OPEN PEER REVIEW

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Peer Review Report for "Relationship Between Lipid Profile and Sepsis Outcome in Intensive Care Unit"

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Review Timeline:

Submit Date: 13 May 2019
Revised Date: 4 Mar 2020
Accepted Date: 12 Mar 2020

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Shabnam Tehrani: Reviewer | **Revision** (0) — 25 Sep 2019

Dear AE,
I Review the article titled “Relationship between Lipid Profile and Sepsis Outcome in Intensive Care Unit”.
Please find below my views concerning the article:
1- Although, this study is a descriptive study, but due to the high incidence and Importance of sepsis, this study is valuable.
2- Introduction, well written.
3- The methodology is fully explained.
4- In the Result section, the Authors should provide a comparative table for all similar studies till now (with a clear search strategy in PubMed, Scopus, Medline and etc.) that includes a year of report/country, age, sex, clinical presentation, TG Level, and outcome.
6- Code of ethics, not mentioned in the article.
7- some of the article references are out of date. Older references from 2010, are not used;
So, this article is accepted and needs major revision.
Thanks.

REFEREE: Reviewer | **Revision** (0) — 6 Jan 2020

Dear AE,

I have read this article several times now, it has been written correctly but there is no brilliant finding in this manuscript.
In my opinion, it is acceptable as a brief report, not an original article.
Thanks.

Bita Pourkaveh: Associate Editor | **Revision** (0) 12 Jan 2020

Dear EIC,
The manuscript is studied, and there are some comments which should be addressed by the author. According to the comments, the document needs major revision.
Kind regards,

Masoud Mardani: EIC | **Revision** (0) 12 Jan 2020

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.
Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Respected Reviewers

Hi,

Thank you very much for your hopeful and essential comments. We exerted the following corrections in our manuscript:

1- The code of ethics, which had briefly been mentioned, was completed and highlighted.

2- In the old version of the manuscript, 13 references were older than in 2010. We accurately updated and double-checked all bibliographies, so, in the revised version, only 3 most relevant articles (highlighted in green) inevitably kept, which are related to 2005, 2007, and 2009.

3- The format of citations and bibliography was set according to your publisher's output style for EndNote.

4- Finally, we performed a systematic search in the leading academic databases, including PubMed, Web of Science, Scopus, Willy Online Library, Springer Link, and Google Scholar again. Then a table (next pages) was prepared, including 25 references about the evaluation of lipid profile in adult patients with sepsis. However, the authors believed that this table is proper for a ‘Systematic Review,’ not for an original paper such as our work. On the other hand, we used all the necessary and relevant resources in the discussion section of our manuscript. If the table is included in the document, it will be very wordy, and the overall arrangement should be changed. For this reason, we will be pleased if you could accept the manuscript in the current format.

Anyway, we are ready again to make any necessary corrections or changes in the manuscript based on your declaration.

Thank you in advance for your considerations.

Best regards,

Corresponding author

Search Methods:

We conducted a review of studies evaluating the lipid profile including total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL) in sepsis and/or septic shock indexed in the **PubMed, Web of Science, Scopus, Willy Online Library, Springer Link,** and **Google Scholar** between Jan. 2000 and Dec. 2019.

Table 1. Description of the studies that evaluated lipid profiles and their association with sepsis and septic shock in adult patients

Study	Location	Study design	Sample	Main Results
Sharma *et al*. (2019) [1]	Brazil	Cohort observational 2 years	27 adult patients with hospital-acquired pneumonia, 23 healthy volunteers as a control	Reduced levels of TC, HDL, LDL, non-HDL cholesterol, apolipoproteins ApoA1 and ApoB100, and Paraoxonase 1 in HAP patients.
Tanaka *et al.* (2017) [2]	France	Prospective observational 3 months	75 adult patients with sepsis	Decreased levels of HDL in patients with sepsis. Need to explore the therapeutic potential of HDL in sepsis was described
Cirstea *et al.* (2017) [3]	Canada	Cohort observational 3 years	200 adult patients with sepsis	Decreased levels of HDL in patients who developed multiple organ failure or died. The level of HDL can provide valuable prognostic information in patients with suspected sepsis and facilitate rapid intervention in patients at increased risk of progression to multiple organ dysfunction.
Novak *et al.* (2017) [4]	Czech Republic	Case-controlled prospective 6 months	26 adult patients divided into 3 groups: SIRS, sepsis, and control	Low levels of TC, HDL were associated with a worse prognosis in SIRS and sepsis
Genga *et al.* (2017) [5]	Canada	Cohort observational 2 years	180 adult patients with sepsis	Low levels of HDL associated with increased risk of sepsis and development of acute renal failure; HDL may be a prognostic factor
Guirgis *et al.* (2017) [6]	USA	Prospective observational 1 year	35 adult patients with sepsis	Increased HDL levels in the first 48 h of sepsis. Use of HDL as a prognostic factor in sepsis
Yamano *et al*. (2016) [7]	Japan	Prospective 4 year	91 adult patients with sepsis	Decreased TC level and increased total bilirubin concentration are associated with poor prognosis in sepsis
Vavrova *et al.* (2016) [8]	Czech Republic	Prospective 6 months	30 adult patients with sepsis + 30 healthy controls	Increased IL10, TNFα, and low levels of HDL and albumin in sepsis. HDL as a useful prognostic factor in sepsis
Zou *et al.* (2016) [9]	China	Prospective 1 year	220 adult patients with SIRS and/or sepsis + 81 controls	In SIRS and/or sepsis, there are reduced values of TC and HDL. The sepsis group had lower HDL values when compared with other groups. The study suggests HDL as a prognostic marker for sepsis
Guirgis *et al.* (2016) [10]	USA	Prospective 4 years	29,690 adults with sepsis, severe sepsis and multiple organ failure	Low LDL levels were associated with increased risk of sepsis, severe sepsis, and multiple organ failure in the long term. However, the same was not observed for HDL
Abdollahi *et al*. (2016) [11]	Iran		107 adult patients with severe sepsis or septic shock, 115 non-septic adult patients	Lower levels of serum lipid profiles in patients with severe sepsis and septic shock. Prognostic role of serum HDL in sepsis and LDL and TG in non-septic patients.
Brodska *et al.* (2015) [12]	Czech Republic	Prospective randomized	150 adult patients SIRS, sepsis, and septic shock	Low TC concentrations at admission were not associated with disease severity.
Lee *et al.* (2015) [13]	Korea	Prospective 6 months	117 patients (average age: 63 years) with sepsis and septic shock	Low HDL, LDL, apolipoprotein A1 levels were associated with higher sepsis mortality and could be considered prognostic markers. However, TG levels were also low
Ngaosuwan *et al*. (2015) [14]	Thailand	Prospective	75 patients with sepsis, 75 without infection and 50 controls	Low TC and HDL levels in patients with sepsis. There were no differences in TG and apolipoprotein V in the three groups
Al-Zaidawi (2014) [15]	Iraq	Prospective	75 patients with burns and sepsis	Reduced levels of HDL in all patients and < 15 mg/dL in those with sepsis and hypertriglyceridemia
Lekkou *et al*. (2014) [16]	Greece	Prospective 29 months	64 patients (average age: 64 years)	Positive association of low HDL and mortality in patients with sepsis. HDL can be a

				predictive marker of severe sepsis
Cappi et al. (2012) [17]	Brazil	Prospective	69 patients (average age: 53 years). Patients evaluated during the first 72 h of sepsis	Lower HDL, LDL, and TC values in sepsis
Barati *et al*. (2011) [18]	Iran	Observational	29 adult patients with sepsis, 41 patients without infection	TC, HDL, and LDL were lower in septic compared non-septic patients
Chiarla *et al*. (2009) [19]	Italy	Review + prospective data	190 patients (average age: 58 years)	Association of an increased level of TC and TG with the severity of sepsis.
Grion *et al*. (2010) [20]	Brazil	Cohort prospective with a control group	51 patients with severe sepsis and 71 controls (average age: 65 years)	Reduced levels of HDL on admission were a risk factor for the development of sepsis in ICU. Each 1 mg/dL increase in HDL resulted in a 3% reduction in the risk of developing sepsis
Tsai *et al*. (2009) [21]	Taiwan		103 cirrhotic adult patients with severe sepsis	Association between reduced levels of HDL and apolipoprotein A-I with disease severity and impaired liver reserve in cirrhotic patients with severe sepsis. A low level of APO A-I is associated with poor prognosis.
Barlage *et al*. (2009) [22]	Germany	Observational	151 adult patients with sepsis	Association between reduced levels of HDL, LDL, apolipoprotein (1 and 2) with mortality
Levels *et al*. (2003) [23]	Netherlands	Prospective	20 adults with sepsis	High levels of CRP, IL6, IL8, LBP, and TNFα, and low levels of TG, VLDL, apolipoprotein (A1 and B) and HDL in sepsis
Lüthold *et al*. (2007) [24]	Switzerland	Observational	101 critically ill adult patients (age: 23 to 86 years)	A positive association between the low levels of HDL and TC with severity
Chien *et al*. (2005) [25]	China	Prospective 1 year	63 patients with severe sepsis (age: 18 to 92 years)	A positive association between the low levels of HDL and apolipoprotein with high levels of TG, IL6, and TNFα in patients with severe sepsis

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Masoud Mardani: EIC | Revision (1) 12 Mar 2020

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.