LETTER TO THE EDITOR

Reponse on Muhammad Bilal, et al. (J Pak Med Assoc. 72, No-5: 839- 842, 2022)

Efficacy of rituximab in patients with rheumatoid arthritis

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Madam, Madam, we have read the article, "Efficacy of rituximab in patient with rheumatoid arthritis" (JPMA, Vol 72, No-5, May2022) with support and agreement on the authors view that internationally much work has been done to explore the treatment modalities with minimum adverse effects among rheumatoid arthritis patients. However, there are some equivocal points that require attention and are hereby enlisted:

1. The title section of the study setting isn't presented

Ans: The site of the study should have been included in the title.

2 The introduction section couldn't give a full idea about thegap in knowledge the current study tried to cover.

Ans: The introduction section focuses on the RTX mechanism of action, safety, and effectiveness in the local Pakistani population. Although internationally, there is extended data available on the safety and efficacy of Rituximab. However, the results of the international studies cannot be generalized due to differences in bone density, cost-effectiveness, and therapy accessibility. Following is the text copied from reference 6 of the original study, which clearly explains the gap in knowledge.

3 "Extensive data on the long-term efficacy and safety profile of RTX are now available, mainly from long-term follow-up of patients participating in the RTX clinical trial programme. Five-year efficacy data from the REFLEX trial extension have recently been reported [4], as have been safety data from a pooled analysis of all RTX clinical trials with a follow-up of 10 years, involving up to 17 courses[5]. However, clinical trials are biased by the requirements of patient exclusion and inclusion criteria, and it is estimated that only about 30% of daily practice patients would be eligible for such studies[6]. Consequently, data obtained in real-life settings are also valuable. Such data from RTX-treated patients have been reported from a number of European registries, although generally involving relatively shorter periods of follow-up."

Ans: More references can be acquired from the author

4. Moreover, the significance of the study wasn't stated clearly.

Ans: As it was clearly mentioned that this pilot study was planned to determine the "efficacy" of Rituximab 2×500mg in RA patients.

5. Regarding the research hypothesis or research question, none was formulated; however, they ensure the entire research methodologies are scientific and valid. Moreover, helps to describe the research study in concrete terms rather than theoretical terms.

Ans: As per the CONSORT guidelines for efficacy studies, it's the responsibility of the author to present a specific objective or hypothesis. In our study, we have clearly mentioned the specific objective as per the guidelines.

6. In relation to the study design, the specific type of research design used to conduct the study wasn't specified.

Ans: This was a descriptive case series of 97 cases, as stated in the methodology section.

In addition, the authors did not provide neither a rationale for selecting the study setting nor setting selection procedure, which may affect the generalizability of the results. Appropriate research setting selection and accurate description is critical since the results might been affected heavily by the study setting.

Ans: Firstly the results of the present study cannot be

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generalized to the entire population as it was a single-center pilot study. Secondly, the site was selected based on the tertiary care setting and patient flow. Lastly, the site was approved by the IRB Committee.

Piloting the data collection instruments was not done despite pilot study is a crucial element of a good study design and it would be important to test the clarity, applicability and time needed for filling in the instruments.

Ans: A validation study of the study instrument was previously conducted in Pakistan, and it was published in JPMA.

Ehsan A, Mushtaq S, Salim B, Samreen S, Gul H, Nasim A. Translation and validation of Modified Health Assessment Questionnaire score in local language Urdu in patients with rheumatoid arthritis presenting in a tertiary care center of Pakistan. J Pak Med Assoc. 2022 Apr 1;72(4):674-8.

7. The data collection instruments weren't tested for both validity and reliability. The validity testing of a data collection instrument is the degree to which it measures what it claims to measure. Reliability refers to the consistency of a measure, in other words, whether the results can be reproduced under the same conditions.

Ans: The literature concerning the validity and reliability of the tool was reviewed before designing the methodology. High reliability has been observed for DAS28, indicated by Cronbach's Alpha.

Supporting references can be acquired from the author.

8. Nothing was mentioned regarding the way of meeting participants or how the participants' responses to study instruments were taken neither at the baseline nor at the follow-up visit.

Ans: The participants were recruited from the study site. The study instrument was translated into a regional language; the principal investigator and clinical research associate helped the participants understand the study objective and instrument.

9. It would be better to advise patients to return for two follow-up visits, one after 12 weeks and one after 24 weeks, instead of one follow-up after 24 weeks, which would help in ensuring the association between study variables.

Ans: In this pilot study, our objective focused on assessing pre and post-interventional change in DAS28 score. Therefore, the data of only one follow-up were included for the study purpose. However, future research with randomized controlled trials and extended follow-up is recommended. We have already mentioned this in our recommendation section.

10. In the results section, no data was presented to assess side effects patients might complain from Rituximab used while the authors mentioned in the introduction section,"internationally much work has been done to explore the treatment modalities with minimum AEs among RA patients". While it is appositive point for the authors to mention this as a limitation of the study.

Ans: Although no "adverse drug reaction" was observed during the entire study. Moreover, the aforementioned comments related to "side-effects" were also addressed at the time of review and revision stages of publication.

11. In the conclusion section, the authors recommended that glucocorticoid premedication does seem to reduce or prevent infusion reaction despite no data was collected or presented in the results section to indicate assessment of the infusion reaction.

Ans: The conclusion section's last line clearly states glucocorticoid premedication does "seem" (seem is a possible explanation) to reduce or prevent infusion reaction.