August 21, 2014

Dear editor,

Please find enclosed the edited manuscript in Word format (file name: 12792-review.doc)

Title: Aetiological factors of Budd-Chiari syndrome in Algeria

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Name of Journal: World Journal of Hepatology

ESPS Manuscript N°: 12792

The manuscript has been improved according to the suggestions of the reviewers

I. Format has been updated.
II. For language improvement, we solicited a professional English language editing company: American Journal experts.
III. Revision has been made according to the suggestions of the different reviewers:
    A. Reviewer 00646393:
        1. “our country” has been replaced by “Algeria” in the text
        2. Indeed, all radiological investigations were performed by the same radiologist. This work is a part of a doctoral thesis carried out by this radiologist and myself. I discussed the clinical and aetiological aspects of the pathology and he addressed the radiological data. He was therefore obliged to achieve himself all the exams even at baseline, and during the monitoring period. This study lasted more than six years. I nevertheless remove this sentence from the text as proposed by the reviewer.
        3. The MR-angiography is safer, because it avoids radiation exposure. On the other hand, I agree with you, this investigation is expensive. The Doppler ultrasound is sufficient for the diagnosis in most cases. Otherwise, if the diagnosis is doubtful, we can perform a CT or MR-angiography according to local availability. For our patients, the problem does not arise, because all these investigations are carried out at the hospital, for free. The patient doesn't pay anything. This is the main advantage of our health care system.
        4. Are our results suitable for other countries around Algeria: I don’t know, insofar as no large ample study has been published about this condition by our neighbors? But according to Budd-Chiari cases reported, the celiac disease and Behçet’s disease also appears frequently found in our area.
    B. Reviewer N°00069819:
        1. This study is prospective. As mentioned above, this work is a part of my doctoral thesis. So, during 6 years, I compiled BCS patients addressed from all over the country, by colleagues, for diagnosis confirmation, aetiological workup and

therapeutic management. All diagnosed patients were followed for at least one year, but that is not the focus of our article

2. The abstract seems to be poorly written, I tried to improve and complete it;
3. The introduction has been enhanced by clinical and epidemiological data as suggested by the reviewer. Etiological variations by ethnicity were discussed in the Discussion section.
4. Demographic and clinical characteristics were summarized in a table
5. Discussion has been completed by a new chapter about factor V Leiden mutation
6. Limitations of the study were mentioned at the end of the discussion, as proposed by the reviewer;
7. Figures which were not related to the text have been removed;
8. For Celiac disease references, I said that 16 cases have been published in the literature until 2012; I was obliged to report references that attest to what I stated above. If it is redundant, I will remove them.
9. Tables were reorganized as directed by reviewer

C. Reviewer 00739301

1. It's a single centre study, but our centre is the reference centre of liver diseases in Algeria. We received patients from whole the country for this work: 61% from central areas, 16.5% from eastern Algeria, 10.4% from the west and 7.8% from the south.
2. The primary Budd-Chiari syndrome is defined as an obstruction (thrombosis, stenosis) of hepatic venous outflow. The secondary BCS is characterized by a compression or invasion of the hepatic veins or the IVC by a tumour process. By convention, like in most published studies ("EN-VIE" study published in Internal Annals of Medicine in 2009), the hepatic vein involvements secondary to cirrhosis or occurring after liver transplantation are excluded. In our centre we had 1 case of Hepatic vein occlusion in a CHILD C advanced cirrhosis and 2 cases of BCS after a liver transplantation. We have chosen to exclude them from the study.
3. The therapeutic aspects of the study are not the purpose of this article.
4. The radiological diagnosis criteria have been added to the text (patients and methods)
5. The definition of primary and secondary BCS has been added to the introduction
6. Tumoral invasion by hepatocellular carcinoma or compression of hepatic venous outflow are considered by definition as a secondary BCS, as mentioned in the definition.
7. The diagnosis of myeloproliferative disease was established using the WHO 2008 revised criteria. JAK2 mutation is a major diagnosis criterion. In our work, testing this mutation was available for less than 50% of the patients, so we were obliged to perform a bone marrow biopsy (BMB) for all the patients. The concordance of the 2 tests (BMB and JAK2 mutation test) was weak in our work. We commented that in the discussion
8. The clinical manifestations of hepatic vein involvement were added in the introduction chapter
9. Inadvertently two tables had been intermixed, the revealing symptoms of BCS and clinical signs at diagnosis. Jaundice revealed BCS in 13.6% of cases, but on

admission to the hospital, this sign was present in 40% of patients. This error has been fixed

10. The pictures Which do not have any relation with the text have been removed
11. For English polishing, we sought a professional translator as mentioned above
12. I focused on one aspect of Budd-Chiari syndrome: aetiological workup. This represents just a little part of my thesis. I think that reducing the study to just inherited BCS will be insufficient.

IV. References and typesetting were corrected

Thank you again for publishing our manuscript in the World Journal of Hepatology

Sincerely yours

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