ROLE OF HDIVC IN CRITICALLY ILL PATIENTS

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INTRODUCTION

- Ascorbic acid popularly known as Vitamin C is a soluble in water, that provides plethora of benefits and advantages to human body. From being vital for body growth to providing shelter against immune degrading diseases and dysfunction , coronary artery diseases, pre and post natal health issues, cancers, stroke, eye diseases
- A study published in *Seminars in Preventive and Alternative Medicine* looks at 100 studies over 10 years and examines budding gains of Vitamin C. Ascorbic acid is one amongst many antioxidants that shields against destruction due to dangerous free radicals, toxins, and pollutants. C Vitamin is the key to a rock-solid and well-functioning immunity.

Some Benefits of Vitamin C given below :

Supports immune system
Induces collagen formation, muscles, and tendons strength
Antihistamine and Antioxidative properties
Prevents iron deficiency and Anaemia

Vitamin C helps interferons in generating cellular defence mechanism against disease pathogens
Vitamin C backs up the functioning of phagocytes
Vitamin C supports both cellular and antibody immunity
Vitamin C increases the production of cytokines which is integral part of immune response
Vitamin C helps in survival of T lymphocytes for cell mediated immune response
Vitamin C backs up circular GMP levels in lymphocytes
Vitamin C in WBC is 80 times higher as compared to its levels in plasma

Table shows ways Vitamin C contributes to the immune system of the body

RESEARCH QUESTION

What role does HDIVC plays in treatment of Critically ill patients?

OBJECTIVES

- **To study the benefits of Ascorbic Acid as a dietary supplementation.**
- **To study the Role of Vitamin C human body during moderate to severe disease pathogenesis.**
- **To study the Role of HDIVC in Critically Ill patients.**

RESEARCH METHODOLOGY

- Secondary Research is based on Narrative literature review.

"PUBMED"	**"https://www.ncbi.nlm.nih.gov/pmc/articles/"**
"RESEARCH GATE"	"https://www.researchgate.net/"
"GOOGLE SCOLAR"	"https://scholar.google.com/"
"SCIENCE DIRECT"	"https://www.sciencedirect.com/"

The **keywords** used to search the publications that are relevant to the aim and the objective of this review were:

Antioxidants, Ascorbic acid, Vitamin C, Biological Availability, Critical illness therapy, Nutritional requirements, Dose-response Relationship, oxidative stress, Biological Availability, Oxidation-Reduction.

Articles published from 2012 -2021 were taken in study and compilation of 14 such articles were done in summarized form for literature review.

REVIEW OF LITERATURE

TABLE 2.1 Summarizes literature review.

Sno	Title	Author/Year	Methodology	Outcome
1.	"Factors Affecting Vitamin C Status and Prevalence of Deficiency: A Global Health Perspective"	"Carr AC, Rowe S. (2020)"	Systematic review	"Deficiency is governed by cultural factors like traditional cooking practices, income strata of countries, Environmental factors, demographic factors such as sex, age and health conditions like weight and pregnancy"
2.	"Effects of oral vitamin C supplementation on oxidative stress and inflammation status in haemodialysis patients"	"Fumeron C, Nguyen-Khoa T"	randomized, open-label trial	"Short-acting oral vitamin C supplements did not affect oxidative stress and inflammatory markers in Haemodialysis patients. Still a higher oral dose could change markers still needs to be studied."

CONTINUATION OF LITERATURE REVIEW

"Rationale and impact of vitamin C in clinical nutrition"	"McGregor GP, Biesalski HK."	Randomized control trial	"In critical patients especially with 3rd degree burns and more, the quick replenishing of low ascorbate levels with high-dose ascorbic acid can reduce circulatory shock, fluid intakes and swelling."
"Vitamin C: should we supplement?"	"Spoelstra-de Man AME, Elbers PWG (2018)"	Case study	"clinical studies related to trauma, ischemia/reperfusion, and sepsis depicts that vitamin C administered reduces oxidative stress & inflammatory markers"
"Functional and physiological role of vitamin C transporters."	"Bürzle M, Hediger MA. (2012)"	Systematic review	"Ascorbic acid is made use for the synthesis of collagen, carnitine, catecholamine"
"Vitamin C and acute respiratory infections."	"Hemilä H, Douglas RM. (2021)"	Conceptual framework of Literature review	"Three controlled trials showed lowering of minimum 80% in the occurrence of pneumonia, and one randomised trial suggested benefits from vitamin C in patients under critical care with pneumonia and bronchitis."

CONTINUATION OF LITERATURE REVIEW

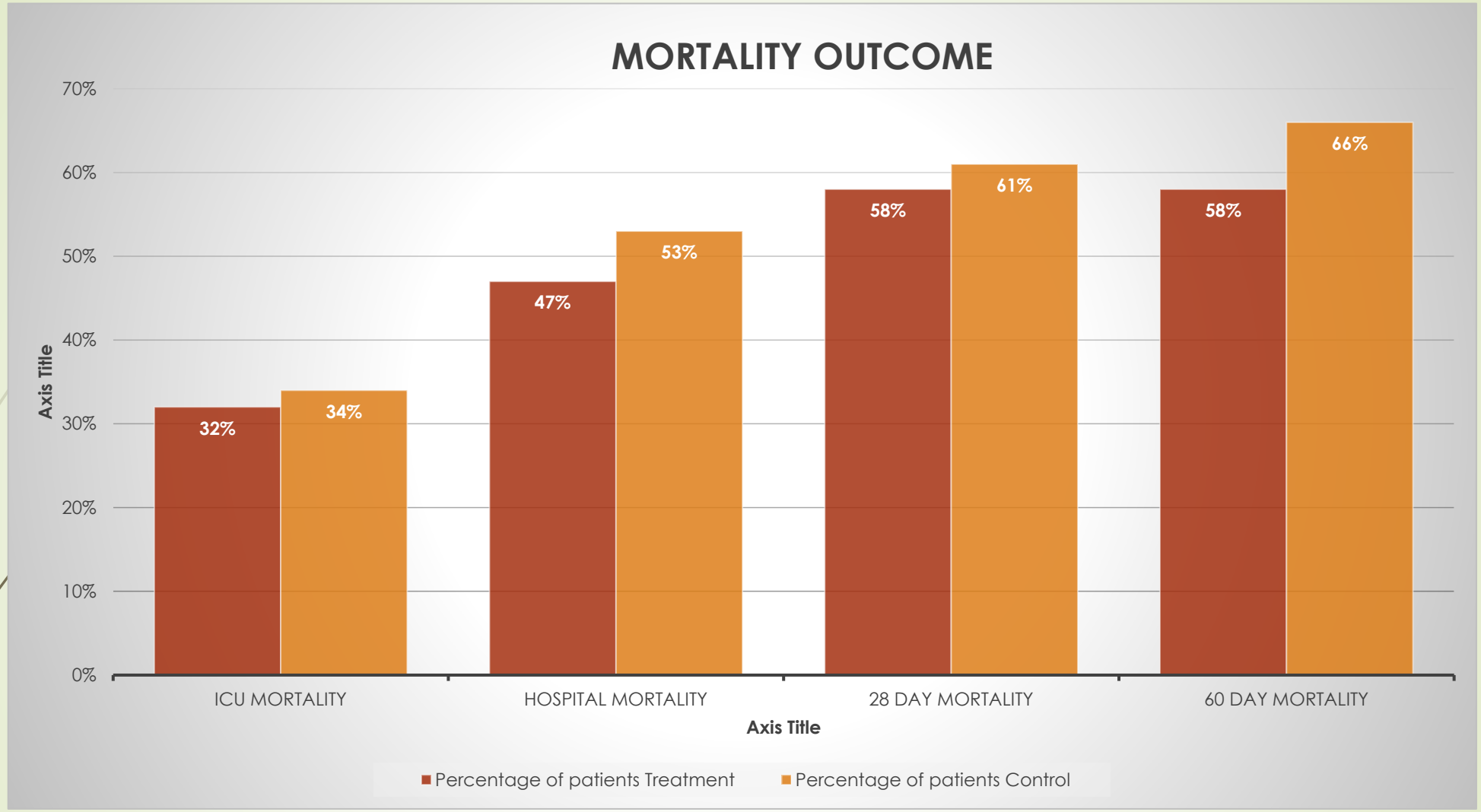
7.	"Dietary vitamin C deficiency depressed the gill physical barriers and immune barriers referring to Nrf2, apoptosis, MLCK, NF-κB and TOR signaling in grass carp (Ctenopharyngodon idella) under infection of Flavobacterium columnare."	"Xu HJ, Jiang WD (2016)"	Systematic review	"Ascorbic acid deficiency (2.9 mg/kg diet) increased reactive oxygen species, malondialdehyde and protein carbonyl."
8.	"Application of methylene blue -vitamin C -N-acetyl cysteine for treatment of critically ill COVID-19 patients"	"Alamdari DH, Moghaddam AB (2020)"	Randomized control trial	"Methaemoglobin and oxidative stress play a pivot role in the critical care of COVID-19 patients"
9.	"Intravenous Vitamin C Administered as Adjunctive Therapy for Recurrent Acute Respiratory Distress Syndrome"	"Bharara A, Grossman C, (2016)"	Systematic review	"Vitamin C in high dose used via parenteral route improved alveolar fluid clearance."
10.	"AA as concurrent treatment for ARDS"	"Fowler Iii AA, Kim C, (2017)"	Systematic review	"On giving HDIVC patient's recovery was fast, and ventilators discontinued in 1 week and patient recovered with no long-term ARDS side effects."

FINDINGS

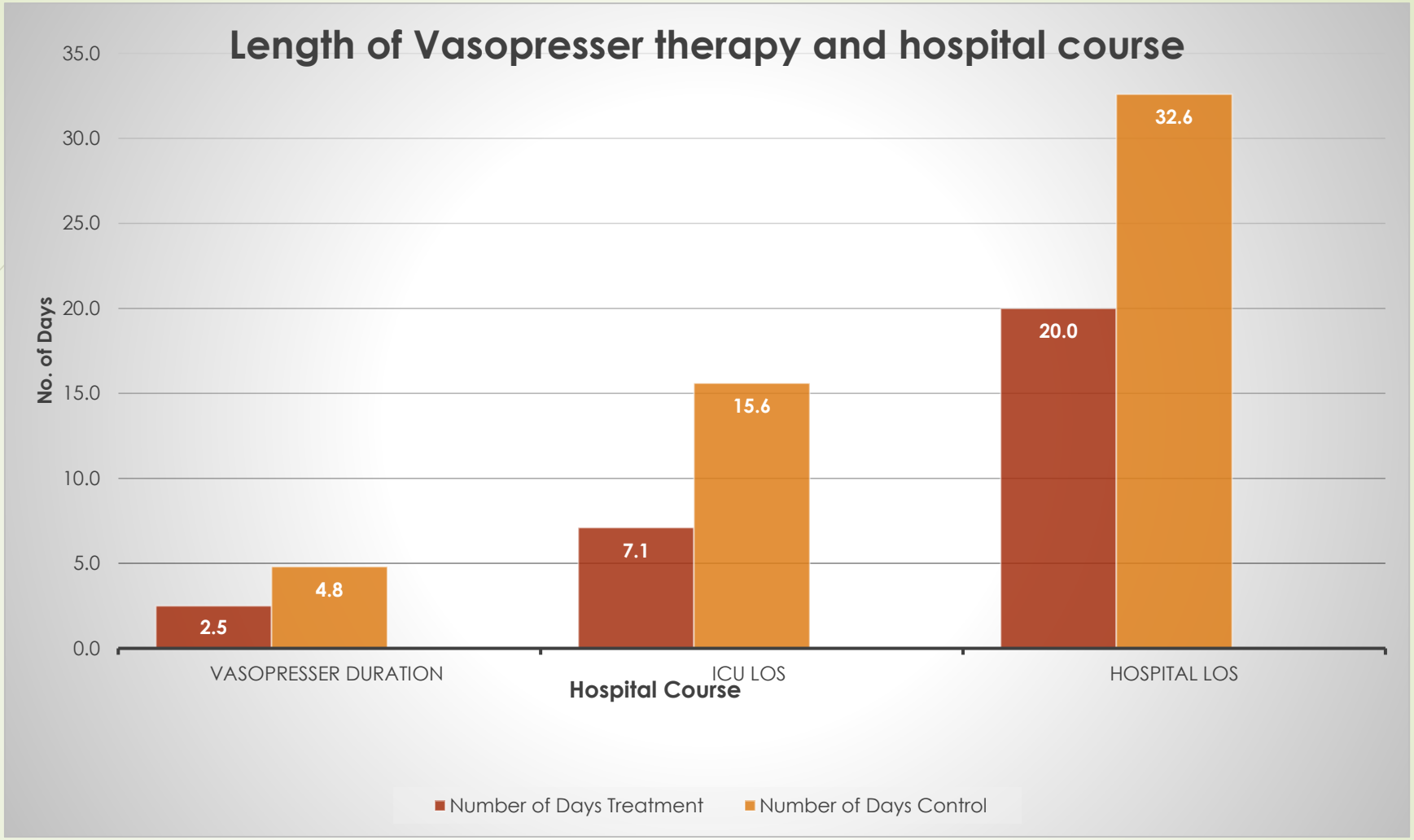
1. Five studies (four randomized controlled trials and one retrospective review) enrolling a total of 142 patients compared with controls, the administration of intravenous vitamin C was associated with a decreased need for vasopressor support (standardized mean difference −0.71; 95% confidence interval (−1.16 to −0.26); p = 0.002) and decreased duration of mechanical ventilation (standardized mean difference −0.5; 95% confidence interval (−0.93 to −0.06); p = 0.03), but no difference was found in mortality (odds ratio 0.76; 95% confidence interval (0.27 to 2.16); p = 0.6). Trends were also noted toward decreased fluid requirements and increased urine output.

2. In another study the included trials enrolled a total of 1210 patients. Intravenous (IV) AA doses of 3-10 g/d reduced the mortality of critically ill patients (OR 0.25; 95% CI (0.14-0.46); $p < 0.001$; $I^2 = 0.0\%$), while low (< 3 g/d) and high AA doses (≥ 10 g/d) had no effect (OR 1.44; 95% CI (0.79-2.61); p = 0.234; $I^2 = 0.0\%$ versus OR 1.12; 95% CI (0.62-2.03); p = 0.700; $I^2 = 0.0\%$). AA was associated with a decreased duration of vasopressor support and mechanical ventilation but did not influence fluid requirement or urine output during the first 24 h of admission. The number of patients suffering from acute kidney injury and the length of intensive care unit or hospital stays were also unaffected by the AA.

Disease Severity Markers	Control (N=38)	Treatment (N=38)
Vasopressors need (%)	76	79
Mean SOFA score ± SD	6 ± 3	6.9 ± 4
Need for Mechanical ventilation (%)	45	50



Shows Mortality in ICU is 2% more when compared to in treatment group, mortality is 6% more in Hospitals for control group, 3% and 8% more within 28 days and 66 days respectively in control group as compared to treatment group



shows the Comparison between the treatment and control in terms of hospital stay, vasopresser duration and ICU stay, LOS in treatment group is visibly reduced to 2.5 days for vasopresser duration, 7.1 days for ICU stay as compared to 15.6 days in control and 20 days for hospital stay as compared to 32.6 days in control

shows SOFA Score comparison between placebo and control, where in treatment SOFA score reduced to 3 from 3.5.

DAYS IN HOSPITAL	SOFA SCORE IN PLACEBO	SOFA SCORE IN TREATMENT GROUP
Day 1	2	3.5
Day 7	6	3

- Analysis :

- The analysis of 8 vitamin C control trials suggested that HDIVC cuts off the use of supported ventilators in critically ill patients The outcome was congruous with antecedent clinical trials depicting that HDIVC shortened the expanse of multiple organ failure and ameliorated the momentary results of circulatory septic shocks. Also, AA levels in blood were indirectly proportional to the incidence of multiple organ failure and death. patients having severe organ failure had a severe hypovitaminosis, for which HDIVC treated the deficiency and improved the organ status. Therefore, the survival was better expected in severely ill patients with a higher SOFA score. The vitamin C administration did not negatively affect patient health and there was decreased ICU stay. Still more data is required to study the treatment benefits in moderate to severe disease prognosis.

QUESTION Does treatment with vitamin C, hydrocortisone, and thiamine lead to a more rapid resolution of septic shock compared with hydrocortisone alone?

CONCLUSION The findings of this clinical trial suggest that treatment with intravenous vitamin C, hydrocortisone, and thiamine does not lead to a more rapid resolution of septic shock compared with intravenous hydrocortisone alone.

POPULATION

133 Men **78** Women

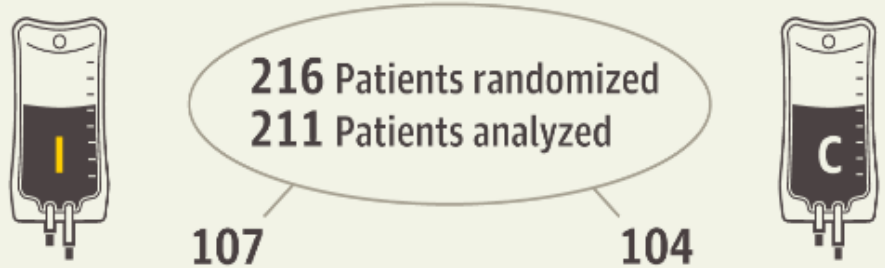
Adult ICU patients meeting Sepsis-3 definition of septic shock

Mean age: **62** years

LOCATIONS

10
ICUs in Australia, New Zealand, and Brazil

INTERVENTION



Intervention

Intravenous vitamin C (1.5 g every 6 hours), hydrocortisone (50 mg every 6 hours), and thiamine (200 mg every 12 hours)

Control

Intravenous hydrocortisone (50 mg every 6 hours)

PRIMARY OUTCOME

Duration of time alive and free of vasopressor administration through day 7

FINDINGS

Median time alive and free of vasopressor administration

Intervention
122 hours (IQR, 76-145 hours)

Control
125 hours (IQR, 82-147 hours)

Median of differences,
-0.6 hours
(95% CI, -8.3 to 7.2 hours); *P* = .83

Fujii T, Luethi N, Young PJ, et al. Effect of vitamin C, hydrocortisone, and thiamine vs hydrocortisone alone on time alive and free of vasopressor support among patients with septic shock: the VITAMINS randomized clinical trial [published online January 17, 2020]. *JAMA*. doi:10.1001/jama.2019.22176

DISCUSSIONS

- Several studies shows that premature recuperation from shock and multiorgan failure can be realized on repeating Vitamin C in dosage of 2 to 3 g given intravenous in conjugation with thiamine in dosage of 100 mg per day, also death can be avoided when pharmacological dose of 2g given intravenous and thiamine in dose of 200-400 mg per day monitored, although these studies are less in number and variates with respect to dosage, time span, pathogenesis and prognosis of disease. Still a lot of biological evidence is required to conform the results. Observational research also shows the synergistic effect of Vitamin C and corticosteroids which is used against septic shock. The use of Vitamin C as oral dose and as i.v. dose in Covid 19 patients has shown to reduce the inflammatory markers and helped in active recovery as well prevention of the viral function, still the research is still active for the viral infection and the role Vitamin C plays in backing up Immunity response to such viruses.

LIMITATIONS:

1.varying degrees of statistical significance between different trials and studies on Vitamin C and use in critical care management.

2.The prognosis is highly dependent on the disease in question, the stage of the pathogenesis of the disease, dose, and immunity response of the patient.

3. Limited data availability on role of vitamin C in other chronic conditions like Cancer and autoimmune diseases.

5.2 STRENGTHS:

1.Enough biological evidence available for the use of ascorbic acid in septic shock and multiorgan failure suggesting positive outcome for other diseases as well resulting in sepsis and multiorgan failure

2.Oral supplementation is of value in maintaining the health of an individual as a very small amount of vitamin C is stored in body and is not actively maintained naturally in the body, an in-depth research on vitamin C and oral supplementation can prevent array of diseases at an early stage.

CONCLUSION

Although there is varying degree of statistical variations in significance between different studies, it is concluded from recent studies that there exists a positive correlation between including Vitamin C as Critical care treatment to patients under high oxidative stress which shortens the stay in ICU as we as reduce the support of mechanical ventilation, although more data is required to prove a causal relationship existing. Vitamin C has great potential to improve the critical care management of the diseases (focusing on sepsis, burns, respiratory infections like ARDS, pneumonia etc) which will in turn reduce the mortality rate in patients.