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Risk factors and prognostic significance of platelet count abnormalities in children with HIV infection on antiretroviral therapy

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Abstract

Objectives:

To establish the incidence, risk factors and correlation with survival of thrombocytopenia and thrombocytosis (T/T) among children with HIV infection (CWH).

Design:

A retrospective nested case control study of patients 0–18 years in five Baylor International Pediatric AIDS Initiative (BIPAI) centers in sub-Saharan Africa, 2004–2014.

Methods:

Clinical and laboratory variables including complete blood counts (CBC) were extracted from the BIPAI electronic medical record system. Incident cases of T/T were identified and frequency-matched on follow-up time with controls with normal platelets. We calculated the prevalence and incidence density of T/T and used conditional logistic regression to evaluate their association with selected clinical variables. We constructed Kaplan–Meier curves and a Cox proportional hazards model to evaluate the impact of T/T on survival.

Results:

Two thousand, one hundred and nine children were sampled. The incidence density of thrombocytopenia was 1 per 57.9 (95% confidence interval [CI] 50.3–66.8) CWH-years. Thrombocytopenia was higher in children with WHO Stage III/IV, lower in children on zidovudine, and had no association with use of lamivudine or nevirapine, CD4⁺ suppression, age, and nutrition status. Thrombocytopenia was independently associated with 2.2-fold higher mortality (95% CI 1.62–3.08). The incidence density of thrombocytosis was 1 per 11.4 (95% CI 10.7–12.1) CWH-years. Thrombocytosis was associated with higher CD4⁺ cell count, younger age, and use of lamivudine or nevirapine, and did not impact survival.

Conclusions:

Platelet count is a clinically valuable biomarker of HIV clinical progression and mortality. Laboratory studies are necessary to elucidate the mechanisms of T/T.

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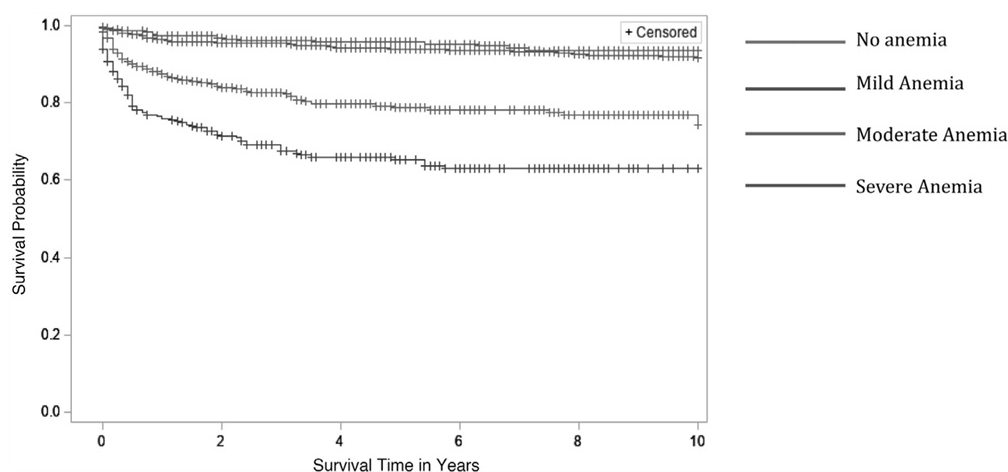
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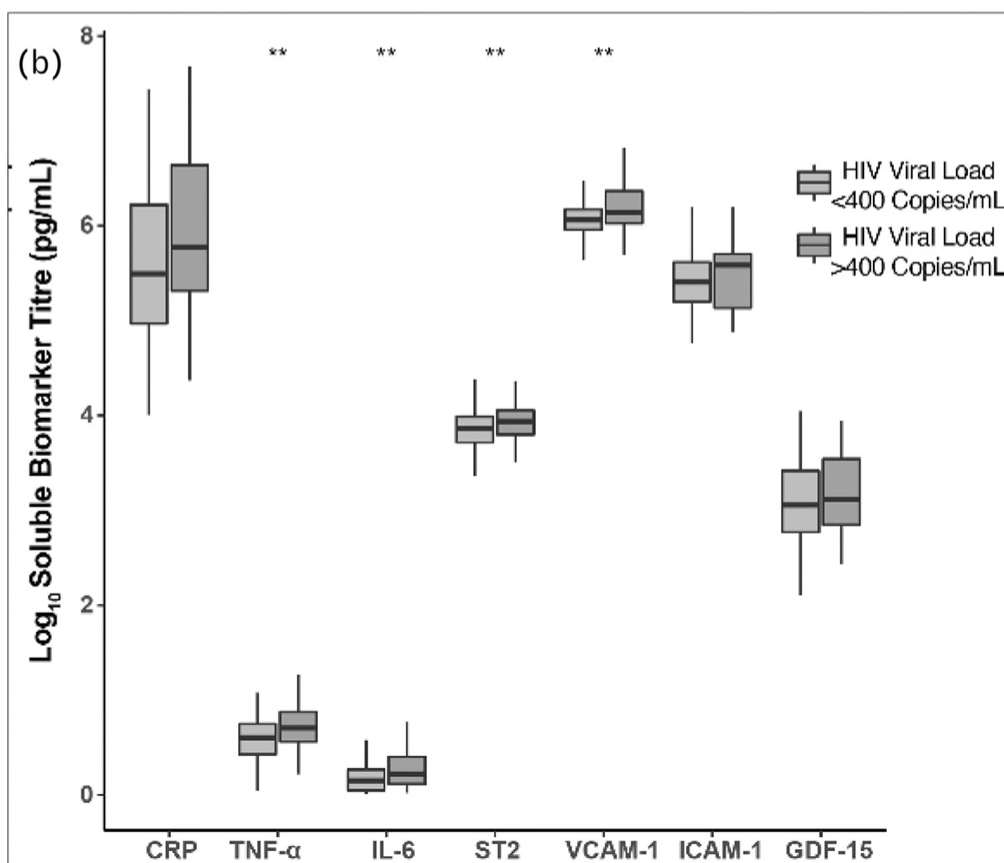
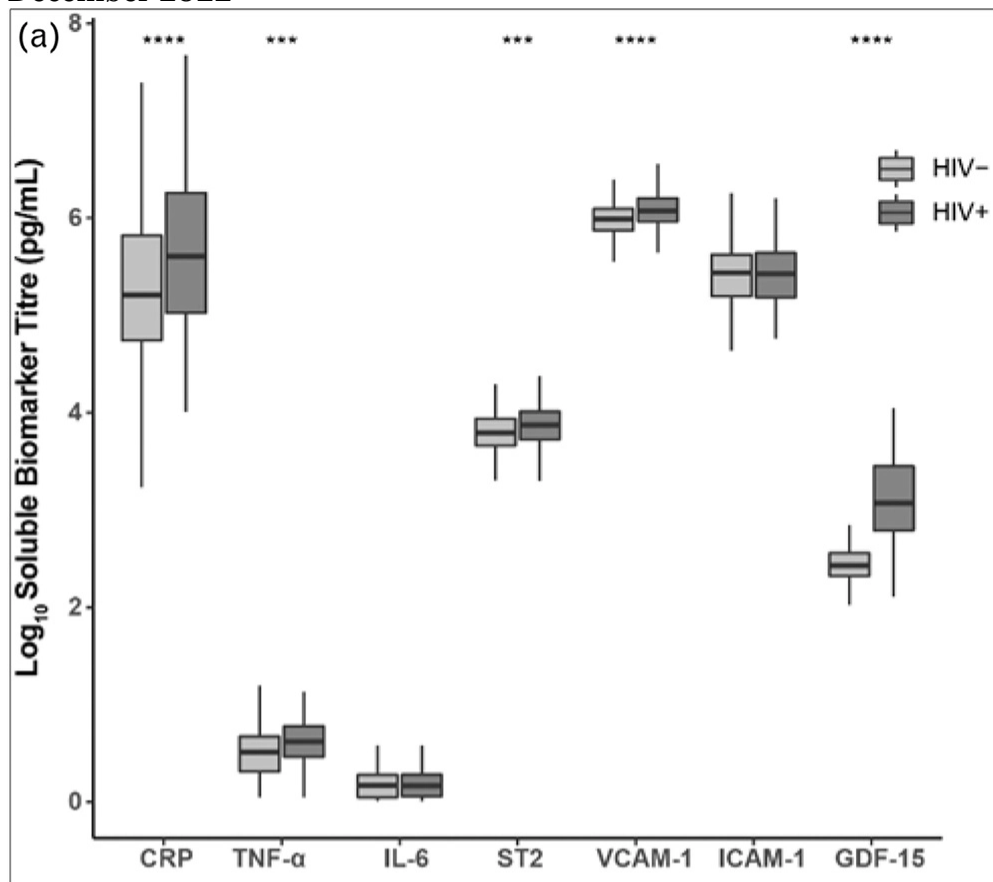
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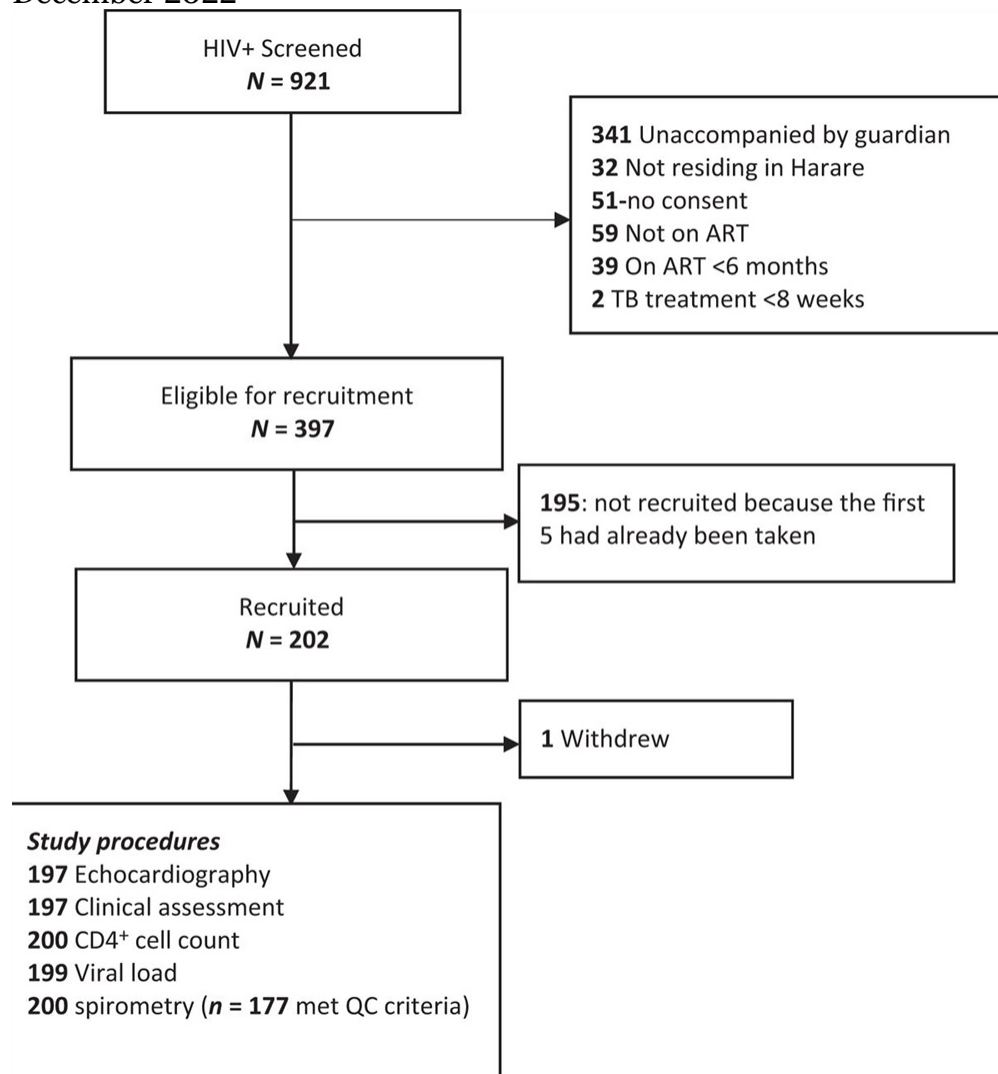
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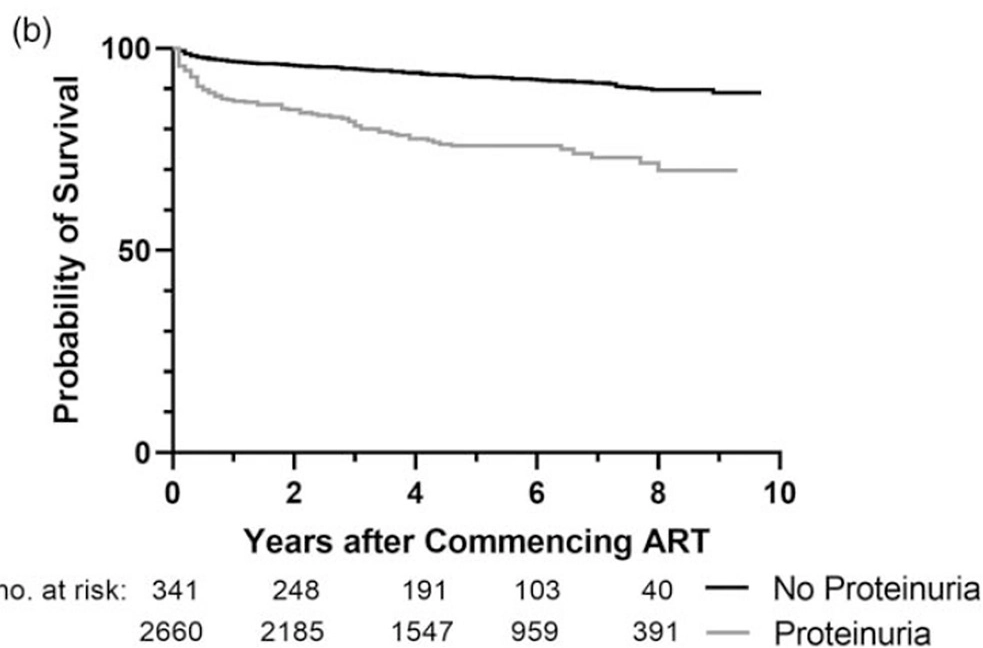
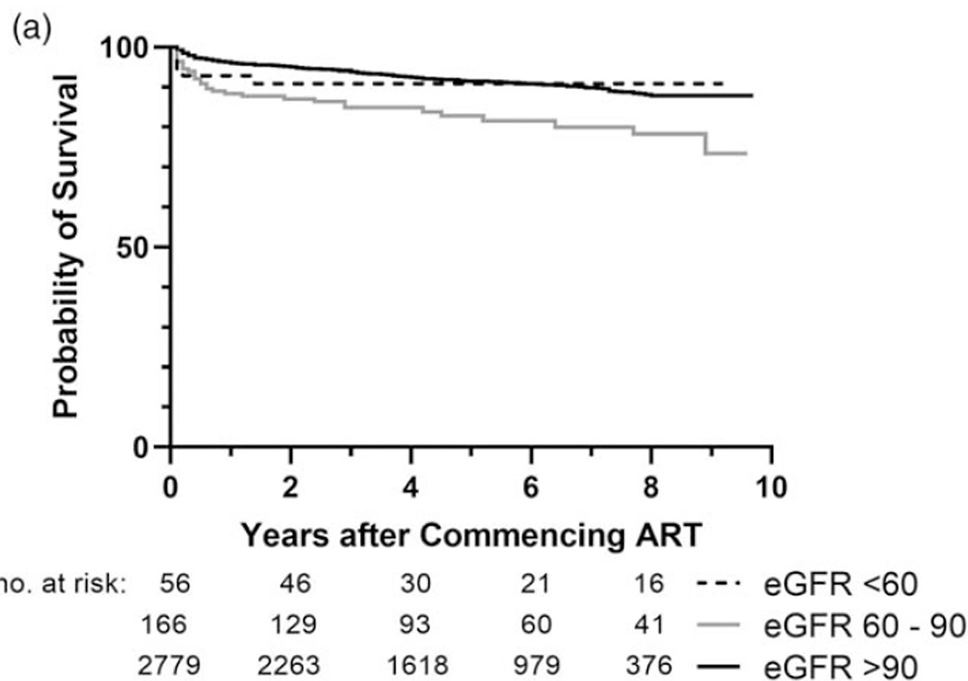
	Group 1 (≤6 months) med [IQR], N (%)	Group 2 (6–24 months) med [IQR], N (%)	Group 3 (≥24 months) med [IQR], N (%)	Overall med [IQR], N (%)	P value*
No. of participants	373	2634	1605	4612	
Demographics					
Age (years)					
<30	31 [25, 40]	34 [28, 42]	40 [33, 46]	36 [29, 44]	<0.001
30–49	168 (45.0)	880 (33.4)	248 (15.5)	1296 (28.1)	<0.001
≥50	174 (46.7)	1500 (57.0)	1096 (68.3)	2270 (60.1)	
Sex (female)	31 (8.3)	254 (9.6)	261 (16.3)	546 (11.8)	<0.001
Race	41 (11.0)	637 (24.2)	562 (35.0)	1240 (26.9)	<0.001
Asian	52 (13.9)	201 (7.6)	130 (8.1)	383 (8.3)	
Black	54 (14.5)	684 (26.0)	647 (40.3)	1385 (30.0)	
Latino/Hispanic	58 (15.5)	395 (15.0)	170 (10.6)	623 (13.5)	
White	191 (51.2)	1254 (47.6)	618 (38.5)	2063 (44.7)	
Other	18 (4.8)	100 (3.8)	40 (2.5)	158 (3.4)	
Geographic location					0.019
United States/Europe/Australia (high)	167 (44.8)	1179 (44.7)	788 (49.1)	2134 (46.3)	
S America/Africa/Asia (low-mid)	206 (55.2)	1455 (55.2)	817 (50.9)	2478 (53.7)	
HIV history					
Likely mode of HIV infection					<0.001
MSM	281 (75.3)	1557 (59.1)	709 (44.2)	2547 (55.2)	
Heterosexual	69 (18.5)	940 (35.7)	751 (46.8)	1760 (38.2)	
Injection drug use	4 (1.1)	23 (0.9)	36 (2.2)	63 (1.4)	
Blood products/Other/Unknown	19 (5.1)	114 (4.4)	109 (6.8)	242 (5.2)	
Months between HIV diagnosis and randomization	2.6 [1.9, 3.4]	7.3 [3.6, 13.3]	51.6 [35.0, 80.2]	12.8 [4.5, 37.0]	<0.001
Unknown HIV infection date	206 (55.2)	1496 (56.8)	1052 (65.6)	2754 (59.7)	<0.001
Months between HIV infection and randomization*	4.8 [4.0, 5.4]	14.3 [9.4, 23.2]	58.0 [40.9, 94.7]	19.5 [9.7, 44.2]	<0.001
Laboratory results					
CD4 ⁺ (cells/μl)	660 [585, 780]	654 [587, 773]	644 [579, 747]	651 [584, 764]	0.007
CD8 ⁺ (cells/μl)	1018 [764, 1358]	1031 [768, 1368]	1070 [796, 1457]	1041 [776, 1400]	0.003
CD4 ⁺ :CD8 ⁺ ratio	0.70 [0.50, 0.90]	0.67 [0.50, 0.92]	0.63 [0.45, 0.86]	0.66 [0.48, 0.89]	<0.001
HIV RNA (copies/ml)	27 199 [8140, 75 431]	13 553 [3330, 44 103]	9744 [2176, 35 769]	12 683 [3041, 43 100]	<0.001
<3000	43 (11.5)	621 (23.6)	476 (29.7)	1140 (24.8)	<0.001
3000–49 999	205 (55.0)	1419 (54.0)	838 (52.4)	2462 (53.5)	
≥50 000	125 (33.5)	590 (22.4)	286 (17.9)	1001 (21.7)	
Treatment assignment					
Immediate	198 (53.1)	1318 (50.0)	777 (48.4)	2293 (49.7)	0.24
Deferred	175 (46.9)	1316 (50.0)	828 (51.6)	2319 (50.2)	

IQR, interquartile range.

*Of those with known HIV infection date: $n = 1858$ (Group 1, $n = 167$; Group 2, $n = 1138$; Group 3, $n = 553$).*Unadjusted P value comparing the three groups. Wilcoxon rank sum test used to compare medians, and Chi-square tests for percents.

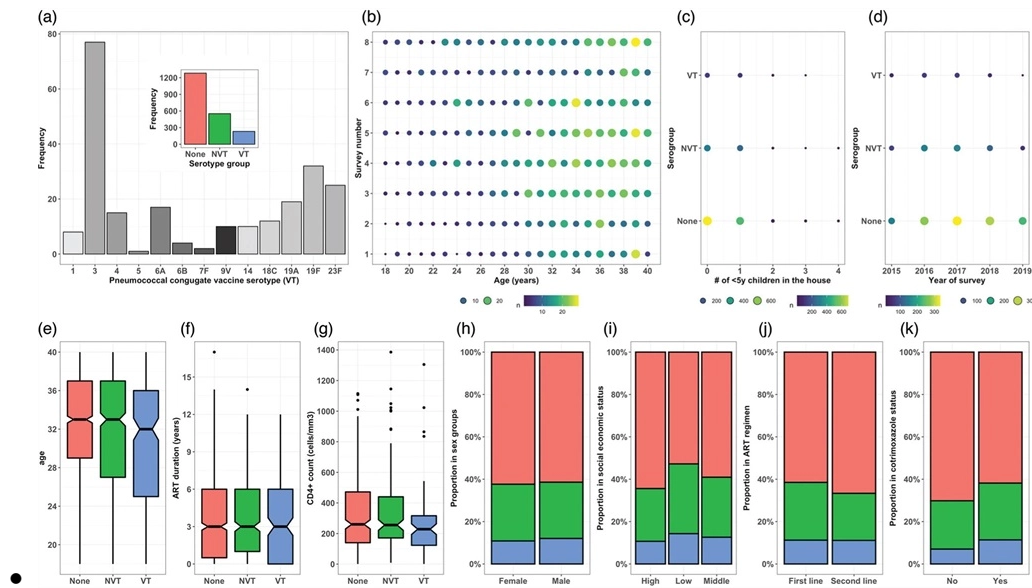
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