THE EUROPEAN SOCIETY OF MEDICINE
Medical Research Archives, Volume 13 Issue 5

RESEARCH ARTICLE

Falciparum Malaria prevents HIV-associated Cervical Cancer in East and Central Africa (Hypothesis)

Prof. **Michael Odida** [1]; Prof. **Helga Rehder** [2]; **Christoph Larsen** [3]; Prof. **Jürgen Freers** [4]; Priv.-Doz.Dr.med. **Rolf Schmauz** [5]

[1] Department of Pathology, Faculty of Medicine, Gulu University, P.O. Box 166, Gulu, Uganda
[2] Institute of Medical Genetics, Medical University Vienna, Austria.
[3] Consulting4Change, Vietnam
[4] Former head of Medicine, Mulago Hospital, Kampala, Uganda.
[5] Corresponding author, Darmklinik Exter, Detmolder Str. 264, 32602 Vlotho, FRG.

OPEN ACCESS

PUBLISHED
31 May 2025

CITATION
Odida, M., Rehder, H., et al., 2025. Falciparum Malaria prevents HIV-associated Cervical Cancer in East and Central Africa (Hypothesis). Medical Research Archives, [online] 13(5). https://doi.org/10.18103/mra.v13i5.6499

DOI
https://doi.org/10.18103/mra.v13i5.6499

ISSN
2375-1924

ABSTRACT

In many parts of the world the human immunodeficiency virus (HIV) and cervical cancer (CC) are associated, but four case-control studies from Mulago University Hospital, Kampala, a highly prevalent area of falciparum malaria (FM), found no association. Adding to Kampala Tanzania and Rwanda with intermediate or low prevalence of FM and OR's of 2.0 and 5.9, respectively, an inverse geographical distribution is noted. Similar to malariotherapy practised in Austria 120 years ago by injecting curable types of malaria HIV might be eliminated by more aggressive attacks of FM. Recently, experts proposed future research on HIV and cancer. Risks accounting for FM should be determined for HIV-associated CC.

Introduction

Cosmopolitan FM as a risk factor deserves high priority in research on cervical cancer. In a prior short communication we reported synergistic and antagonistic interactions with FM and CCrisk from HPV.[1] In a second assessment the question is what FM may do to HIV. In Kampala and surrounding areas FM is highly prevalent.[1] Four case-control studies conducted between 1989 and 2011 at Mulago University Hospital showed no association (Table 1).[2-6] Confidence intervals (CI) of the risk for HIV always included the value of the odds ratio (OR) of 1·0. In the fourth and last study (Odida, personal communication) the OR amounted to 1·09 (95% CI 0·72-1·65).[7] Accordingly, the attractive hypothesis was formulated that FM prevents CC from HIV, i.e. shows antagonistic interaction in the risk for HIV-asssociated CC. An attempt is made to search the literature to support further this assumption.

Table 1: Risks (OR's) of case-control studies on the association between HIV and Cervical Cancer in East and Central Africa

Country Author	Year of study publication	OR*	(LCI - UCI)	Cases +	-	Ctrls. +	Ctrls. -
Uganda Schmauz	1984-5 1989	0.23	(0.04-1.28)	2	32	5	18
Uganda Sekirime	1993-5 2007	1.27	(0.58-2.80)	18	98	15	105
Uganda Newton	1994-8 2001	1.6	(0.7-3.6)	21	65	18	78
Uganda Odida#	2004-6 2011	1.09	(0.72-1.65)	55	238	54	254
Tanzania Kahesa	2007 2008	2.9 2.0	(1.4-5.9") (1.1-3.9+)	29	138	16	138
Rwanda Mpunga	2012-16 2018	5.9	(3.8-9.2)	113	447	42	918

#personal communication; "multi-, +bivariate analysis; *all studies used 95% CI except the first study from Uganda using 90% CI.Odds Ratio (OR), lower, upper confidence interval (LCI, UCI).

Material and Methods

The data bases PubMed and Google were used extensively. In this way, the report on malariotherapy was detected.[8] A main source was a global report on HIV and CC.[2] Only case-control studies were accepted. Prevalence of malaria in the populations where CC risks from HIV had been measured[9, 10] was taken from the country-wide malaria profile or malaria map and own observations[11,12,1] and was graded as low, intermediate and high.

Results

One argument to strengthen the hypothesis is historical malariotherapy applied first by the Nobel Laureate Julius Wagner-Jauregg, Professor of Psychiatry in Vienna, Austria, in the late 19th and early 20th century.[8] Patients with progressive paralysis, a late stage of neurolues, were inoculated plasmodia from easily curable types to kill the spirochaetes by high pyrexia. However, not all cases achieved remission. Since it is highly prevalent in Kampala,[1] FM may be superior in controlling adverse infections than repeated injections with less aggressive types. Epidemiological observations are matched by a remarkable treatment modality.

Perhaps more favourable are inverse geographical distributions observed in East and Central Africa. When comparing the countries Rwanda and Tanzania the risk estimates obtained from case-control studies in national referral hospital-centers were 5·9 and 2·0, respectively.[9, 10] In Kampala the values are zero (Table 1).[3-7] Prevalence of FM shows the opposite trend. In national referral centres hospital populations reflect frequencies of diseases as seen in the country. In both Rwanda and Tanzania the highlands show little malaria, but in the lowlands in the East and in the East and West, respectively, it is common.[11,12] The conclusion is that in Rwanda the CC-risk from HIV is high, since women are infected rarely with FM. In Tanzania the risk is intermediate. For the majority the prevalence of FM is high, only for a small segment of the population it is low as in most areas of Rwanda. Finally, as documented in the preceding study among patients and visitors of Mulago Hospital, Kampala, prevalence of FM is very high.[1] All women showed antibodies, and the risk is zero. The decrease in HIV-risk together with an increase in the prevalence of FM may suggests an antagonistic interaction between FM and HIV, both risk factors for CC. Indeed, FM may prevent CC- risk from HIV.

Discussion

In a recent proposal concerted efforts by a panel of experts arrived at a consensus on directions for research on HIV and cancer.[13] As others,[14] they did not consider FM although a case-control study and geographical inferences had implicated it to be a possible risk factor in malignant lymphomas and CC.[15-18]

Single CC risks from FM are always zero. Interactive estimates with HPV are mainly synergetic.[1] If the hypothesis holds, interaction with HIV would be the opposite, namely antagonistic. No interactions were detected between HPV and HIV,[6] but risks accounting for FM need to be determined in the web of causation of CC, particularly in the vaginal microbiome or bacterial vaginosis including Gardnerella vaginalis.[19]

For future vaccination strategies results from case-control studies may provide leads how to clear this sector of public health concern.[20] For a possible minority of CC negative for HPV women vaccinated in childhood against

FM and without protection from HPV-vaccination will there be prevention of HIV-associated CC?

Funding.

The study received private financial support from Priv.-Doz. Rolf Schmauz.

Acknowledgements

In memory of the late M.S.R. Hutt, Professor of Pathology, Makerere University, Kampala, Uganda and Dr. J. Higginson, first director of IARC, Lyon, France, pioneers in Geographical Pathology.

References

1. Odida M, Löscher T, Rehder H, Schmauz R. Malaria and Cervical Cancer Risk from HPV in Kampala, Uganda. *Epidemiol Public Health* 2024; 2: 1040-3.
2. Stelzle D, Tanaka LF, Lee KK, et al. Estimates of the global burden of cervical cancer associated with HIV. *Lancet Glob Health* 2021; 9: e161–9.
3. Schmauz R, Okong P, De Villiers E -M., *et al*. Multiple infections in cases of cervical cancer from a high-incidence area in tropical Africa. *Int J Cancer* 1989; 43:805–9.
4. Sekirime WK, Gray R. HIV Infection among Uganda Women with Cervical Cancer: a retrospective study. *Gynecol Obstet Invest* 2007; 63: 222–8.
5. Newton R, Ziegler J, Beral V, *et al*. A case-control study of human immunodeficiency virus infection and cancer in adults and children residing in Kampala, Uganda. *Int J Cancer* 2001; 92: 622–7.
6. Odida M, Sandin S, Mirembe F, Kleter B, Quint W, Weiderpass E. HPV types, HIV and invasive cervical carcinoma risk in Kampala, Uganda: a case-control study. *Infect Agent Cancer* 2011; 6: 8.
7. Odida M (personal communication, 2024).
8. Freitas DRC, Santos JB, Castro CN. Healing with malaria: a brief historical review of malariotherapy for neurosyphilis, mental disorders and other infectious diseases. *Rev Soc Bras Med Trop* 2014; 47: 260–1.
9. Mpunga T, Znaor A, Uwizeye FR, *et al*. A case–control study of HIV- infection and cancer in the era of antiretroviral therapy in Rwanda. *Int J Cancer* 2018; 143:1348–55.
10. Kahesa C, Mwaiselage J, Wabinga HR, Ngoma T, Kalyango JN, Karamagi CA. Association between invasive cancer of the cervix and HIV-1 infection in Tanzania: the need for dual screening. *BMC Public Health* 2008; 8: 262.
11. Rwanda Malaria Profile *(Google, accessed July, 13th, 2024)*
12. Tanzania Malaria Map *(Google, accessed July, 13th, 2024)*
13. Engels EA, Shiels MS, Barnabas RV, et al. State of the science and future directions for research on HIV and cancer: Summary of a joint workshop sponsored by IARC and NCI. *Int J Cancer* 2024; 154: 596–606.
14. Sitas F, Parkin DM, Chirenje M, Stein L, Abratt R, Wabinga H. Part II: Cancer in Indigenous Africans—causes and control. *Lancet Oncol* 2008; 9: 786–95.
15. Schmauz R, Mugerwa JW, Wright DH. The distribution of non-Burkitt, non-Hodgkin's lymphomas in Uganda in relation to malarial endemicity. *Int J Cancer* 1990; 45: 650–3.
16. Cook-Mozzafari P, Newton R, Beral V, Burkitt DP. The geographicl distribution of Kaposi's sarcoma and lymphomas in Africa before the AIDS epidemic. *Br J Cancer* 1998; 78(11): 1521-1528.
17. Odida M, Schmauz R, Lwanga SK. Grade of malignancy of cervical cancer in regions of Uganda with varying malarial endemicity. *Int J Cancer* 2002; 99: 737–41.
18. Carpenter LM, Newton R, Casabonne D, Ziegler J, Mbulaiteye S, Mbiddde E, Wabinga H, Jaffe H, Beral V. Antibodies against malaria and Epstein-Barr virus in childhood Burkitt-lymphoma: A case-control study in Uganda. Int J Cancer 2008;122, 1319-1322.
19. Abou Chacra I., FenollarF., Diop K. What Do We Currently Know? *Front Cell Infect.Microbiol. 2022 Jan 18;1:672429*
20. Datoo MS, Dicko A, Tinto H, et al. Safety and efficacy of malaria vaccine candidate R21/Matrix-M in African children: a multicentric, double-blind, randomised, phase 3 trial. *Lancet* 2024; 403: 533-544.

