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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 57663

Title: Type 1 diabetes and associated autoimmune diseases

Reviewer's code: 02945812
Position: Editorial Board
Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: India

Author's Country/Territory: Germany

Manuscript submission date: 2020-06-25

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-08-11 16:01

Reviewer performed review: 2020-08-13 12:51

Review time: 1 Day and 20 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

This is a good study. However, few minor modifications are required in the manuscript: 1. Core tip needs modification. The second sentence is too long. 2. The information related to prevalence of autoimmune diseases and antibodies among relatives are not matching in abstract/results and figure 4. 3. Few mistakes are there in figures 3 & 4 e.g. DNS.

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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 57663

Title: Type 1 diabetes and associated autoimmune diseases

Reviewer's code: 00597793
Position: Peer Reviewer
Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: Germany

Manuscript submission date: 2020-06-25

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-08-15 00:44

Reviewer performed review: 2020-08-15 01:13

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

This study examines the clinical factors associated with multiple autoimmunity in people with T1DM. The results appear valid I have several suggestions 1. INTRODUCTION - it is too long and meandering. The first paragraph can be removed. Simply state that T1DM is associated with other AI disorders and you are reporting your own experience. Indeed the authors do not mention the purpose of the study in the INTRO. 2. METHODS - refer the reader to the table of the autoimmune conditions and the immune markers. There is no point in listing them in the text. 3. You can take some of the information in the INTRO and put in the DISC section. 4. RESULTS "...AID. In average, we did observe 1.88 associated AID. More patients with AID were followed than patients with T1D only; hence ." What is 1.88? Something is missing..... More patients with AID were followed than T1D alone - please explain this. Not clear as written 5. DISC - "screening for 21 hydroxylase deficiency should be done" This is too strong a statement. the disease is rare. Perhaps "should be considered".

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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 57663

Title: Type 1 diabetes and associated autoimmune diseases

Reviewer's code: 03671072
Position: Editorial Board
Academic degree: PhD

Professional title: Honorary Research Fellow, Research Scientist

Reviewer's Country/Territory: China

Author's Country/Territory: Germany

Manuscript submission date: 2020-06-25

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-08-14 03:30

Reviewer performed review: 2020-08-19 08:04

Review time: 5 Days and 4 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

This article provided detailed demographical and serological comparisons between T1D patients and those with associated autoimmune diseases (AID). The authors conducted long-term, longitudinal observational study on those patients and their first-degree relatives. While the association of glandular and non-glandular AID in T1D patients has already been well characterized; this study provided useful information on gender-specific and late onset characteristics with T1D-associated AID. The major shortcoming of this article was some data described not being displayed quantitatively. This study was well designed, with clear definition for the diagnosis of different AID. However, a few minor modifications would make this article of better quality: 1. In comparing the demographic data, the authors stated the average time interval between the onset of T1D and glandular AID was much shorter than that between T1D and non-glandular AID. It would be more convincing to provide the quantitative figures. The same apply more T1D+AID relatives were affected by AID when compared to T1D relatives. 2. In the clinical and serological data of relatives, it would be advisable to display the relationship between prevalence of autoantibodies and occurrence of AID. Currently, only the former information was provided. 3. Could the authors provide an explanation of the prevalence of most autoantibodies assayed in T1D relatives being higher than that in T1D+AID relatives? The trend was completely opposite as observed in T1D and T1D+AID patients. 4. Please provide the normal range of all autoantibodies assayed in this study. Currently, only part of them were provided in Table 1.

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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 57663

Title: Type 1 diabetes and associated autoimmune diseases

Reviewer's code: 03490568
Position: Editorial Board
Academic degree: MSc, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: India

Author's Country/Territory: Germany

Manuscript submission date: 2020-06-25

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-08-13 06:58

Reviewer performed review: 2020-08-26 02:42

Review time: 12 Days and 19 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

The manuscript submitted by Frommer and Kahaly is indeed a long-term longitudinal study (spanning over 20 years) on demographic, serological and clinical features in subjects with T1D versus those with T1D and associated AID. The study is well conceived and executed over a fairly large number of subjects and their relatives highlighting important observations over this time period. The data is sound enough and conclusions are well drawn. However, there are certain points in various sections of the manuscript that require more details and explanations for the better understanding of the reader. Introduction: 1. The article cited the reference of IDF 2013. Recent information according to the latest IDF data is recommended. 2. The role of innate immune cells in initiation of T1D (and related AID) should be described. Additionally, the role of cytotoxic CD8+ T cells as principle mediators of beta cell damage must be clearly mentioned. Methods: 3. In addition to the antibodies, any data available on CD4+ or CD8+ T cells or neutrophils (particularly at the onset of the disease) in T1D vs T1D with AID subjects, might be useful. 4. Were tTG-IgA levels performed for CD subjects during the observation period? Results: The prevalence of Ab against various other tissues was found to be higher in patients with T1D+AID. This result is expected as the subjects were grouped on the basis of this criteria. However, it would be interesting to find out whether any particular AID specific antibody, had a correlation with 1.) any of the T1D associated antibodies or 2.) any other AID (as shown in figure 3). This might be useful in clustering autoantigens/autoantibodies in various AID. Figure 1 (Pathogenesis of T1D - Cellular Crosstalk) is lacking important cells and other pathways involved in autoimmunity which have recently emerged in the past few years. Therefore, this figure can be updated with more recent information. Besides, there are a few grammatical errors in the manuscript that also need to be addressed.