

RESEARCH

Open Access



Brief communication: coagulation profiles of HIV positive patients on antiretroviral therapy (ART) at the Mampong Municipal Hospital, Ashanti-Region, Ghana: a case control study

Freddie Boateng Opoku^{1†}, Akua Koaso Yalley^{1*†}, Nicholas Israel Nii-Trebi¹, Ekoutiame Ahlin^{2,3}, Abena Asefuaba Yalley⁴ and Ransford Kyeremeh¹

Abstract

This study aimed to ascertain how the current two ART regimens used in Ghana affected HIV patients' coagulation profiles. A case-control study was conducted on 102 HIV positive patients at the Mampong Municipal Hospital. Coagulation parameters measured showed APTT was normal in majority of ART-experienced participants but prolonged in majority of ART-naïve participants. The mean platelet count was significantly higher in ART-experienced participants. No significant differences were found between the coagulation profiles of ART-experienced patients on two different drug regimens. In conclusion, current ART can enhance the coagulation profiles in HIV-infected patients, by improving platelet count and APTT.

Keywords Antiretroviral therapy, Human immunodeficiency virus, Coagulation profile, Activated partial thromboplastin time, Platelet count, International normalized ratio

Introduction

Currently, the antiretroviral therapy (ART) drug combination Tenofovir + Lamivudine + Efavirenz (TDF + 3TC + EFV), referred to in this study as regimen 1 (R1) which is an integrase strand transfer inhibitor (INRTI)-based regimen and Tenofovir + Lamivudine + Dolutegravir (TDF + 3TC + DTG), referred to in this study as regimen 2 (R2), a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen are the two ART mostly being administered at the Mampong Municipal Hospital, Ashanti Region, Ghana for HIV first-line or second-line treatment. Coagulation parameters remain to be fully described since Ghana switched to integrase strand transfer inhibitor (INRTI)-based

[†]Freddie Boateng Opoku and Akua Koaso Yalley contributed equally to this work.

*Correspondence:

Akua Koaso Yalley
akyalley@ug.edu.gh

¹Department of Medical Laboratory Sciences, School of Biomedical and Allied Health Sciences, University of Ghana, P.O. Box KB 143, Accra, Ghana

²Free University of Berlin, Kaiserswerther Str. 16-18, 14195 Berlin, Germany

³Center for Research and Opinion Polls (CROP), Boulevard du 30 aout, Carrefour La Pampa, Immeuble Cleveland building, 5 BP 568, Lome, Togo

⁴Zukunftscolleg, Department of Politics and Public Administration, University of Konstanz, 78464 Konstanz, Germany



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

regimen a few years ago. In order to analyze the potential impact of the two ART regimens on coagulation profiles, this study compared the coagulation profiles of HIV patients on ART to those of newly diagnosed HIV patients who were yet to be put on ART. The rationale behind the study is that though HIV infection causes coagulation problems, there is conflicting information about the effect of ART regimens on coagulation profiles since the drugs can cause liver damage which can lead to coagulation problems [1].

Methods

Study plan/study area/study participants

This case-control study compared the coagulation profiles of HIV patients receiving ART (ART-experienced) to newly diagnosed HIV patients who had not yet initiated ART as the control group (ART-naïve). A sample size of 102 participants was used, which comprised 52 ART-experienced and 50 ART-naïve individuals. The following categories of patients were excluded from the study: patients who refused to participate, those who had bleeding problems and those receiving anticoagulant therapy unrelated to their infection status; those with myeloproliferative disorders; those who had liver diseases and patients taking medications other than ART. Apart from participant ART status, the baseline difference between the two groups were the percentage of females were slightly higher and there were no participants below 25 years in the ART-experienced group as compared to the control group. The Mampong Municipal Hospital's Retroviral Clinic was the recruitment site for the study participants. The hospital serves the entire Mampong municipality in the Ashanti region of Ghana, and is an area made up of 55% rural settlements and 45% urban settlements [2]. Study participants were from all walks of life. Clinical and demographic data were gathered by means of a questionnaire.

Blood sample collection and processing

Under aseptic conditions, 1 to 4 ml of blood were collected from participants and the following tests were run on the samples; Platelet count, Activated Partial Thromboplastin Time (APTT) estimation, Prothrombin Time (PT) Estimation and International normalized ratio (INR).

Statistical analysis

Data was entered into IBM Statistical Package for Social Sciences (SPSS) statistics for Windows, version 21.0 (IBM Corporation, Armonk, NY), STATA MP/14.1 (Statacorp LLC, Texas, USA) and Microsoft Excel (2016 version) and analyzed. For various variables, data was expressed using the means, percentages and standard deviations. Unpaired T-test analysis was performed to elucidate

the difference between means of ART-experienced participants and ART-naïve participants; between means of Female ART-experienced participants and female ART-naïve participants; between means of male ART-experienced participants and male ART-naïve participants; and between means of the two different ART regimens. Fisher's exact test was used to assess potential associations between categorical variables (Gender and ART adherence). Statistical significance was set at $P < 0.05$.

Results

General characteristics of study participants and baseline differences

One hundred and two (102) participants were included in this study out of which 63% were female. The majority of participants (66%) were above 36 years. Of the ART-experienced participants, 17 (32.7%) were males and 35 (67.3%) were females. Of the ART-naïve participants, 21 (42%) were males and 29 (58%) were females. Whereas 100% of ART-experienced participants were above 25 years, 66% of the ART-naïve participants were above 25 years (with 14% below 18 years).

Coagulation profile of study participants against reference standards

To evaluate the coagulation profiles of both ART-experienced and ART-naïve individuals against reference standards, Platelet count, PT, INR and APTT values were measured and their individual values compared to their respective biological reference ranges [3]. For both ART-naïve and ART-experienced participants, majority had prolonged PT (~ 16 s). Similarly, a majority of ART-naïve and ART-experienced participants had high INR values above the biological reference interval of 0.80–1.30. APTT values of 33 ART-experienced participants representing the majority fell within the standard reference range of 30–40 s. On the other hand, a greater percentage of ART-naïve participants (60%) had prolonged APTT values (~ 40 s). A summary of the data is shown in Fig. 1.

Comparing the coagulation profile of ART versus ART-naïve participants

To compare the coagulation profiles of ART participants to those of ART-naïve participants, the mean values of the various parameters as shown in Table 1 were compared using an unpaired T test. The mean platelet count was significantly higher in patients on ART compared to the ART-naïve participants ($p < 0.05$). Differences seen in the other 3 parameters were not statistically significant.

Effects of different ART regimen on coagulation profile

The effects of different combination of ART regimen on platelets, PT, INR and APTT were also investigated. Participants on R1 appeared to have a higher mean platelet

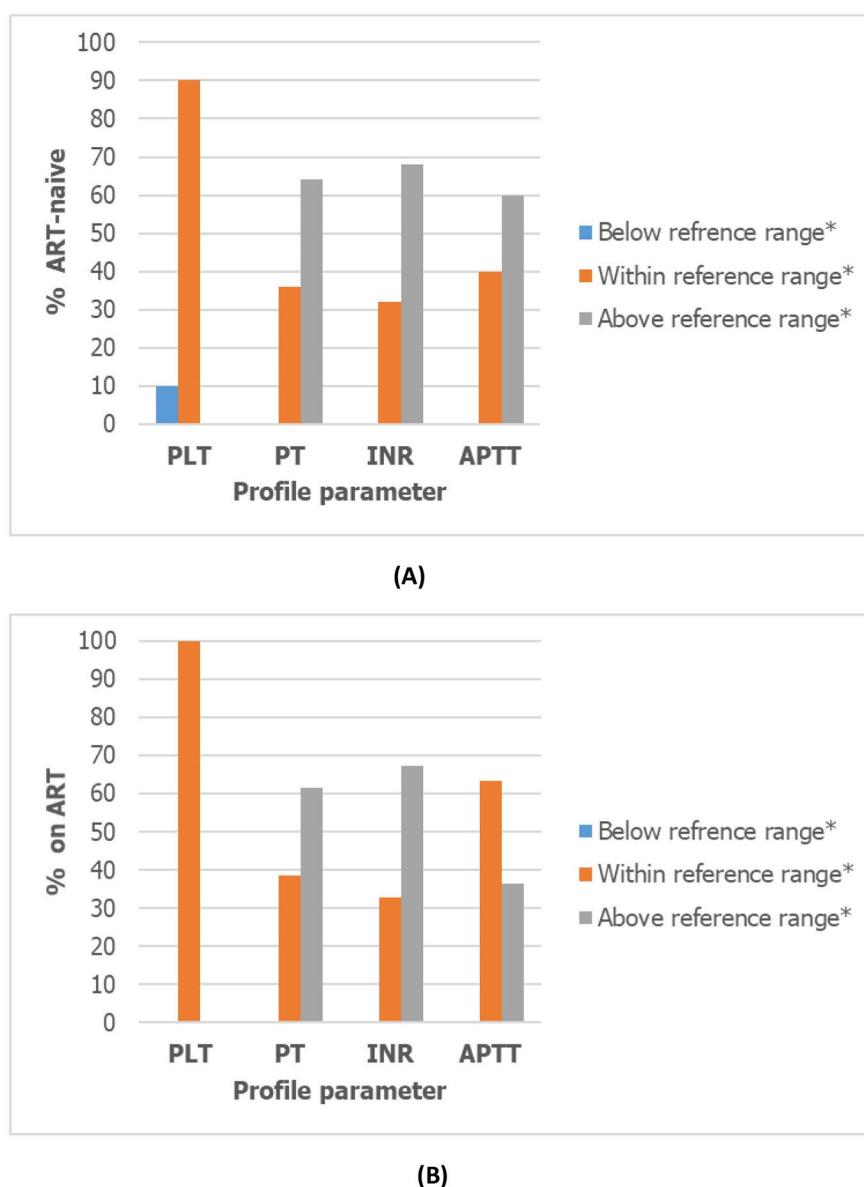


Fig. 1 Coagulation profile of study participants against reference standards **(A)**: Displays percentage of ART-naïve participants within and outside the standard reference ranges of the indicated parameters; **(B)**: Displays percentage of ART-experienced participants within and outside the standard reference ranges of the indicated parameters. PLT=Platelet count; PT=Prothrombin Time; INR=International Normalized Ratio; APTT=Activated Partial Thromboplastin Time; *Reference ranges: PLT($\times 10^9/L$): 150–450; PT (sec): 11–16; INR: 0.80–1.30; APTT (Sec): 30–40

count compared to those on R2. However, this difference did not reach statistical significance ($p=0.827$). Also, no statistically significant differences were observed in the means of PT, INR and APTT between participants on R1 and those on R2.

Effects of inconsistent use of ART on the coagulation profiles of HIV positive participants

Forty five (86.5%) out of the ART-experienced participants indicated not skipping any doses of the ART drugs. The prevalence of full ART adherence in females

was 88.6% whereas that of males was 82.4%. The difference was however not statistically significant ($p=0.670$). In addition, there was no significant difference between coagulation profiles of fully adherent and partially adherent participants.

Discussion

In this study, the results show that participants on ART had significantly higher average platelet count as compared to ART-naïve patients. This indicates that ART may help improve the platelet count of HIV-infected people.

Table 1 Comparing average coagulation profiles of ART participants against ART-naïve participants. Shows average values of the indicated parameters and accompanying *P*-values

Parameters	ART Status	Number (N)	Mean \pm SD	<i>P</i> -value
PLT ($\times 10^9$ /L)	ART-experienced	52	320.10 \pm 63.29	0.00
	ART-naïve	50	238.82 \pm 75.18	
PT (sec)	ART-experienced	52	23.36 \pm 15.77	0.059
	ART-naïve	50	18.61 \pm 7.97	
INR	ART-experienced	52	2.06 \pm 1.41	0.054
	ART-naïve	50	1.62 \pm 0.76	
APTT (sec)	ART-experienced	52	40.60 \pm 8.01	0.084
	ART-naïve	50	43.06 \pm 6.08	

PLT = Platelet count; PT = Prothrombin Time; INR = International Normalized Ratio; APTT = Activated Partial Thromboplastin Time; SD = standard deviation

Only 10% of the ART-naïve participants had platelet counts indicative of thrombocytopenia. Thrombocytopenia was also noted in reports from other research though it was unclear if the HIV patients were on HIV drugs [4, 5].

INR in a greater proportion of both subjects and controls were above the biological reference interval. In addition, APTT values of the majority of ART-experienced participants was normal. However a higher proportion of ART-naïve participants had prolonged APTT values when compared to the reference range. This is consistent with studies indicating that antiphospholipids or lupus anticoagulants, which were shown to occur in HIV patients as indicated in studies in Nigeria and USA, have been linked to prolonged APTT [6–9]. Also, average APTT values were lower in the ART-experienced compared to the ART-naïve patients albeit not statistically significant.

It is normally anticipated that HIV's hypercoagulable state would result in shorter PT and APTT readings [10, 11]. However, in this investigation, the PT values in the HIV patients receiving ART and the ART-naïve controls showed a haemorrhagic tendency to be prolonged as observed in other studies among HIV positive subjects studies [7, 12, 13]. The liver plays a crucial role in coagulation and a problem therein may cause PT and APTT to be prolonged, predisposing HIV patients to bleeding tendencies. Difference in PT values between ART-experienced and ART-naïve participants was not statistically different as has been shown in a similar study [14].

This study showed that the particular ART regimen administered to patients had no apparent selective advantage in enhancing the coagulation profile in HIV patients receiving ART. In addition, no significant difference was observed in coagulation profiles between fully ART adherent participants and partially ART adherent participants, neither was there a significant difference in prevalence of male versus female drug compliant participants.

The study reported here had a number of limitations. The sample size was relatively low. Length of time patients had been on ART as well as viral load of ART-experienced participants and how that affected their coagulation profile was not factored into the analysis. Furthermore, the role of comorbidities like coinfections with other viruses such as hepatitis B [15], that could also affect outcomes of coagulation studies were not addressed. Hepatitis B is a sexually transmitted disease just as HIV is with highest endemicity found in sub-Saharan Africa [16] and hence one would expect to find coinfection among participants. Future studies would address all the above mentioned limitations.

In conclusions, the study demonstrated that any of the 2 ART regimens used for HIV first-line or second-line therapy could enhance the coagulation profile in HIV-infected patients by improving platelet count and APTT. To the best of our knowledge, this is the first coagulation profile studies in Ghana on these current ART combinations.

Abbreviations

HIV	Human Immunodeficiency Virus
ART	Antiretroviral Therapy
INRTI	Integrase Strand Transfer Inhibitor
PT	Prothrombin Time
APTT	Activated Partial Thromboplastin Time
INR	International Normalized Ratio
NNRTI	Nucleoside Reverse Transcriptase Inhibitor
TDF	Tenofovir
3TC	Lamivudine
EFV	Efavirenz
DTG	Dolutegravir

Acknowledgements

The authors acknowledge the guidance and mentorship of Mr Enos Kwame Adepa (Principal Laboratory Technician, AAMUSTED-Mampong) and the support of the GNPC foundation.

Author contributions

Conceptualization, F.B.O., A.K.Y. and R.K. N.I.N-T.; methodology, F.B.O. and A.K.Y.; formal analysis, F.B.O., A.K.Y. and E.A.; investigation, F.B.O.; writing—original draft preparation, F.B.O. A.K.Y. and R.K.; writing—review and editing, F.B.O., A.K.Y., N.I.N-T, E.A., A.A.Y. and R.K. All authors reviewed the manuscript.

Funding

No external funding was received for this study.

Data availability

The data that support the findings of this study are available in the open science framework repository, <https://doi.org/10.17605/OSF.IO/FVB9G>.

Declarations

Ethics approval and consent to participate

The School of Biomedical and Allied Health Sciences (SBAHS), University of Ghana, and Ghana Health Service Ethics Review Committee (GHS-ERC) were consulted for ethical clearance and approval was granted (Identification / approval numbers: SBAHS/AA/MLAB/18037891/2021–2022 and GHS-ERC:042/09/22 respectively). Before collecting the data and samples, written informed consent were obtained from participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 1 July 2024 / Accepted: 12 October 2024

Published online: 22 October 2024

References

1. Getawa S, Adane T. Coagulation parameters in human immunodeficiency virus infected patients: a systematic review and Meta-analysis. *AIDS Res Treat*. 2022;2022(1):6782595.
2. Mampong municipal assembly. Composite budget for 2023–2026: available online at <https://mofep.gov.gh/sites/default/files/composite-budget/2023/AR/Mampong.pdf> accessed August 26th 2024. 2023.
3. Pagana K, Pagana T, Pagana T. Mosby's Diagnostics and Laboratory Test reference. St Louis: Elsevier; 2019.
4. Abdollahi A, Shoar N, Shoar S, Rasoulinejad M. Extrinsic and intrinsic coagulation pathway, fibrinogen serum level and platelet count in HIV positive patients. *Acta Medica Iranica*. 2013;472–6.
5. Sullivan PS, Hanson DL, Chu SY, Jones JL, Ciesielski CA, Group AASoD. Surveillance for thrombocytopenia in persons infected with HIV: results from the multistate adult and adolescent spectrum of Disease Project. *JAIDS J Acquir Immune Defic Syndr*. 1997;14(4):374–9.
6. Awodu O, Adebayo A, Famodu A. Effects of anti-retroviral therapy on haemostatic and haemorheological parameters in HIV/AIDS patients. *Port Harcourt Med J*. 2011;5(3).
7. JAIYEOLA AA, HAEMOSTATIC PARAMETERS AMONG HAART NAÏVE HIV/AIDS. PATIENTS IN UNIVERSITY OF ILORIN TEACHING HOSPITAL, ILORIN. *Faculty of Pathology*. 2015.
8. Bloom EJ, Abrams DI, Rodgers G. Lupus anticoagulant in the acquired immunodeficiency syndrome. *JAMA*. 1986;256(4):491–3.
9. Ndakotsu MA, Salawu L, Durosinmi MA. Lupus anticoagulant in Nigerian patients living with human immunodeficiency virus/acquired immunodeficiency syndrome. *Journal of Microbiology, Immunology, and Infection* = Wei Mian Yu Gan ran Za Zhi. 2009;42(1):69–73.
10. Orlovic D, Smego RA. Hypercoagulability due to protein S deficiency in HIV-seropositive patients. *Int J Collaborative Res Intern Med Public Health*. 2009;1(6):0.
11. Abdullah WZ, Moufak SK, Yusuf Z, Mohamad MS, Kamarul I. Shortened activated partial thromboplastin time, a hemostatic marker for hypercoagulable state during acute coronary event. *Translational Res*. 2010;155(6):315–9.
12. Ephraim RKD, Ahadzie JE, Adu P, Boachie J, Agbodzakey H, Adoba P, et al. Abnormal coagulation profile in people living with HIV-AIDS on combined antiretroviral therapy: findings from a case-control study in the Ho municipality, Ghana. *Pan Afr Med J*. 2018;29(1):1–5.
13. Walter O, Anaebo QBN, Obeagu EI, Okoroiwu IL. Evaluation of activated partial Thromboplastin Time and Prothrombin Time in HIV and TB patients in Owerri Metropolis. *J Pharm Res Int*. 2022;29–34.
14. Raman RT, Manimaran D, Rachakatla P, Bharathi K, Afroz T, Sagar R. Study of basic coagulation parameters among HIV patients in correlation to CD4 counts and ART status. *J Clin Diagn Research: JCDR*. 2016;10(5):EC04.
15. Khan J, Rahim S, Akhtar RR, Shafique U, Prevalence OF, Hepatitis'B'and'C', and Importance of coagulation profile in patients presenting to orthopaedic ward of a tertiary care hospital. *Pakistan J Public Health*. 2019;9(3):132–4.
16. Vessellee DB, Yalley AK, Adjei DN, Appeaning M, Odoom PN, Kyeremeh R, et al. Prevalence of Hepatitis B Virus infection among inmates at the Monrovia Central Prison, Liberia. *Trop Med Infect Disease*. 2023;8(3):139.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.