European Journal of Inflammation

Original Research Article

Evaluation of circulating $CD4^+CD25^+CD127^{-/low}$ regulatory T cells in newly diagnosed hepatitis C-infected patients

European Journal of Inflammation
Volume 22: 1–7

DOI: 10.1177/1721727X241242701
journals.sagepub.com/home/eji
Sage

Morvarid Asadipour[1,*], Soolmaz Khansalar[1,*], Fatemeh Rezaei Kahmini[2], Mahsa Eshkevar Vakili[1], Mohammad Reza Ataollahi[3], Mohammad Ali-Hassanzadeh[4], Keivan Shams[1], Zahra Faghih[5] and Kurosh Kalantar[1,2,6]

Abstract

Objectives: Hepatitis C virus (HCV) is one of the most global health problems with 2.5% prevalence worldwide. It seems that regulatory T (Treg) cells, which are able to modulate the host immune responses, play a substantial role in the immunopathogenesis of HCV infection. In this study, we evaluated the distribution of Treg cells in HCV-infected patients and its correlation with viral load and clinical manifestations.

Methods: Peripheral blood mononuclear cells (PBMCs) were collected from 14 newly diagnosed HCV-infected patients and 23 age- and sex-matched healthy subjects, and the frequency of CD4+CD25+CD127−/low Treg cells was determined by flow cytometry.

Results: Our results showed that the mean level of CD4+CD25+CD127−/low Treg cells in HCV-infected patients was significantly higher than that in healthy control subjects (8.2 ± 1.48% vs 5.4 ± 0.36%, $p < .05$). However, there was no statistical correlation between Treg cells frequency and viral load or clinical manifestations.

Conclusion: A higher proportion of Treg cells in HCV-infected patients might indicate their critical role in viral persistence and candidate them as a new target of immunotherapy to improve antiviral immunity.

Keywords

hepatitis C virus, regulatory T cells, viral persistence, Hepatitis C virus-infection, flow cytometry

Date received: 1 May 2023; accepted: 12 March 2024

[1]Department of Immunology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Autoimmune Diseases Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Department of Immunology, School of Medicine, Fasa University of Medical Science, Fasa, Iran
[4]Department of Immunology, School of Medicine, Jiroft University of Medical Sciences, Jiroft, Iran
[5]Shiraz Institute for Cancer Research, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[6]Department of Bacteriology and Immunology and the Translational Immunology Research Program (TRIMM), The University of Helsinki and HUSLAB, Helsinki University Hospital, Helsinki, Finland

*Morvarid Asadipour and Soolmaz Khansalar participated equally in this study, if there is an option for co-first author, please mention these two authors as first authors.

Corresponding author:
Kurosh Kalantar, Department of Immunology, School of Medicine, Shiraz University of Medical Sciences, Zand str., Shiraz 71348-45794, Iran.
Email: kalantark@sums.ac.ir

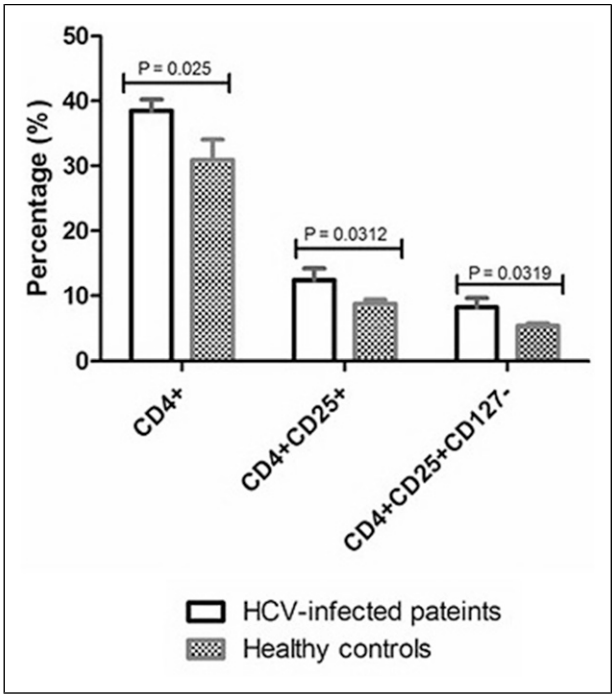

Figure 2. Altered frequencies of CD4+, CD4+CD25+ and CD4+CD25+ CD127−/low cells in the peripheral blood of HCV-infected patients. PBMCs were isolated from the whole blood of HCV-infected patients and healthy controls. CD4+, CD4+CD25+ and CD4+CD25+ CD127−/low populations were more significantly frequent in HCV-infected patients compared to healthy controls. Data are shown as mean ± SEM, and $p < .05$ was considered statistically significant.

Several studies have shown a positive correlation between the viral load and Treg cells proportion in HCV-infected patients.[18,20,36] However, we found no correlation between the percentage of Treg cells and HCV RNA copy number. In to the same line with our study, Pearson *et al.* have reported no significant association between HCV RNA titer and Treg cells percentage.[21] These differences between studies might be related to different reagents and methods used or the sample size. In this study, we also examined the correlations between Treg cells frequency and clinical parameters, such as alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP) levels and platelet counts; the results revealed that clinical manifestations did not correlate with Treg frequency. Our study was in accordance with those of previous studies, which reported no correlation between the percentage of Treg cell; serum ALT and AST levels; and platelet counts.[18,36,37]

The main limitation of our study was small sample size. The other one was that we were unable to isolate and assess the function of CD4+CD25+CD127−/low T cells during co-culture with PBMCs. Therefore, further experiments, which focus more on the phenotype and function of Treg cells during acute HCV infection, with increased sample size are needed to increase our knowledge about the role of Treg cells in the resolution or persistence of HCV infection.

Study limitations

Different Treg subsets in hepatitis C-infected patients are not evaluated in this study which can be applied in future studies.

Conclusion

In conclusion, we demonstrated elevated proportions of CD4+ CD25+ CD127−/low Treg cells in the initiation of HCV infection. This result suggests that Treg cells may play a substantial role in HCV viral persistence and the establishment of long-lasting infection. However, precise mechanisms of Treg cells in HCV-infected patients remain completely clarified and large-scale studies are needed to define the exact mechanisms of Treg cells in HCV infection.

Acknowledgments

The authors would like to thank Shiraz University of Medical Sciences, Shiraz, Iran and also Center for Development of Clinical Research of Nemazee Hospital and Dr Nasrin Shokrpour for editorial assistance.

Author contributions

K.K and S.Kh and Z.F devised the study plan, M.A and M.A.H collected the data, M.E.V and S.KH were responsible for data analysis, Z.F F.R.K interpreted the data, MR.A and K.SH drafted the manuscript, and K.K and M.AH supervised the whole process and gave constructive advice. All authors have made contributions to the current work.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by Shiraz University of Medical Sciences under grant number 14848.

ORCID iD

Kurosh Kalantar https://orcid.org/0000-0002-9160-9449

References

1. Hoofnagle JH. Course and outcome of hepatitis C. *Hepatology* 2002; 36(5 Suppl 1): S21–S29.
2. Petruzziello A, Marigliano S, Loquercio G, et al. Global epidemiology of hepatitis C virus infection: an up-date of the