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2 **Human Herpesvirus 8 seroprevalence among blood donors in Mali**

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22 Fax: +33142177411; E-mail: arnoldgermalonga@gmail.com ; gervillienarnoldmalonga@aphp.fr

23 **Short title:** HHV-8 seroprevalence in blood donors

24 **ABREVIATIONS:** Human Herpesvirus 8 (HHV-8), Latent Associated Nuclear Antigen 1
25 (LANA-1), Indirect Immunofluorescence Assay (IFA), Kaposi’s Sarcoma associated Herpesvirus
26 (KSHV).

27 **WORD COUNT:**

28 Abstract: 200

29 Main text: 1021

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39 **ABSTRACT**

40 **Background:** In sub-Saharan Africa, the Human Herpesvirus 8 (HHV-8) is endemic but with
41 disparities between regions and population studied. Although the virus remains mostly latent, there
42 is some evidences that blood transfusion may represents one of the transmission way for this virus.
43 Here, we evaluated HHV-8 seroprevalence among blood donors in Mali.

44 **Materials and Methods:** This cross-sectional study recruited blood donors from the Blood
45 Transfusion Center at Gabriel Touré Hospital, Bamako. Serum was used for the detection of latent
46 HHV-8 IgG directed against LANA-1 by an indirect immunofluorescence assay (IFA). HIV-1,
47 HBV, HCV and Treponema pallidum were also screened.

48 **Results:** HHV-8 seroprevalence was 10.4% in Malian blood donors. None of the socio-
49 demographic characteristics were associated with HHV-8 infection, although there is a tendency
50 of a higher HHV-8 seroprevalence among participants living in Bamako than those not living there.
51 One individual had co-infection HHV-8/HBV, another HHV-8/HCV while another had HCV and
52 Treponema pallidum. None has been tested positive for HIV infection.

53 **Conclusion:** This intermediate seroprevalence in Malian blood donors suggests that the risk of
54 HHV-8 transmission by transfusion should be considered. Further investigations are needed to
55 assess impact of HHV-8 in polytransfused patients residing in an endemic area for this virus.

56

57 **KEYWORDS**

58 HHV-8; Seroprevalence; Blood donors; Transfusion; IFA; Mali

59

60 INTRODUCTION

61 Human herpesvirus 8 (HHV-8), also known as Kaposi's sarcoma associated herpesvirus (KSHV),
62 causes several neoplastic diseases and is responsible of all forms of KS. HHV-8 infection is not
63 ubiquitous, but endemic in Sub-Saharan Africa, some parts of Eastern Europe and Mediterranean.
64 HHV-8 seroprevalence varies between different populations and it is commonly found in human
65 immunodeficiency virus (HIV)-positive individuals and men who have sex with men (MSM) ^{1,2}.
66 The exact route of transmission is still very much debated. Some studies report that saliva is
67 implicated as the main vehicle of transmission in sub-Saharan children; others, on the other hand,
68 support the hypothesis of horizontal transmission in adulthood ^{2,3}. It should be noted that, HHV-8
69 can be transmitted by blood transfusion. Ensuring good haemovigilance remains a major public
70 health problem in sub-Saharan Africa and more particularly in low-income countries on the African
71 continent ⁴. Various studies provide strong evidence of HHV-8 transmission by blood transfusion
72 in sub-Saharan Africa. A Ugandan study carried out on patients receiving transfusion; tested for
73 anti-HHV-8 antibodies pre- and post-transfusion, showed that 43% received blood seropositive for
74 HHV-8 and seroconversion risk was significantly higher in recipients of HHV-8 seropositive blood
75 ⁵. In addition, this area is described as highly endemic for this virus. Some sub-region countries
76 reported HHV-8 seroprevalences in blood donors of 14%, 22% and 57% in Burkina-Faso, Central
77 African Republic and Tanzania, respectively ^{2,6,7}. In Mali, HHV-8 studies in blood donors are
78 almost absent while the most dreaded post-transfusion infections are viral in origin. We
79 investigated the prevalence of antibodies directed against HHV-8 latent associated nuclear antigen
80 1 (LANA-1) by use of an indirect immunofluorescence assay (IFA) in blood donors from Bamako
81 and its periphery.

82

83 MATERIALS AND METHODS

84 This cross-sectional study included 229 parental and voluntary non-remunerated blood donors,
85 without clinical evidence of Kaposi Sarcoma recruited from November 2019 to January 2020 at
86 the Blood Transfusion Center at Gabriel Touré Hospital in Bamako, Mali. After collecting socio-
87 demographic characteristics, serum was collected for HIV-1, HBsAg, HCV and syphilis screening
88 in Bamako blood bank laboratory. The detection of HHV-8 antibodies directed against LANA-1
89 Immunoglobulin G (IgG) by IFA using the BC- 3 cell line infected with HHV-8 but not with
90 Epstein Barr virus (Figure 1 and Supplementary Figure 1) was performed as previously described
91 in the virology department of the Pitié-Salpêtrière Hospital, Paris, France ⁸. This technique uses
92 unstimulated cells (sensitivity 80 - 85%, specificity nearly 100%). Samples reactive at a 1:50
93 dilution were considered positive (Figure 1, A and C, Supplementary Figure 1, A, B, C and F).
94 Note that, the term “equivocal HHV-8 serology result” was used when after twice tests in some
95 patients, we had an indeterminate result, i.e. ambiguous, fluorescent slide on reading (Figure 1, B
96 and Supplementary Figure 1, D). Continuous variables were described with median and
97 interquartile range [IQR] and categorical variables as numbers and percentages. GraphPad software
98 was used to perform nonparametric tests, Mann–Whitney U test for quantitative data, Fisher exact
99 t test for qualitative data. Confidence interval was 95% (95%CI) and $p < 0.05$ was considered
100 significant.

101

102 RESULTS AND DISCUSSION

103 We showed that 10.4% of this population of apparently healthy blood donors in Mali had HHV-8
104 antibodies. None of them had clinical evidence of KS. The socio-demographic characteristics, the

105 geographical setting and HIV-1, HBsAg, HCV and syphilis (*Treponema pallidum*) screening of
106 the 229 blood donors are described in Table 1. The median age was 29 [IQR, 23-35] years. The
107 majority of blood donors were male (58%), residing in Bamako (89%), attending the center for a
108 parental blood donation (99%) and more than two-thirds have reached primary school or less
109 (69%). None of the socio-demographic characteristics tested were associated with HHV-8
110 infection, although there is a tendency of a higher HHV-8 seroprevalence among participants living
111 in Bamako than those not living there. One individual had co-infection with HHV-8 and HBV,
112 another with HHV-8 and HCV while another had one with HCV and *Treponema pallidum*. None
113 has been tested positive for HIV infection. Consistent with previous studies in Burkina-Faso,
114 Central African Republic and Tanzania, this blood donor population is young and predominantly
115 male ^{2,6,7}. The 8 (4%) blood donors with equivocal HHV-8 serology results were excluded in our
116 seroprevalence estimation. This is the first study to investigate HHV-8 seroprevalence in blood
117 donors in Mali showing a moderate seroprevalence around 10%. Many samples had negative HHV-
118 8 serology (Figure 1, D and Supplementary Figure 1, E). This seroprevalence is relatively close to
119 that has been reported in blood donors population in Burkina Faso ⁷. However, other studies carried
120 out in blood donors from the sub-region report high prevalence of up to 57% ^{2,6}. Differences in
121 assays used, ethnic groups of the sampled populations, cultural practices (pre-masticating baby
122 food, use of medicinal herbs), environmental factors (volcanic soil, exposure to iron) and
123 geographic location of these countries in the area described as the KS belt could be the reason for
124 observed differences in HHV-8 seroprevalence ⁹⁻¹¹. However, since the majority of transfusions
125 are whole blood, the presence of HHV-8 in the peripheral compartment does not exclude its
126 transmission, even in the absence of clinical symptoms. Especially since the Malian
127 recommendations in terms of transfusion safety do not prescribe leukodepletion steps while HHV-
128 8 is mostly latent in B lymphocytes.

129 Our study has some limitations; (i) the relative low sensitivity of the indirect immunofluorescence
130 test used leads to a possible underestimation of seroprevalence in our population, (ii) the patients
131 included in our study were all asymptomatic to KS, thus the comparison of fluorescence intensity
132 of serology, and in view of the HHV-8 quantification in peripheral compartment, between
133 symptomatic and asymptomatic patients could not be study; (iii) finally, the sample size studied is
134 limited and probably explains why the statistical results do not have rich significance.

135 In conclusion, this intermediate seroprevalence among blood donors in Mali suggests that the risk
136 of transmission of HHV-8 by transfusion should be considered. Further studies are needed on the
137 evaluation of HHV-8 transmission via blood transfusion in Africa, especially in children with
138 homozygous sickle cell disease, who generally require several transfusions, and who live in an area
139 of high HHV-8 seroprevalence.

140

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147 **DATA AVAILABILITY STATEMENT**

148 The data that support the findings of this study are available from the corresponding author upon
149 reasonable request.

150

151 **CONFLICT OF INTEREST STATEMENT**

152 The authors have disclosed no conflicts of interest.

153 **AUTHOR CONTRIBUTION STATEMENT**

154 AJ, AIM, VC and AGM designed and planned the study. SD, FTT, ZM, AB, OF and AIM included
155 the study patients and acquired the data. EC, SM, GAM conducted the experiments. GAM and AJ
156 analyzed and interpreted the data. GAM, AJ, AGM wrote the manuscript. GAM, AJ, AIM, VC and
157 AGM revised the manuscript. All the authors read and approved the final manuscript.

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200 and volcanic soil in southern Italy. *The Lancet*. 1996;347(9005):905. doi:10.1016/S0140-
201 6736(96)91388-4

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203 **Table 1: Sociodemographic and medical data according to HHV-8 serological status in the**
 204 **229 blood donors recruited**

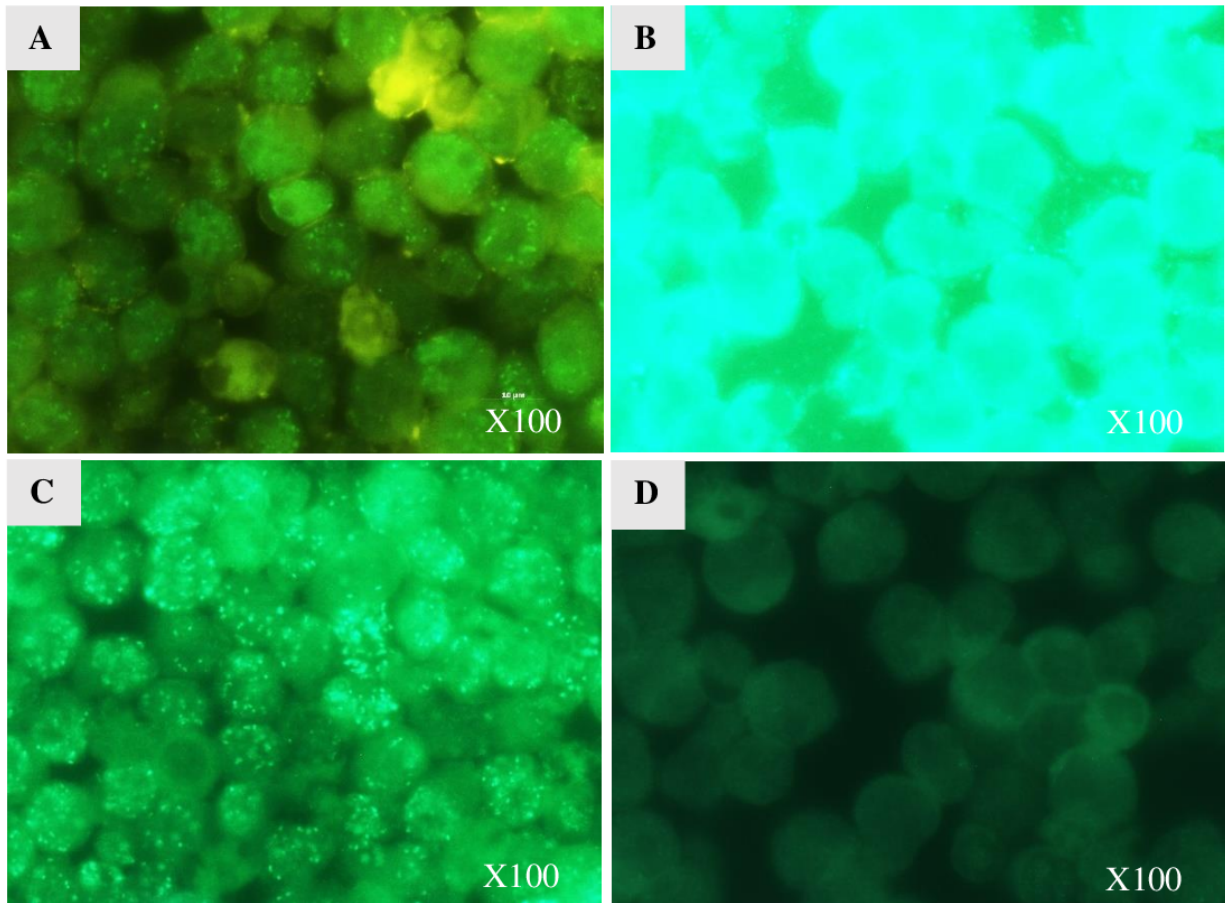
Characteristics	Total No. (%)	HHV-8 seropositive		HHV-8 seronegative		P value
		No.	%	No.	%	
All	229	23	10.4	198	89.6	
Age,						
median (IQR), years	29 (23-35)	32 (25-37)		28 (23-35)		0.24
Age group, years						
18-30	138 (60.3)	11	47.8	124	62.6	0.25
31-40	60 (26.2)	9	39.1	50	25.3	
41-50	28 (12.2)	2	8.7	22	11.1	
> 50	3 (1.3)	1	4.4	2	1	
Gender						
Male	133 (58.1)	12	52.2	115	58.1	0.65
Female	96 (41.9)	11	47.8	83	41.9	
Education level						
None	99 (43.2)	8	34.8	84	42.4	0.47
Primary	60 (26.2)	6	26.1	54	27.3	
Secondary	42 (18.3)	5	21.7	36	18.2	
Higher	28 (12.2)	4	17.4	24	12.1	
Marital status						
Single	79 (34.5)	8	34.8	70	35.4	> 0.99
Married	150 (65.5)	15	65.2	128	64.6	

Geographical setting						
Bamako	203 (88.6)	18	78.3	179	90.4	0.08
Around Bamako	26 (11.4)	5	21.7	19	9.6	
Type of blood donation						
Parental donors	226 (98.7)	23	100	195	98.5	> 0.99
Volunteers donors	3 (1.3)	0	0	3	1.5	
HIV-1 status						
Positive	0	0	0	0	0	NC
Negative	229 (100)	23	100	198	100	
HBsAg status						
Positive	22 (9.6)	1	4.4	20	10.1	0.70
Negative	207 (90.4)	22	95.6	178	89.9	
HCV status						
Positive	6 (2.6)	1	4.4	4	2	0.42
Negative	223 (97.4)	22	95.6	194	98	
T. pallidum status						
Positive	5 (2.2)	0	0	4	2.02	> 0.99
Negative	216 (94.3)	22	95.6	187	94.4	
Not specified	8 (3.5)	1	4.4	7	3.6	

HIV: Human Immunodeficiency virus 1; HBsAg: Hepatitis B surface antigen; HCV: Hepatitis C virus; IQR: Interquartile; No: number; NC: non calculated.

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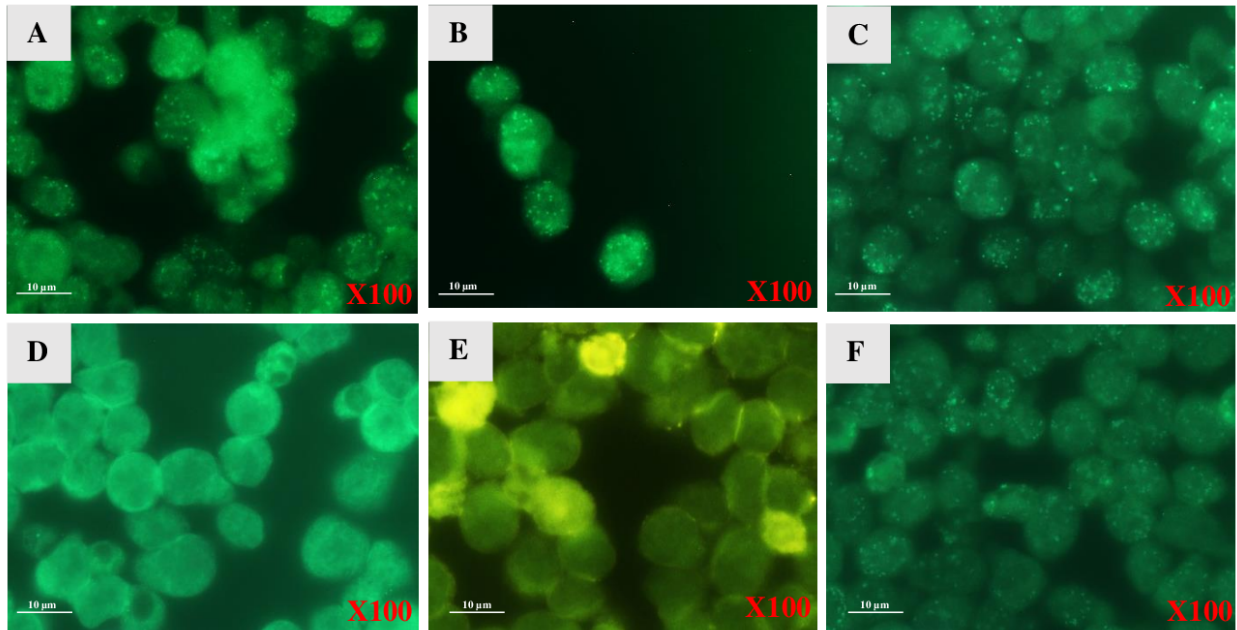
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Figure 1: Indirect Immunofluorescence assay for the qualitative detection of HHV-8 IgG antibodies directed against the LANA-1 protein. *The positivity for HHV-8 antibodies is revealed by the presence of dots in the nucleus. (A) positive sample at 1:50 dilution; (B) indeterminate result sample at 1:50 dilution (equivocal HHV-8 serology): ambiguous result, hyper fluorescence on reading; (C) strongly positive sample at the 1:50 dilution; (D) negative sample at 1:50 dilution.*



217

218 **Supplementary Figure 1: Pictures of Indirect Immunofluorescence assay for the detection of**
 219 **HHV-8 IgG antibodies directed against the LANA-1 protein. *The positivity for HHV-8***
 220 ***antibodies is revealed by the presence of dots in the nucleus. Positive sample at 1:50 dilution***
 221 ***(A); strongly positive sample at the 1:50 dilution (B) (C); indeterminate result sample at 1:50***
 222 ***dilution (equivocal HHV-8 serology): ambiguous result, presence of small dots in the cytoplasm***
 223 ***and fluorescence on reading (D); negative sample at 1:50 dilution (E); Positive control at 1:50***
 224 ***dilution (F).***

225