BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

**ARTICLE DETAILS**

| TITLE (PROVISIONAL)                                                                 | The analysis of risk factors for diabetic kidney disease progression: a single-center and cross-sectional experiment in Shanghai |
|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| AUTHORS                                                                          | Liu, Wen; Du, Juan; Ge, Xiaoxu; Jiang, Xiaohong; Peng, Wenfang; Zhao, Nan; Shen, Lisha; Xia, Lili; Hu, Fan; Huang, Shan |

**VERSION 1 – REVIEW**

| REVIEWER                           | Aktas, Gulali                                                              |
|------------------------------------|---------------------------------------------------------------------------|
|                                    | Bolu Abant İzzet Baysal University                                         |
| REVIEW RETURNED                    | 26-Feb-2022                                                               |

**GENERAL COMMENTS**

Dear Authors
I carefully read and reviewed the paper titled "The analysis of risk factors for diabetic nephropathy progression: a single-center experiment in Shanghai". It is an original contribution studied risk factors of diabetic nephropathy development in patients with Diabetes mellitus. My comments are as follows:

Title: concise

Abstract: Well summarizes the text. However, inflammation is involved in the processes of DN development, therefore, I recommend adding inflammation another keyword.

Introduction: Objectives and rationale are clear. However, association between inflammation and DN should be emphasized. Recently, Care Time study showed increased burden of inflammation in subjects with diabetic kidney injury compared to those without (doi: 10.1016/j.pcd.2021.08.015.). Indeed, antiinflammatory molecules have been shown to pose nephroprotective effects in diabetic nephropathy (doi: 10.3390/antiox10121920). Improvement of the background data accordingly is required.

Methods: Clearly expressed. Statistics are accurate. No revisions required in this section.

Results: Given in an easy to follow way. Tables improved the readiness. Figure is informative enough.

Discussion is fair and to the point. However, I recommend stating the importance of the study findings in regard of clinical utility.

References: Up to date, mostly. Yet, 3 of them are older than 10 years. In addition, ref / looks incomplete.

In general, I think the manuscript is worthy for consideration for publication, however, it should be revised accordingly before re-evaluation..

| REVIEWER                           | Santoro, Domenico                                                        |
|------------------------------------|                                                                          |
|                                    | Universita degli Studi di Messina, Division of Nephrology                |
| REVIEW RETURNED                    | 14-Mar-2022                                                             |
GENERAL COMMENTS

In this cross-sectional study, the authors aimed to investigate the risk factors for “diabetic nephropathy” development and the difference between patients with long course of type 2 diabetes mellitus and those with short duration of diabetes. The topic of this study is quite interesting but several improvements should be performed.

The most recent nomenclature for renal involvement in course of diabetes is “Diabetic Kidney Disease”, you can find more in the most recent KDIGO, when the consensus group writes “[…] we adopt the current clinical approach of treating most presentations of diabetes and CKD similarly, modifying the approach as appropriate according to albuminuria or eGFR category. We avoid the term “diabetic kidney disease” to avoid the connotation that CKD is caused by traditional diabetes pathophysiology in all cases, although this term is entirely appropriate when this limitation is recognized. We also avoid the term “diabetic nephropathy,” an outdated term for which there is currently no consensus definition”.

For a better definition of DKD in your population, repeated microalbuminuria measurements should be performed and analyzed.

In the introduction section, I suggest you to underline the role of therapeutic inertia in diabetic kidney disease setting and the major burden of the aggressive Diabetic Kidney Disease in Youth-Onset Type 2 Diabetes.

One of the main aspects of the diagnosis and the staging of diabetic kidney disease is the renal biopsy. You should mention the fact that this is a necessary tool to distinguish the renal involvement related the diabetic condition or an underlying glomerulonephritis.

A subgroup analysis by gender can give added value to your study.

I appreciated the use of the STROBE statement checklist for your research.

I suggest you also to further explain the meaning of the results of your study. For example, why free triiodothyronine was considered a protective factor for DN in T2DM patients? See the study “Association of thyroid function with insulin resistance: data from two population-based studies. Eur Thyroid J. 2022 Feb 28;11(2):e210063. doi: 10.1530/ETJ-21-0063. PMID: 35085102”.

VERSION 1 – AUTHOR RESPONSE

For reviewer 1,
1) Abstract: We added inflammation to the keyword. (page3, line7)
2) Introduction: We further elaborated the relationship between diabetic kidney disease and inflammation in the introduction based on the comments given by reviewer 1, the association between inflammation and DKD has been emphasized. (page4, line19-21, page5, line1-2)
3) Methods: Clearly expressed. Statistics are accurate. No revisions required in this section.
4) Results: Given in an easy to follow way. Tables improved readability.
5) Discussion: We further discuss the importance of the findings in terms of clinical application. (page 16, line1-4)
6) References: We have added the most recent literature mentioned by the reviewers to complete reference.

For reviewer 2,
1) We found more information in the latest KDIGO, confirming that diabetic kidney disease (DKD) fits the definition better. Therefore, we make corresponding changes. For more accurate diabetic kidney disease, we perform repeated microalbuminuria measurement and analysis.

2) We emphasized the role of therapeutic inertia in diabetic kidney disease setting and the major burden of the aggressive Diabetic Kidney Disease in Youth-Onset Type 2 Diabetes in the introduction section. We made some adjustments. (page5, line2-6)

3) We mentioned the fact that the renal biopsy is a necessary tool to distinguish the renal involvement related to the diabetic condition or an underlying glomerulonephritis in the part of Patients and Methods. (page7, line12-16)

4) We analyze subgroup according to gender and draw some conclusions. Women should pay attention to controlling inflammation and triglycerides, and men strictly control blood pressure, avoiding abdominal obesity in both men and women will bring great benefits. (page15, line15-22)

5) Further explanation of the meaning of the results of our study have been shown in the article. (page15, line8-10)