Prognostic factors for mortality among patients with visceral leishmaniasis in East Africa: systematic review and meta-analysis

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Aim

Visceral leishmaniasis (VL), or kala-azar, is a neglected tropical disease which is deadly if untreated.

The average VL case fatality rate in East Africa was 2% in 2015, but this proportion can be markedly higher in specific subgroups, such as in VL and HIV co-infected patients among whom the case fatality rate can be as high as 39%.

Understanding which factors have prognostic value may help to focus clinical management and reduce case fatality.

However, information about prognostic factors is scattered and conflicting. Hence, the classification of VL severity remains poorly defined.

We conducted a systematic review and meta-analysis to identify prognostic factors for mortality among VL patients in East Africa.

Figure 1. MSF VL treatment centre in North West Ethiopia (Abdurafi Health Centre)

Methods

The review protocol was registered in PROSPERO (CRD42016043112).

We included studies published in English after 1970 describing VL patients treated in East African health facilities.

To be included, studies had to report on associations between clinical or laboratory factors and mortality during admission or during VL treatment, with a minimal study size of ten patients.

Conference abstracts and evaluations of genetic or immunological prognostic factors were excluded.

We searched for studies in MEDLINE and four other databases in December 2018. To assess risk of bias in observational studies and clinical trials, we used the Quality in Prognostic Studies (QUIPS) tool.

For factors reported in at least five studies, we did a meta-analysis. For the different predictors, we performed a fixed effects and random effects meta-analysis of the odds ratio of mortality.

Since we pooled studies conducted in different settings and with high heterogeneity, the main conclusions were based on the random effects model.

The amount of heterogeneity was quantified with the I square statistic (I^2), which expressed the proportion of variation across studies that is due to heterogeneity.

Figure 2. MSF VL Treatment centre in South Sudan (Lankien Hospital)

Results

We included 48 studies in the systematic review, describing 150,072 VL patients of whom 7,847 (5.2%) died.

The studies were conducted in Ethiopia, Sudan, South Sudan, Uganda and Kenya.

Table 1: Main prognostic factors for mortality among VL patients

Prognostic factor	Pooled OR[a]	Lower 95% CI	Upper 95% CI	I^2 (%)
Jaundice	8.27	4.99	13.71	12
HIV positive	4.60	3.24	6.54	27
Tuberculosis	4.06	1.83	9.01	62
Age >45 *vs.* age 15-45 years	3.69	2.72	5.02	53
Oedema	3.52	1.77	7.03	85
Bleeding	3.37	2.62	4.34	0
Low haemoglobin (≤6.5 g/dl)	3.26	2.16	4.93	83
Severe malnutrition	2.42	2.07	2.85	0
Long duration of illness (≥2 months)	1.82	1.29	2.57	68
Age<5 *vs.* age 15-45 years	1.59	1.28	1.98	27
Large spleen size (≥10 cm)	1.27	1.02	1.56	30

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; [a] OR from random effects model.

Conclusions

These prognostic factors can be easily identified by health professionals in resource-constrained settings.

Future prognostic studies within East Africa evaluating novel or other prognostic markers should consider these as “core” prognostic factors for inclusion in multivariable analysis.

A limitation is that many of the studies used routine data and were retrospective in nature. Consequently, only a limited number of prognostic factors were assessed in most studies.