Dettaglio abstract

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Title: Predictors of mpox duration and severity in an Italian multicenter cohort (Mpox-ICONA)

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Abstract
Background: Mpox is a pivotal example of how old viral pathogens can cause new outbreaks with novel clinical presentation and new routes of transmission. This analysis explores potential predictors of mpox severity and duration, and mpox virus (MPXV) persistence in relevant biological fluids after healing.
Method: Italian multicenter cohort study in the network of Icona Foundation. Severe cases were defined as those hospitalized or with proctitis, pharyngotonsillitis, ocular lesion, or >20 skin lesions, and recovery as the resolution of all mucocutaneous lesions. Predictors of mpox duration and severity were assessed by multivariable linear and logistic models, respectively. A stepwise backward process was fitted for the selection of variables in both multivariate models, using HIV status as a priori predictor. Assessment of early MPXV viral load (VL) as a predictor of severity was done by Student T-Test and logistic regression model.
Results: Between 11 May 2022 and 28 Jan 2023, 352 pts were enrolled (Fig A), 350 male, mean age 39 yrs (range 19-75), 158 (45.02 %) PLWH. The mean time to mpox resolution, in 319 pts with complete follow-up, was 23.15 days (95% CI 21.54-24.77): duration (Fig B) was significantly longer in pts with proctitis (+7.62 days), pharyngitis (+5.98 days), lymphadenopathy (+3.47 days), age >46 years (+4.40 days) and in PLWH with <350 CD4 (+14.29 days). Multivariable analysis for severity predictors (Fig C) showed that presentation with fever (OR 2.91; p<0.001), lymphadenopathy (OR 1.88), diarrhea (OR 4.43), peri-anal (OR 1.92) and face lesions (OR 1.92) were significantly associated with severe mpox. Quantitative determination of VL in the upper respiratory tract (URT) was available for 118 pts (74 mild and 44 severe). Mean Ct-value was 36.00 (95%CI 34.28-37.73) and 29.68 (95%CI 27.47-31.87) in mild and severe cases, respectively (P<0.001; Fig D). By logistic model the probability of developing severe disease had a strong inverse association with Ct-value, dropping by 10% per Ct (OR 0.90 95%CI 0.85-0.95; p<0.001; Fig E). Finally, we found that MPXV persists in body fluids despite clinical recovery: a detectable amount of MPXV was found in sperm (12/28 pts), urine (3/47), anorectal (8/38), and URT (18/73) specimens in recovered pts with a minimum Ct value of 26.
Conclusion: Clinical presentation with systemic symptoms (fever and lymphadenopathy), diarrhea, peri-anal and face lesions could predict the development of severe mpox. The occurrence of

proctitis/pharyngitis implies a longer disease duration, as does an advanced HIV infection with a low CD4 count, consistent with literature data. Remarkably, our results suggest that MPXV is a virulent pathogen with a direct association between VL and disease severity and with viral shedding that may persist even after clinical recovery in several anatomical sites. Urgently need to assess whether the persistence of MPXV in biological samples after clinical recovery may lead to a status of persistent infectivity.

(A) Description of the enrolled population

Population	Patients features	Num (N=352)	%
Epidmiological feature	Age	77	21.94%
	Male	350	99.43%
	Caucasian	233	66.38%
	Vaccinated	36	10.26%
	Omo-bisexual	331	94.30%
	Sexual transmission route	314	89.46%
	HIV neg	194	55.27%
	HIV pos >350 CD4	140	39.89%
	HIV pos ≤350 CD4	18	5.13%
Clinical presentation and symptoms	Severe disease	121	34.47%
	Hospedalized	69	19.66%
	Fever	228	64.96%
	Lymphadenopathy	197	56.13%
	Myalgia	54	15.38%
	Sore throat	39	11.11%
	Fatigue	73	20.80%
	Headache	52	14.81%
	Diarrhea	17	4.84%
	Pharyngitis	40	11.40%
	Proctitis	44	12.54%
Lesions distribution	Peri-anal lesion	128	36.47%
	Face lesion	158	45.01%
	palmar-plantar lesion	54	15.38%
	Penile lesions	160	45.58%
	Groin lesion	10	2.85%
	Lower limbs lesion	77	21.94%
	Upper limbs lesion	85	24.22%
	Ocular lesions	6	1.71%
	More than 20 lesions	25	7.12%

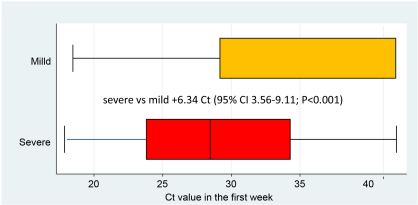
(B) Predictors of mpox duration by fitting a linear regression model

Patients feature		Unadjusted analysis				Multivariable analysis			
		Time to recovery (day)			P-value	Time to recovery difference (day)			P-value
		Mean	95% CI			Mean	95% CI		
Lymphadenopathy	no	21.13	19.58	22.68	0.038	base			
	yes	24.58	22.07	27.10		3.47	0.30	6.64	0.032
Sore throat	no	23.28	21.47	25.09	0.673	base			
	yes	22.21	19.91	24.51		-3.16	-7.99	1.68	0.200
Lower limbs lesion	no	22.67	20.67	24.66	0.263	base			
	yes	24.89	22.99	26.78		2.55	-1.14	6.25	0.175
Pharyngitis	no	22.33	21.34	23.32	0.007	base			
	yes	29.08	17.69	40.47		5.98	1.16	10.79	0.015
Proctitis	no	22.14	21.17	23.11	0.001	base			
	yes	30.23	19.12	41.33		7.62	2.98	12.26	0.001
Age	18-45	22.53	21.43	23.64	0.162	base			
	46 +	25.28	19.14	31.42		4.40	0.67	8.13	0.021
HIV class	HIV neg	22.48	20.36	24.60	<0.001	base			
	HIV pos >350 CD4	22.14	19.66	24.62		-0.88	-4.08	2.32	0.590
	HIV pos ≤350 CD4	38.63	31.62	45.63		14.29	7.14	21.45	<0.001

(C) Predictors of severe mpox by fitting a logistic regression model

Patients feature		Unadjusted analysis				Multivariable analysis			
		Risk for severe disease			P-value	Risk for severe disease			P-value
		OR	95% CI			OR	95% CI		
Fever	yes	3.83	2.25	6.53	<0.001	2.91	1.63	5.21	<0.001
	no	base				base			
Lymphadenopathy	yes	2.37	1.49	3.77	<0.001	1.88	1.10	3.21	0.020
	no	base				base			
Fatigue	yes	0.99	0.58	1.70	0.979	0.60	0.32	1.11	0.102
	no	base				base			
Diarrhea	yes	4.98	1.78	13.88	0.001	4.43	1.37	14.31	0.013
	no	base				base			
Peri-anal lesion	yes	2.63	1.67	4.14	<0.001	1.92	1.16	3.19	0.012
	no	base				base			
Face lesion	yes	2.35	1.50	3.68	<0.001	1.92	1.16	3.18	0.011
	no	base				base			
Penile lesions	yes	0.70	0.45	1.09	0.115	0.60	0.36	1.01	0.054
	no	base				base			
HIV class	HIV neg	base				base			
	HIV pos >350 CD4	0.95	0.60	1.51	0.367	0.77	0.46	1.29	0.325
	HIV pos ≤350 CD4	1.94	0.73	5.12		1.65	0.56	4.88	0.362

(D) CT-value in the upper respiratory tract during the first week of disease (P-values are reported according to Student T-test)



(E) Association between severe disease and CT-values in the upper respiratory tract during the first week of disease