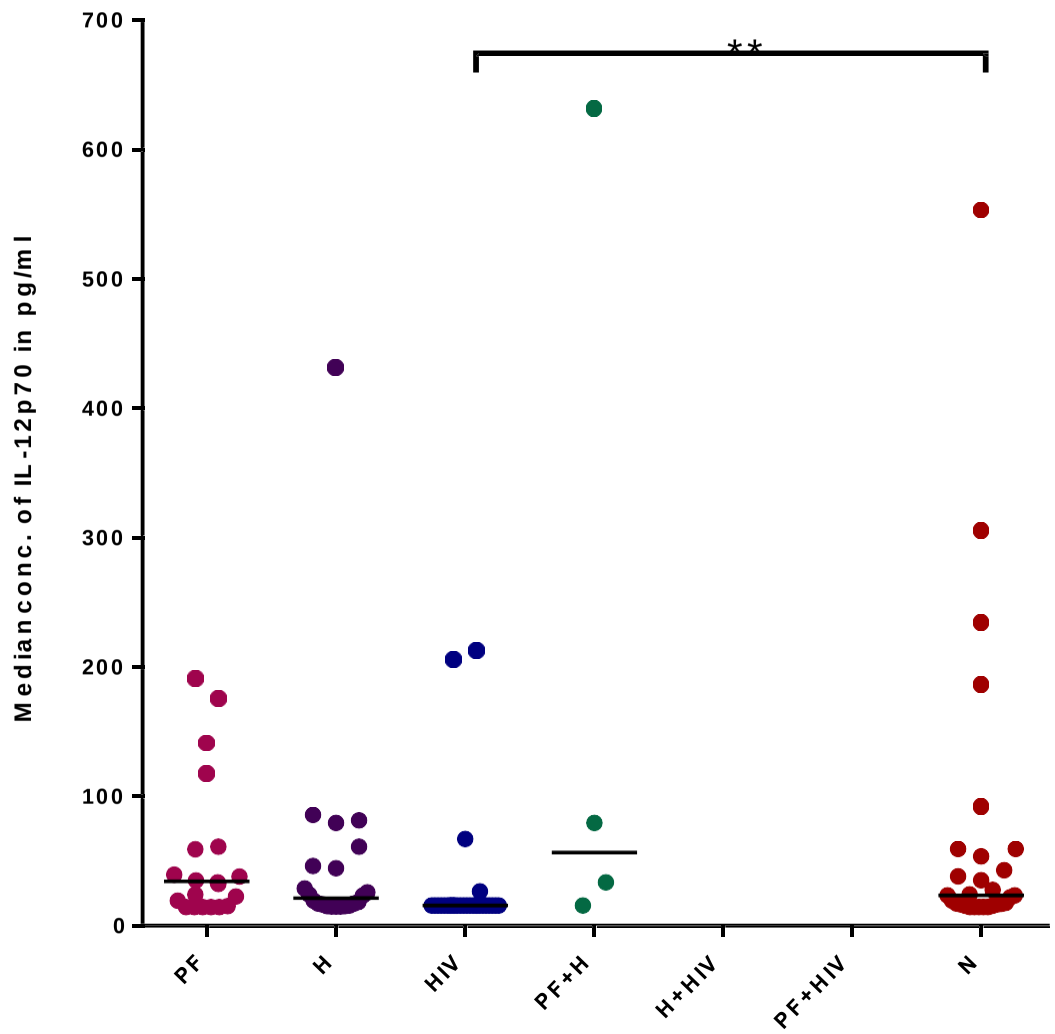
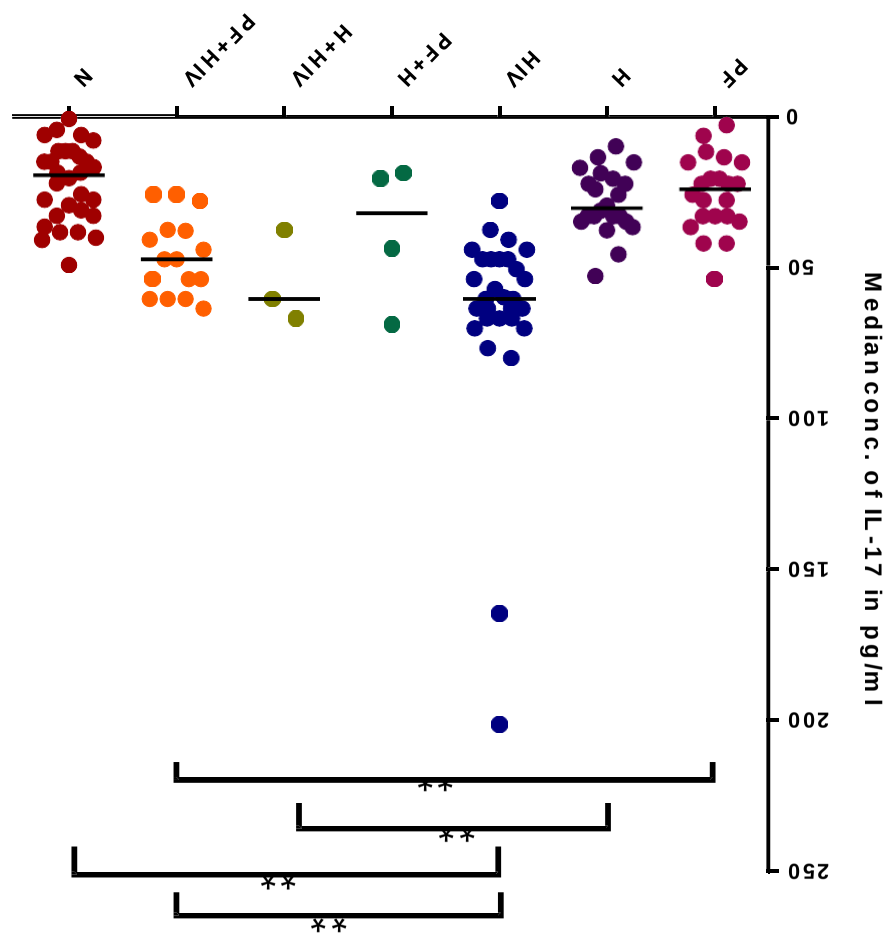

Median conc. of IL-6 in ng/ml
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
**
**
PF
H
HIV
PF+H
H+HIV
PF+HIV
N


**
700
600
500
400
300
200
100
0
Medianconc. of IL-12p70 in pg/ml
PF
H
HIV
PF+H
H+HIV
PF+HIV
N


N
PF+HIV
H+HIV
PF+H
HIV
H
PF
0
50
100
150
200
250
Median conc. of IL-17 in pg/ml
**
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Limitation

- Few cases of co-infection of *Plasmodium* and helminthes
- Few cases of co-infection of HIV and helminthes.
- Reduced capacity to make strong statistical inferences is reduced.
- More studies with larger number of co-infection cases will further increase the body of existing knowledge on impact of co-infection on immunological profile.

Background

- The sub-Saharan region of Africa is the most endemic for *P. falciparum* and HIV infections (UNAIDS, 2014; WHO, 2014).
- The burden of helminthes is also relatively high (Pullan *et al.*, 2014).
- Helminthic infection influenced susceptibility and severity of *Plasmodium* and HIV infections in pregnancy (Egwunyenga *et al.*, 2001; Ndibazza *et al*., 2013).
- Pregnancy-induced immune responses also affected by inflammation or infectious diseases (Marzi *et al.,* 1996).