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LETTERS TO THE EDITOR

Laboratory features of 160 CCHF confirmed cases in Zabol of Iran: A 10-year study

We have read with interest recent communications to this journal which highlight the difficulties in diagnosis and management of Crimean—Congo hemorrhagic fever (CCHF).[1] CCHFv RNA test is not available in many regions and the results take too long. Therefore, practitioners have to rely on laboratory test results for CCHF diagnosis. There is a lack of evidence-based criteria for the disease and practitioners are not sure if they are hospitalizing, isolating and discharging a CCHFv positive case. In order to detect main laboratory changes in CCHF patients we evaluated laboratory results of 160 confirmed CCHF cases in Zabol-Iran. Every year several cases of CCHF are reported from Sistan and Baluchestan province of Iran. Zabol is a city in north east of Sistan and Baluchestan and is neighbored with Afghanistan in which CCHF is endemic (see Fig. 1).[2,3] In this study 153 (95.6%) of patients recovered and this may be due to the awareness of health care providers of laboratory, clinical and epidemiological characteristics of the disease.[4] Most of the patients in this study were males 128 (80%) with mean age of 32.86 (SD: 13.67). Fever was the most prevalent symptom of the disease which was seen in 159 (99.4%) of patients. Headache (in 92.5% of cases), myalgia (in 90% of cases), vomiting (in 69.4% of cases), and bleeding (in 62.5% of the cases) were other important clinical symptoms.

Having a look at laboratory findings in these patients reveals that the most prevalent changes in blood indexes were thrombocytopenia and prolongation of aPTT. The serum concentration of hepatic enzymes were also elevated in a large proportion of patients and AST and LDH have increased in almost all of them. Leukopenia and Anemia were other less prevalent laboratory findings in this study. CRP was also evaluated and were positive in almost half of the patients. During hospitalization a more marked change in blood indexes perceived including Plt and leukocyte count and Hb and it is related to the pathological progress of the disease.

Laboratory aspects of CCHF has been considered in several studies. It has been shown that thrombocytopenia, Leukopenia, Anemia, Prolongation of aPTT and serum elevation of AST, ALT, LDH, Creatinine, and bilirubin can be considered as probable laboratory indications of CCHF positive cases.[5—8]

In this study we also compared laboratory and standard criteria references for categorizing patients. The results suggest that laboratory references were more successful in detecting CCHF cases but we need to establish some case control studies to revise the present criteria for probable CCHF case definition. Some of other indexes including CPK

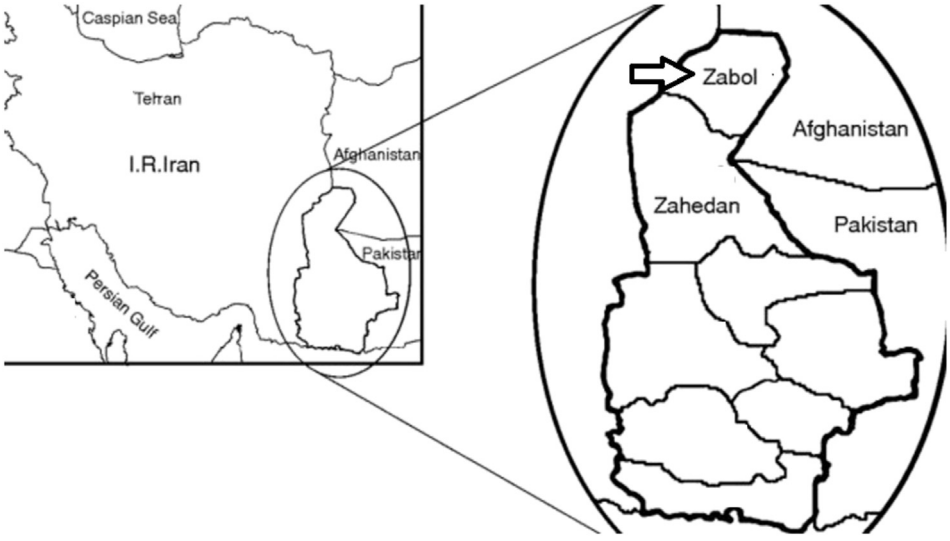

Fig. 1 The location of "Zabol" in Sistan and Baluchestan province of Iran.

Table 1 Hematological and biochemical parameters of CHF cases at first day of hospitalization (Mean ± SD and percentage of patients with higher and lower than normal).

	Laboratory reference				CCHF diagnostic criteria		
	CCHF cases (n = 160)	Normal range	Higher than normal (%)	Lower than normal (%)	Normal range	Higher than normal (%)	Lower than normal (%)
Total leukocyte count ($\times 10^9$/L)	4.81 ± 3.71	4–11	11 (6.9)	95 (59.4)	3–9	13 (8.1)	55 (34.4)
Platelet count ($\times 10^9$/L)	55.32 ± 42.68	150–450	0 (0)	155 (96.9)	100–450	0 (0)	133 (83.1)
Hemoglobin (HB)	13.47 ± 1.95	M: 14–18 F: 12–16	0 (0)	76 (47.5)	–	–	–
Prothrombin time (PT) (Sec)	17.92 ± 9.26	11–14	83 (51.9)	1 (0.6)	–	–	–
Activated partial thromboplastic time (aPTT) (Sec)	55.55 ± 22.68	25–35	137 (85.6)	0 (0)	–	–	–
Erythrocyte sedimentation rate (ESR) (mm/hr)	17.41 ± 13.80	0–20	54 (33.8)	–	–	–	–
Total bilirubin (mg/dl)	1.37 ± 1.38	0.2–1.2	36 (22.5)	0 (0)	–	–	–
Creatinine (Cr) (mg/dl)	1.07 ± 0.87	0.5–1.2	29 (18.1)	4 (2.5)	–	–	–
Creatine phosphokinase (CPK) (U/L)	1092.47 ± 1763.52	22–198	123 (76.9)	0 (0)	–	–	–
Aspartate aminotransferase (AST) (U/L)	501.84 ± 1300.26	12–37	144 (90)	16 (10)	Below 100	117 (73.1)	–
Alanine aminotransferase (ALT) (U/L)	225.17 ± 407.86	3–25	142 (88.8)	0 (0)	Below 100	95 (59.4)	–
Alkaline phosphatase (ALP) (U/L)	331.86 ± 326.46	40–147	129 (80.6)	0 (0)	–	–	–
Lactate dehydrogenase (LDH) (U/L)	1178.41 ± 1207.29	88–230	146 (91.3)	0 (0)	–	–	–

The reference range of Hb, PT, aPTT, ESR, Total bilirubin, Cr, CPK, ALP and LDH have not been presented in Criteria of CCHF diagnosis.

and LDH has been considered in this study which may also be used in case definition protocols (see Table 1).

As far as authors know it is the first time that this large numbers of confirmed CCHF cases in such a long time period (10 years) are presented. As many of this laboratory changes can be evident at early stages of the disease, considering the results of this study would be of great importance to identify probable CCHF cases and to timely initiate appropriate treatment and preventive procedures. This may lead to marked reduction of case fatality rate and person to person transmission of the disease.

Conflicts of interest

There is no conflict of interest.

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The history of plasma viral load and CD4 count impacts the size of HIV-1 reservoir

Dear Editor,

We read with great interest the article: "Impact of late presentation of HIV infection on short-, mid- and long-term mortality and causes of death in a multicenter national cohort: 2004–2013".[1] The size of latent reservoir also highly impacts the course of HIV infection. Higher cellular HIV-1 DNA levels have been associated to a rapid disease progression in treatment-naïve patients.[2] In treated patients with high HIV-1 DNA levels, a rapid virological rebound was observed at treatment interruption.[3] In contrast, low levels of HIV-1 DNA have been observed both in elite controllers and post-treatment controllers.[4,5] HIV-1 DNA levels vary considerably among successfully controlled patients and the impact of the treatment on the reservoir size seems very low over time. We investigated in routine practice, determinants that may be associated with low HIV-1 DNA levels in patients with suppressed viral load (VL).

A retrospective cross-sectional study was conducted in the HIV unit of Tourcoing general hospital, France. All patients have signed the ethics board-approved consent form. Patients under ART with plasma RNA VL <20 copies/mL since at least 6 months and who underwent HIV-1 DNA quantification, were included in the study. The quantification of total HIV-1 DNA level was performed in whole blood using a real-time PCR assay (Biocentric, Bandol, France) as previously described.[6] Categorical variables were expressed as frequencies and percentages. Quantitative variables were expressed as medians [interquartile range (IQR)]. Associations of HIV-1 DNA levels with patients' characteristics were studied using linear regression analyses. Then, HIV-1 DNA levels were separated in two groups, one with HIV-1 DNA levels <2 log copies/10^6 PBMCs and the other with HIV-1 DNA levels >3 log copies/10^6 PBMCs. Comparisons were made using univariate and then multivariate logistic regression.

A total of 500 patients were included in the study. At the date of HIV-1 DNA quantification, the median age was 48 years and 74% of patients were males. Most of patients (73.3%) were infected with a subtype B virus since a median period of 11.5 years and were treated since 9.4 years with a median of 4 different regimens. The median CD4 count and CD4 nadir were 607 cells/μL and 238 cells/μL, respectively. The median pre-ART RNA VL was 4.8 log copies/mL, and plasma RNA was undetectable since 2.8 years. The median HIV-1 DNA level was 3 log copies/10^6 PBMCs.

The analysis of the whole population (Table 1) showed that HIV-1 DNA levels were not associated with the sex ($p = 0.06$) and the HIV-1 subtype ($p = 0.07$). Likewise, HIV-1 DNA levels were not correlated to CD4 cell count ($p = 0.63$), CD8 count ($p = 0.98$), and the delay between HIV-1 diagnosis and initiation of treatment ($p = 0.94$). A correlation was found between HIV-1 DNA levels and age ($p = 0.021$), duration of ART ($p = 0.005$), CD4 T cell nadir ($p < 0.0001$), the number of ART regimens ($p = 0.008$), the pre-ART plasma RNA VL ($p < 0.0001$) and the time since plasma RNA VL was undetectable ($p = 0.0001$).

In multivariate analysis, CD4 nadir and the time since undetectable RNA VL were found to be independently and negatively associated with HIV-1 DNA levels, while a positive relation was found with pre-ART plasma RNA VL (Table 1).

In order to confirm the impact of these factors on HIV-1 DNA levels, we chose to compare 2 groups of patients who

Table 1 Factors associated to HIV-DNA levels: results of linear regression results.

Variables	Bivariate analysis		Multivariate analysis	
	β (±SEM)	p	β (±SEM)	p
Age	0.006 (±0.002)	0.021	–	–
Sex (men)	0.11 (±0.06)	0.061	–	–
HIV-1 subtype (non B)	−0.11 (±0.06)	0.07	–	–
Duration between diagnosis and ART (/year)[a]	0.0006 (±0.004)	0.94	–	–
Duration of antiretroviral treatment (/year)	0.01 (±0.04)	0.005	–	–
CD4 cell count (100 cells/μL)	−0.005 (±0.01)	0.63	–	–
Nadir CD4 cell count (100 cells/μL)	−0.09 (±0.02)	<.0001	−0.08 (±0.02)	<.0001
CD8 cell count (100 cells/μL)	−0.0002 (±0.008)	0.98	–	–
Pre-ART plasma HIV-1 RNA VL (copies/ml)[a]	0.17 (±0.03)	<.0001	0.10 (±0.03)	0.002
Time since undetectable plasma HIV-1 RNA (year)	−0.04 (±0.01)	0.0001	−0.04 (±0.01)	<.0001
Number of ART lines	0.02 (±0.02)	0.008	–	–

[a] Variables transformed in log10.