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BACKGROUND: Herpetic meningoencephalitis is the most frequent form of sporadic fatal encephalitis in the world and accounts for 10-20% of all viral encephalitides. There were studies assessing the outcomes particularly by comparing the efficacies of antiviral drugs in the past. To the best of our knowledge, no datum exists in the literature on the mortality indicators of HME patients with definite microbiological diagnosis. Thus, our study makes use of the largest case series ever reported in the literature to provide data for the predictors of unfavorable outcome in HME cases.

METHODS: This multicenter study enrolled HME patients from referral participant centers in 10 countries (Croatia, Czech Republic, Denmark, Egypt, France, Iraq, Italy, Lebanon, Slovenia, and Turkey). The study had a retrospective design and included patients hospitalized between 2000 and 2013. Only the adult patients with HME over the age of 15 were enrolled. Dr Lütfi Kirdar Training and Research Hospital's Review Board in Istanbul approved the study.

The inclusion criteria were as follows:

1. Symptoms and/or signs of parenchymatous disease of the brain such as focal neurological signs, seizures, decreased consciousness or disorientation often concomitant with fever and pathological neuroradiology or neurophysiology findings
2. Positive CSF-PCR result for HSV-1 or HSV-2 or both.
3. The unlikely presence of another parenchymatous disease of the brain.

Unfavorable Outcome included death and sequelae.

RESULTS: In this study, 501 patients with microbiologically confirmed HME were enrolled from 35 referral centers in 10 countries [Turkey (n=144), Denmark (n=127), France (n=64), Slovenia (n=54), Croatia (n=32), Iraq (n=30), Czech Republic (n=23), Italy (n=12), Lebanon (n=8), Egypt (n=7)]. However, 438 patients were found to be eligible for outcome analysis and 63 HME cases were excluded due to missing data.

In this study 44 (10 %) patients died and 188 (42.9 %) experienced unfavorable outcome. Hence, 232 (52.9 %) cases experienced

unfavorable outcome. The results of multivariate analysis are presented in the table. The interrelation between the elapsed time since the onset of symptoms to anti-viral treatment and unfavorable outcome is presented in the figure.

CONCLUSION: Advancing age, lower GCS scores, delayed start of antivirals exceeding one week in particular, and new onset of convulsions seem to increase unfavorable outcome in HME. Thus, it appears that both host and therapeutic parameters contribute to success in these cases.

Table. Final model including independent predictors of unfavorable outcome

	OR [1]	95% CIs		p
		Low	High	
Age (years)	1.04	1.02	1.05	0.000
Glasgow coma scale	0.84	0.77	0.93	0.000
Elapsed time [2]				
>2 days <=7	1.80	1.16	2.79	0.009
>7 days	3.75	1.72	8.15	0.001
New onset convulsion [3]	1.61	0.93	2.76	0.088
constant	1.08	0.27	4.43	0.910

[1] OR, odds ratio

[2] Elapsed time between unset of symptoms and administration of anti-viral treatment

[3] Newly unset convulsion before hospital admission