

Review Form 1.7

Journal Name:	Journal of Advances in Medicine and Medical Research
Manuscript Number:	Ms_JAMMR_110622
Title of the Manuscript:	Investigation of the Antioxidant Effect of Varied Doses of Ascorbic Acid in Burn Patients: A Randomized Controlled Study.
Type of the Article	Original Research Article

Review Form 1.7

PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<p>Compulsory REVISION comments</p> <p>1. Is the manuscript important for scientific community? (Please write few sentences on this manuscript)</p> <p>2. Is the title of the article suitable? (If not please suggest an alternative title)</p> <p>3. Is the abstract of the article comprehensive?</p> <p>4. Are subsections and structure of the manuscript appropriate?</p> <p>5. Do you think the manuscript is scientifically correct?</p> <p>6. Are the references sufficient and recent? If you have suggestion of additional references, please mention in the review form.</p> <p><u>(Apart from above mentioned 6 points, reviewers are free to provide additional suggestions/comments)</u></p>	<p>1) There are large gender differences in each group. This is not addressed in the Discussion, vis-à-vis hormonal effects on proteinuria or MDA levels, for example.</p> <p>2) The %TBSA of the burn in group 3 is much less than in groups 1 & 2 and could easily distort results.</p> <p>3) Table 3 shows no difference in post-treatment proteinuria (P=0.128) yet the authors state that there is a difference in Figure 2 caption and in the Results reporting.</p> <p>4) There is no dose-response relation between the dose of ascorbic acid and serum MDA changes. Caption for Table 4 states “mean decrease in serum MDA was highest for patients on the higher dose of ascorbic acid.” However, Group 1 median was 0.04, Group 2 median was 1.0, and Group 3 was 0.1 umol/ml. Perhaps the data for Groups 2 & 3 are reversed by mistake?</p> <p>5) Discussion states “The burn patients that received 8mg/kg/hr of ascorbic acid recorded significantly greater decrease in serum MDA...”. The data as presented do not support this.</p> <p>6) Figure 2 shows greater decrease in proteinuria in Group 2 than in Group 3, so the statement “Similarly, there was a marked decrease in proteinuria in the group of burn patients treated with 8mg/kg/hr of ascorbic acid compared to the other 2 groups.” Is not supported. Again, perhaps the data for the 2 groups is reversed.</p> <p>7) Authors point out the temporal decline in serum MDA after burns, but no data is presented between the 3 groups controlling for time prior to presentation.</p> <p>8) There is not correlation between the %TBSA burn and serum MDA, calling into question the significance of monitoring MDA as a marker at all. Conversely, proteinuria is a common finding after severe burn. Though its mechanism is still unclear, it is considered clinically significant and any treatment which reduces proteinuria after severe burn has potential for therapeutic value. Because of this, I recommend publication but only after significant revision. The authors need to ensure all data for the groups is where it should be. The emphasis should be on the proteinuria effects, with some discussion of MDA reduction possibly being related to the mechanism of action. Far less emphasis should be placed on the MDA in the paper since they don't correlate to much of anything.</p>	<p>1. The gender disparity in the recruited sample has been addressed in the discussion.</p> <p>2. We reported in the results section that the %TBSA in group 3 was significantly lower compared to groups 1 and 2. This disparity was imposed by chance owing to the randomization process. The difference could constitute a limitation to the study as we highlighted in the discussion section of the manuscript.</p> <p>3. Table 3 shows that comparison across the three groups revealed no statistically significant difference in both the pre-treatment and post-treatment urine protein concentration. However, Table 4 (New insert) displays within-group comparison of mean malondialdehyde and proteinuria among the study groups. The mean malondialdehyde for participants in Group 2 was significantly higher at baseline, 2.5 ± 0.6 when compared with post-intervention values, 1.5 ± 0.3, (paired t test=6.943, P<0.001). Similarly, the mean proteinuria for participants in Group 2 was significantly higher at baseline, 327.0 ± 108.3 when compared with post-intervention values, 224.8 ± 37.3, (paired t test=3.255, P=0.010). Also, the mean proteinuria for participants in Group 3 was significantly higher at baseline, 315.6 ± 70.5 when compared with post-intervention values, 259.9 ± 37.2, (paired t test=2.960, P=0.018)]. These results were captured in Figure1 and Figure2.</p> <p>4. Tables 4 and 5 clearly demonstrate a dose-response relationship with ascorbic acid therapy in both serum MDA and urinary protein concentration. There is no reversal of median data. We cross-check median using the mean and not SD in this instance of skewed data.</p> <p>5. For clarity, we have inserted a new Table 4 of within-group comparison, to depict the significant reduction in serum MDA in the patients that received 8mg/kg/hr of ascorbic acid. Table 4 also reveals significant reduction in proteinuria in the burn patients that received 8mg/kg/hr and 2mg/kg/hour of ascorbic acid injection, but not in the placebo group. The illustrations in Figure 1 and Figure 2 support the findings.</p> <p>6. Figure 2 shows greater decrease in proteinuria in Group 2 than in Group 3 and Group 1 burn patients. However, the data from Table 4 indicates that the decreases were statistically significant in both Groups 2 and 3, but not in Group 1 patients. The reports are</p>

Review Form 1.7

		<p>supported, and no group data was reversed.</p> <p>7. The authors did not have the investigation of the temporal course of MDA levels as an objective of the study. Nevertheless, in the methodology it was stated that only burn patients presenting within 48 hrs of the trauma were included in the study.</p> <p>8. Elevation in serum MDA is an acknowledged marker of oxidative stress and lipid peroxidation in burn trauma. However, several characteristics of the burn trauma determine the severity and impact of burn injury, including % TBSA, inhalation component, burn thickness, burn mechanism, among others. So far, this study and some others appear to suggest poor correlation between %TBSA and the degree of oxidative stress. Future studies should strive to investigate the correlation between other burn trauma characteristics and the degree of oxidative stress.</p>
Minor REVISION comments		
1. Is language/English quality of the article suitable for scholarly communications?		
Optional/General comments		

PART 2:

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Are there ethical issues in this manuscript?	(If yes, Kindly please write down the ethical issues here in details)	