

Title: Clinical Characteristics and Outcomes of Cytomegalovirus Disease in HIV-Negative Non-Transplant Patients, a Propensity Score Match Analysis

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Background

Cytomegalovirus (CMV) infects millions in the US and is a source of comorbidity among immunocompromised patients. There is limited data on clinical characteristics or outcomes among HIV-negative, non-transplant (NHNT) patients in population-based cohorts.

Objective

We aim to evaluate a multicenter US-based network to obtain clinical characteristics and outcomes of NHNT patients with CMV disease and explore potential prognostic clinical characteristics implicated in increased morbidity and mortality.

Methods

This is a US-based multicenter, population-based, retrospective cohort study. We queried TrinetX, a global research network, to identify patients with a CMV disease by ICD-10-CM codes and serum and PCR > 5000 IU/mL. We captured comorbidities diagnosed within 90 days of CMV infection diagnosis, symptoms noted within 30 days, and outcomes of interest at 30 days and 1 year. Primary outcome was all-cause mortality. Secondary outcomes were hospitalization and CMV disease related complications. We performed a propensity score-matched analysis comparing clinical characteristics among patients who survived versus non-survivors at 90 days.

Results

We found 1123 patients with evidence of CMV disease. Mean patient age was 53 years, 48% men and 50% white. Aplastic anemia and neoplasms were the most common comorbidities (Table 1). Thromboembolism was a common complication (15%). Half of the patients had dyspnea, fever, abdominal pain, and nausea. CMV disease was associated with 14%, 22%, and 26% mortality at 30 days, 90 days, and one year, respectively. 35% of patients required hospitalization within 30 days. After propensity score matching, we had 278 patients in each

cohort. Dyspnea and weakness were linked to increased 90-day mortality (Figure 1). Purpura, encephalopathy, and sepsis were more common in patients who died. High CMV serum viral load and ferritin were associated with increased mortality.

Conclusions

NHNT patients with CMV disease often have underlying comorbidity, commonly aplastic anemia, and neoplasms. CMV disease was associated with thrombosis and high risk of hospitalization and mortality. Vascular disease, sepsis, high viral load, and cell lysis markers were prognostic factors for mortality in this cohort.

Table 1. Characterization of clinical characteristics of patients with CMV Disease in HIV-Negative Non-Transplant Patients. Overall description, comparison of non-survivors vs. survivors (90 days after index event).

Variable Mean ± SD, N (%)	Overall, N = 1123	Non-survivors, N = 234	Survivors N = 889	P-value
Demographics				
Age at Index	53 ± 18	65.1 ± 15.3	56.6 ± 18.2	< 0.0001
Male	543 (48%)	106 (45%)	437 (49%)	0.2867
Female	579 (52%)	128 (55%)	451 (51%)	0.2867
White	579 (52%)	142 (61%)	516 (58%)	0.4766
Hispanic or Latino	253 (23%)	41 (18%)	212 (24%)	0.0386
Not Hispanic or Latino	788 (70%)	166 (71%)	622 (70%)	0.7899
Black or African American	104 (9%)	20 (9%)	84 (9%)	0.6685
Asian	85 (8%)	20 (9%)	65 (7%)	0.528
Comorbidities				
Aplastic Anemia	894 (80%)	213 (91%)	681 (77%)	< 0.0001
Neoplasms	710 (63%)	159 (68%)	551 (62%)	0.0958
Essential hypertension	662 (59%)	154 (66%)	508 (57%)	0.0173
Purpura	619 (55%)	171 (73%)	448 (50%)	< 0.0001
Acute Respiratory Failure	480 (43%)	171 (73%)	309 (35%)	< 0.0001
Malnutrition	452 (40%)	127 (54%)	325 (37%)	< 0.0001
Pleural Diseases	444 (40%)	122 (52%)	322 (36%)	< 0.0001
Hypotension	436 (39%)	128 (55%)	308 (35%)	< 0.0001
Neutropenia	397 (35%)	93 (40%)	304 (34%)	0.1169
Type 2 Diabetes Mellitus	394 (35%)	95 (41%)	299 (34%)	0.0483
Sepsis	390 (35%)	159 (68%)	231 (26%)	< 0.0001
Lymphoid Malignancies	369 (33%)	85 (36%)	284 (32%)	0.2084
Venous Embolism and Thrombosis	343 (31%)	86 (37%)	257 (29%)	0.021
Other and Unspecified				
Encephalopathy	310 (28%)	109 (47%)	201 (23%)	< 0.0001
Heart Failure	292 (26%)	93 (40%)	199 (22%)	< 0.0001
Symptoms				
Malaise and Fatigue	623 (55%)	134 (57%)	489 (55%)	0.5473
Fever, Unspecified	600 (53%)	111 (47%)	489 (55%)	0.0253
Dyspnea	592 (53%)	130 (56%)	462 (52%)	0.3361
Nausea and Vomiting	561 (50%)	99 (42%)	462 (52%)	0.0082
Abdominal and Pelvic Pain	557 (50%)	102 (44%)	455 (51%)	0.0374
Cough	458 (41%)	82 (35%)	376 (42%)	0.0433
Weakness	444 (40%)	110 (47%)	334 (38%)	0.0089
Aphagia and Dysphagia	289 (26%)	81 (35%)	208 (23%)	0.0005
Medications				
Anticoagulants	931 (83%)	214 (91%)	717 (84%)	0.0044
Antineoplastics, antimetabolites	348 (31%)	58 (25%)	290 (33%)	0.0206
Antineoplastics, other	387 (34%)	92 (39%)	295 (33%)	0.081

Benzodiazepines	946 (84%)	214 (91%)	732 (82%)	0.0007
Bronchodilators	839 (75%)	201 (86%)	638 (72%)	<0.0001
Glucocorticoids	1023 (91%)	225 (96%)	798 (90%)	0.0025
Hydrocortisone	658 (59%)	159 (68%)	499 (56%)	0.0012
Loop Diuretics	747 (67%)	196 (84%)	551 (62%)	<0.0001
Pituitary (Peptide Hormones)	267 (24%)	115 (49%)	152 (17%)	<0.0001
Tacrolimus	270 (24%)	32 (14%)	238 (27%)	<0.0001
Lab Values				
CMV Serum Viral Load (IU/mL)	31,236 ± 253,512	28,570 ± 133,784	14,855 ± 110,337	0.7763
CD4+ T Cell Count (Cells/mL)	509 ± 1,606	190 ± 224	408 ± 458	0.0054
Leukocytes (10 ³ Cells/μL)	9.23 ± 14.6	27.5 ± 269	8.6 ± 7.53	0.0393
Neutrophils (10 ³ Cells/μL)	581 ± 2,621	257 ± 2074	579 ± 2409	0.0782
aPTT	36.3 ± 16.3	37.4 ± 28.2	23 ± 20.6	< 0.0001
INR	1.33 ± 1.25	1.88 ± 4.86	1.29 ± 1.26	0.0021
PT	14.9 ± 3.98	17.4 ± 11.5	14.9 ± 6.39	< 0.0001
Ferritin (mg/dL)	2,359 ± 4,092	5654 ± 15869	1710 ± 3267	< 0.0001
Bilirubin (mg/dL)	1.76 ± 4.65	5.3 ± 9.3	1.15 ± 2.94	< 0.0001
Lactate Dehydrogenase (U/L)	497 ± 544	839 ± 1060	435 ± 525	<0.0001

Figure 1. Selected critical variables associated with CMV mortality at 90 days after propensity score matching.

