

## Reviewer Comments:

### Reviewer 1

#### Methodology:

1. Sample Selection Bias: The study only included patients discharged from a single tertiary care center, potentially limiting the generalizability of the findings. There's no discussion of how representative this sample is of the broader population of myocardial infarction patients in Pakistan.

**Response:** Including patients from a single tertiary care center is a limitation, which is mentioned in the manuscript. This study is the first of its kind in Pakistan and sets the ground for future research to include a more diverse sample from multiple centers to enhance the representativeness and applicability of the findings.

2. Exclusion Criteria: Excluding patients who died after discharge or had cancer within 2 to 4 years of myocardial infarction could introduce bias and limit the comprehensiveness of the findings. These exclusions may eliminate important subsets of patients who could provide valuable insights into quality of life after myocardial infarction.

**Response:** Our study is qualitative, including patients who died after discharge was not feasible since they could not be interviewed. Additionally, excluding patients with cancer was necessary to ensure that changes in quality of life were attributed to myocardial infarction only, rather than cancer-related issues. This approach aimed to maintain the focus and validity of our findings on the post-MI population.

3. Consent Process: Verbal consent was obtained over the phone, which may not be as robust as written consent, particularly for sensitive health information. Additionally, the process of obtaining consent via telephonic calls could introduce bias as patients who agree to participate may differ systematically from those who decline.

**Response:** Given the constraints of our study, including geographical and logistical challenges, telephonic consent was the most practical approach. To ensure the robustness of the consent process, a single interviewer conducted all interviews. This consistency helped reduce potential bias that could arise if multiple interviewers were involved. The interviewer followed the same detailed script to explain the study's purpose, procedures, risks, and benefits thoroughly to all interviewees.

4. Single Interviewer: While having a single interviewer can reduce variability in data collection, it may not eliminate bias entirely, especially if the interviewer has preconceived notions or lacks cultural sensitivity.

**Response:** To address this, the interviewer, who is also from Pakistan and familiar with the cultural norms, adhered to a structured interview guide to minimize the influence of personal biases. The interviewer's cultural background helped ensure sensitivity and understanding during

the data collection process. The interviewer also underwent extensive training in qualitative interviewing techniques (described in methodology).

5. Questionnaire Choice: While the WHOQOL-BREF is a validated instrument, its appropriateness for the Pakistani context is not explicitly discussed. Cultural and linguistic differences may impact the validity of responses.

**Response:** In our study, we used a validated Urdu version of the WHOQOL-BREF, which has been culturally and linguistically adapted for the Pakistani population. This version is cited in the methodology section (<https://pubmed.ncbi.nlm.nih.gov/29951429/>). Using the validated Urdu version helps ensure that the instrument accurately reflects the cultural and language differences of our participants, thereby enhancing the validity of the responses.

6. Statistical Analysis: The statistical analysis section lacks detail regarding the specific tests used and how variables were controlled for in multivariate regression. Additionally, there's no mention of addressing potential confounding variables such as age, gender, or comorbidities in the analysis.

**Response:** We chose not to run multivariate regression for the majority of variables to avoid adding unnecessary complexity to the results. However, for tobacco use, we did perform a multivariate regression analysis since the biological plausibility was not well established. This analysis plan was approved by Dr. Jasmit Shah, PhD Biostatistics and Bioinformatics, to ensure rigorous evaluation.

- Tests Used: We have detailed the specific statistical tests used, including Wilcoxon and Kruskal-Wallis tests, for analyzing relationships between sociodemographic and clinical characteristics and different aspects of QoL as described in WHOQOL-BREF.
  - Multivariate Regression: While we did not conduct a full multivariate regression for all variables, we accounted for potential confounding variables such as age, gender, and comorbidities in the analysis of tobacco use. This was necessary due to the lack of clear biological plausibility for the impact of tobacco use on QoL outcomes.
  - Confounding Variables: We acknowledge the importance of controlling confounding variables. In the analysis of tobacco use, adjustments were made for PTCA, ejection fraction, age, total number of comorbidities, and gender. These adjustments were performed using non-parametric linear regression to ensure the robustness of the findings.
7. Data Presentation: The study presents median and interquartile range for continuous variables, but there's no indication of the sample size or the distribution of these variables, which limits the interpretability of the findings.

**Response:** As described in the statistical analysis subsection of the methodology (page 4), the data is not normally distributed, thus non-parametric tests were used, and median (IQR) are presented in the results.

8. Ethical Considerations: While ethical approval was obtained from the Ethics Review Committee, there's no discussion of potential conflicts of interest or funding sources that could influence the study's design or interpretation.

**Response:** There are no conflicts of interest, and the funding source for the study was an intramural fund provided by the Brain and Mind Institute, Aga Khan University. These details are described on page 13 of the manuscript.

## Results:

### 1. Inconsistency in Total Participants:

The text states, "440 patients formed our final study cohort," but the sum of males (300) and females (140) is only 440, not considering other exclusions mentioned (e.g., refusals, deaths).

**Response:** Thank you for your feedback. Upon reviewing the data, we confirm that the total number of participants included in the study is 440. The breakdown is as follows:

Total patients discharged with MI: 990

Patients that could not be contacted: 291

Remaining: 699

Patients discovered to have died: 112

Remaining: 587

People who did not give consent: 146

Remaining: 441

Patient diagnosed with Cancer: 1

Remaining: 440

The final study cohort includes 300 males and 140 females, totaling 440 participants, which is consistent with the exclusions mentioned.

We appreciate your attention to detail and hope this clarifies the reported figures.

### 2. Total Monthly Income Percentage Issue:

The percentages for the total monthly income of the household add up to more than 100%.

Specifically:

5.5% (<50,000)

18.0% (>50,000 to <100,000)

29.5% (100,000 - 250,000)

18.4% (>250,000)

28.6% (Unknown)

Total: 99.6%, which should be exactly 100% when considering rounding errors.

**Response:** The total percentages for monthly income add up to 100%. We have verified the original data, and the sum should indeed be 100%.

### 3. Inconsistent Data for Education:

The text states that the majority of participants had completed graduation. However, the table shows:

Primary: 20.2%

Matric/Intermediate: 35.7%

Graduation: 40.7%

This does not clearly indicate a majority, as the sum of the categories is 96.6%, implying missing data or rounding issues.

**Response:** We have clarified in the text and table to reflect that the percentages represent the available data, acknowledging a small percentage of missing information.

Revised Table:

Primary: 20.2%  
Matric/Intermediate: 35.7%  
Graduation: 40.7%  
Missing data: 3.4%

4. Gender Discrepancy:

In the introductory part, it is mentioned that 18.5% of females died during the telephone follow-up. However, this percentage is not reconciled with the final gender distribution provided.

**Response:** Out of the n=699 people who were successfully contacted, 112 were reported deceased by their family members, comprising 14.4% of males and 18.5% of females. After excluding these deaths, along with patients who did not give consent (n=146) and one patient diagnosed with cancer, the final study cohort included 440 participants. The gender distribution of these 440 participants is accurately provided in the table, with 68.2% males and 31.8% females.

5. Misalignment in Marital Status Data:

The total percentage for marital status adds up to 100%, but this does not align perfectly with the total number of participants, given the small discrepancy in rounding:

Married: 79.1%

Unmarried/widow/widower/separated: 20.9%

Total: 100%, but any rounding issues should be explicitly noted or corrected.

**Response:** The total percentage for marital status categories is 100%.

Married: 79.09 ~79.1%

Unmarried/widow/widower/separated: 20.91~20.9%

Total: 100%

6. Typographical and Formatting Errors in Table:

Age data has incorrect formatting for IQR; it should be "63.0 (56-72)" instead of using separate rows.

In the total monthly income category, ">50,000 to < 100,000" shows "79.0" instead of just "79," which should be 18.0% or have consistent formatting.

**Response:** We have revised the formatting.

7. Typographical Errors in Payor Information:

The categories for primary payor do not sum up correctly due to missing separators and extra spaces.

**Response:** We have made the correction for Rs 50,000. Now, they add up correctly

8. Data on Comorbidities:

The text mentions specific percentages for comorbidities, but the sum exceeds 100%, indicating possible overlapping comorbidities not accounted for in the analysis:

1 comorbidity: 28.2%

2 comorbidities: 43.4%

3 comorbidities: 20.9%

4+ comorbidities: 4.6%

Total: 97.1%, which needs explanation if comorbidities overlap.

**Response:** There was a minor rounding off error. There are no overlaps. The sum is 100% now. We have revised as follows: The study revealed that a majority of the participants had multiple comorbidities, with **28.2%** (n=124) having **1** comorbidity, **43.4%** (n=191) having **2** comorbidities, **20.9%** (n=92) having **3** comorbidities, and **4.6%** (n=20) having **4 or more** comorbidities. Only **2.9%** (n=13) of the participants had **ischemic heart disease (IHD), without any other comorbidities**.

9. Internal Consistency and Missing Data:

The median and IQR for QoL scores should consistently use "median (IQR)" notation and explain if any categories are missing or need additional context.

**Response:** We have revised this and added the correct notation, "median (IQR)", wherever missing. There are no missing categories.

10. Incorrect P-Values:

In the Wilcoxon and Kruskal-Wallis test results, some p-values are shown with extra digits or spaces, e.g., "81 (69,100)" and "81 (75,91)" need consistent formatting for easier interpretation:

**Response:** The table has been reformatted. All the median values (IQR) are rounded off to 3 significant figures.

11. Redundant Data:

Repetition of percentages and figures in multiple sections without reconciliation, such as gender and marital status.

**Response:** We have removed the redundant mention of gender percentages in the discussion section. The percentages are initially mentioned in the sociodemographic section, then presented in the table for comparison with different types of QoL, and finally in the results section because they are significant. This structured repetition ensures clarity and emphasizes its importance in the study's findings.

## **Discussion:**

1. The mortality rates reported as 16.02%, 14.4% for males, and 18.05% for females do not align with the earlier data that said 18.5% of females died. This discrepancy should be clarified.

**Response:** We apologize for the typing error. It is 18.05% and has been corrected in the results.

2. It mentions a study in Pakistan showing a 20.3% cumulative mortality rate but does not provide a proper citation.

**Response:** Correct citation has been added.

3. The discussion about the differences in QoL scores compared to other countries is vague. It should explain the cultural or contextual factors more specifically.

**Response:** The discussion has been expanded to explain cultural and contextual factors influencing QoL scores.

4. The section on physical health issues after discharge needs more detail on what specific interventions could be implemented.

**Response:** The section on physical health issues after discharge has been improved with specific interventions, such as effective rehabilitation programs and counselling of the patients.

5. Missing Citations:

Some statements, such as the need for early intervention and the reference to a study conducted in another tertiary hospital in Pakistan, lack proper citations. The text mentions multiple studies without providing proper references or linking to the studies.

**Response:** All the citations have been rechecked and added or removed accordingly.

6. Redundant Information:

The statement about higher education, being married, and higher income levels being associated with better QoL is repeated without adding new insights.

**Response:** It has been changed to avoid redundancy.

7. Language and Tone Issues:

Phrases like "one of the first QoL investigations of its kind in Pakistan" and "Our main findings can be summarized as follows" should be more formal and specific. Some sentences are overly complex and could be simplified for clarity.

**Response:** Language and tone have been revised to be more formal and specific. Overly complex sentences have been simplified for clarity.

8. Inadequate Discussion on Methodological Limitations:

The discussion should address methodological limitations, such as potential biases in data collection, sample size limitations, and the impact of lost follow-up cases.

**Response:** All of these have been added to the limitations section.

9. Inconsistent Use of Terminology:

The text switches between terms like "HRQoL" and "QoL" without clear definitions or consistency.

**Response:** Terminology has been standardized throughout the text, consistently using "HRQoL" with clear definitions provided.

10. Unsubstantiated Claims:

The statement that "specific rehabilitation programs for women need to be further explored" lacks a foundation in the results or discussion.

**Response:** More context has been added from the cited study to support this statement.

11. Contextualizing Findings:

There should be a clearer connection between the findings and the local healthcare context in Pakistan, considering sociocultural factors and healthcare infrastructure.

**Response:** These have been added.

## **Reviewer 2**

### **Summary and Overall Impression:**

This manuscript presents a single-center cross-sectional study conducted at a tertiary care hospital in Karachi, Pakistan, aimed at assessing the Quality of Life (QoL) among post-Myocardial Infarction (MI) patients. Using the WHOQOL-BREF questionnaire, the study investigates various sociodemographic and clinical factors affecting QoL in this population. The findings indicate that physical health is the most impacted domain, with significant associations between QoL scores and factors such as gender, income, education, and comorbidities.

Overall, the study addresses an important gap in understanding QoL outcomes in post-MI patients in Pakistan. The manuscript is technically sound in its approach. The methodology is robust, and the statistical analysis is sound. However, some areas require further clarification and improvement.

**Response:** Thank you for your thorough and constructive review. We are pleased that you find our study technically sound with strong methodology. We appreciate your recognition of the importance of our research in addressing QoL outcomes in post-MI patients in Pakistan. We will carefully address the points that require clarifications to enhance the quality of our manuscript.

Point 1: Please provide Full name before using abbreviation for the very first time in the text. For example, in the Introduction section, LCIM abbreviation is used without its complete term.

**Response:** We have addressed this comment and added full names of abbreviations used for the first time.

Point 2: Availability of Data:

Issue: The manuscript mentions that data were collected from electronic records and patient interviews, but it does not detail the data availability for the research community.

Recommendation: Clearly state the availability of the dataset used for the study. If there are any restrictions on data sharing, explain them and provide information on how interested researchers can request access to the data.

**Response:** The dataset used for this study is only accessible to the study team and is not publicly available due to institutional policies and patient confidentiality concerns. We have added this information to the manuscript. (page 13)

Point 3: The manuscript involves complex statistics so the METHODS section must be reviewed by an expert statistician.

**Response:** This analysis plan was approved by Dr. Jasmit Shah, PhD Biostatistics and Bioinformatics, to ensure rigorous evaluation.

Minor Issues:

1. Language and Formatting:

Issue: There are minor language and formatting issues throughout the manuscript.

Recommendation: Conduct a thorough proofread to correct any grammatical errors and ensure consistent formatting, particularly in tables and figures.

**Response:** Thank you for pointing this out. We have thoroughly reviewed the manuscript again to ensure consistent formatting and correcting any grammatical errors.

## 2. Ethical Considerations:

Issue: The manuscript mentions ethical approval and informed consent but could provide more details.

Recommendation: Include the ethics approval number and a more detailed description of the informed consent process to assure readers of the study's adherence to ethical standards.

**Response:** Ethical approval number and more details about consent process have been added to the section (page 13).

By addressing these issues, the manuscript can be significantly improved, enhancing its clarity, comprehensiveness, and impact. The study provides valuable insights into the QoL of post-MI patients in Pakistan, and with these revisions, it has the potential to contribute meaningfully to the existing literature.