



Functional and Integrative Wellness Medicine and its effect on General Health Quality of Life among Chronic illness patients – A Scientific Outcome Analysis

Effectiveness of Wellness therapy in improving health

Sujitha S¹, Rajmohan M², Arul K³, Sindhu R⁴, Prabu D⁵, Dinesh Dhamodhar², Lubna Fathima⁴, Sowndarya Madugula¹

¹Post Graduate, Department of Public Health Dentistry, SRM Dental College, Bharathi salai, Chennai.

²M.D.S., Reader, Department of Public Health Dentistry, SRM Dental College, Bharathi salai, Chennai.

³General Physician, Nulife Wellness Centre, Chennai, India.

⁴M.D.S., Senior Lecturer, Department of Public Health Dentistry, SRM Dental College, Bharathi salai, Chennai.

⁵M.D.S., Ph.D., Professor and HOD, Department of Public Health Dentistry, SRM Dental College, Bharathi salai, Chennai.

Corresponding Author: Dr. Rajmohan M, M.D.S.,
Reader, Department of Public Health Dentistry, SRM Dental College
Bharathi Salai, Chennai.

ABSTRACT:

Background: A holistic view of the individual is the hallmark of Integrative Medicine, which combines the best practices of conventional medicine and complementary and alternative medicine to meet each patient's unique needs most safely and cost-effectively possible. **Aim:** The study aims to determine whether integrated therapies, including Extracorporeal Blood Oxygenation and Ozonation (EBOO), Major Auto Haemotherapy (MAHT), Vitamin C IV infusions, and chelation therapy, can help treat chronic medical conditions and normalize blood parameters. The study also evaluates the effectiveness of integrated therapy in terms of pain management, mobility, sleep, amnesia, depression, appetite, and bowel movements. **Materials and method:** A retrospective hospital record-based research study on chronic diseases was conducted using secondary data obtained from all the case records of patients who underwent integrated therapy at Wellness Centre in Chennai, India, from 2019-2023. A Chi square test was used to analyze the relationship between age, gender, and response to treatment for the various chronic diseases. One-way ANOVA was used to determine the effect of integrated therapy in normalizing the blood parameters. Statistical analysis was carried out using SPSS 27.0 software. **Results:** Out of 47 patients examined, 77.6% showed improved general health, and almost 48.8% were relieved from pain. Also, there is a significant (<0.001) difference in normalizing the abnormal blood parameters. **Conclusion:** The results are unambiguous that individuals with chronic diseases have benefited greatly from integrative therapy. Future advancements in patient care will be facilitated by the advent of a holistic approach to treatment that incorporates integrated therapy and traditional medicine.

Keywords: Complementary and Alternative Medicine, Traditional Medicine, Ozone therapy, General Wellness Therapy, Non-Communicable Diseases.



INTRODUCTION:

In India, Health life expectancy, the average number of years a person lives with full health from birth, is 60.3, quite less than the World estimate of 63.7 as of 2019. According to Global Cancer Observatory (GLOBOCAN), 2022, the top causes of death for both sexes in 2019 were found to be Ischemic Heart Disease (IHD), Chronic Obstructive Pulmonary Disease (COPD), Diabetes Mellitus (DM), Stroke, Fatty liver, diarrheal disease, and autoimmune disorders.¹

Conventional therapy relies too much on expensive technology to solve health problems, even when ineffective. As an adjuvant to conventional medicine, complementary therapy can be used as a safe and effective mode of intervention. Integrative medicine focuses on healing by considering everything about a person, including the body, mind, and spirit.² Integrated medicine comprises modern or conventional medicine, traditional medicine, Complementary and Alternative Medicine (CAM), and holistic therapy. It is based on the belief that health and healing are more important than diseases and interventions; thus, integrating medicine has a broader meaning and mission. As part of this approach, patients and doctors work to maintain health by considering lifestyle factors, such as diet, exercise, rest and sleep quality, and living relationships.

At the first-ever World Health Organization Global Summit on Traditional Medicine 2023, held on August 18, a diverse and unique group of partners and stakeholders expressed their commitment to making the most of evidence-based traditional, complementary, and integrative medicine. By 2030, we hope to achieve universal health coverage and the Sustainable Development Goals to improve the well-being of people and the planet.³

By utilizing a holistic understanding of the individual, Integrative medicine incorporates the best practices from both worlds of conventional medicine and CAM is customized to meet each patient's unique needs most safely and cost-effectively.⁴ Urbanization has been problematic in India due to many barriers and obstacles, resulting in a miserable situation for the rural Economy.⁵ To bring the nation's public health infrastructure up to international standards, it must fortify its critical healthcare delivery, which can only be done by hiring more healthcare providers and bringing in more expensive equipment.⁶ The rising costs of health care combined with the high mortality rate and morbidity of chronic diseases now account for the majority of our health care expenditures. Instead of waiting till a disease manifests to treat it, integrative



medicine emphasizes disease prevention and early detection. By choosing a healthier lifestyle, we can reduce the incidence of heart disease, diabetes, and cancer.²

There is a lack of good guidelines on how to treat and manage a number of chronic illnesses, although the history and course of disease burden are very much studied. As a consequence, treatment burden is a distinct concept from disease burden and symptom burden. Chronic illnesses can be treated in a number of ways, such as through radiation therapy, physical therapy, psychiatric treatment, or surgery. The prevention and treatment of chronic illnesses can be challenging, especially when multiple systemic complications are elicited. The biggest disadvantage of conventional practice is that such treatment is unnecessary because a disorder or disease is often self-limiting. Expensive tests are commonly done just "to be sure," thereby subjecting the patient and the economy to a significant financial burden.

Although shreds of evidence show a better response to integrated therapy, it still needs to be explored. Unfortunately, patients fall for inappropriate, non-standardized, and unapproved treatment protocols. This study evaluates the effectiveness of integrated medicine in treating chronic medical conditions in terms of improving Quality of Life (QoL) and normalizing blood parameters.

MATERIALS AND METHOD:

Study site: A retrospective hospital record-based cohort study of chronic diseases was conducted using secondary data obtained from Wellness Centre in Chennai, Tamil Nadu, India. All the case records of patients undergoing integrated medicine for various chronic illness conditions from 2019 to 2023 were recruited upon proper informed consent. Out of 118 patients who underwent integrated therapy, 47 case records were eligible to be included in the study. The study population was included based on the International Classification of Diseases – 10th revision (ICD-10)⁷. Various chronic diseases of the circulatory system, central nervous system, respiratory system, gastrointestinal system, neuromuscular disorders, endocrinal system, excretory system, infectious diseases, and blood disorders.

Eligibility criteria: All medical records of patients aged 15 or above were included in the study. Patients with informed consent for using their medical records for research purposes were in the study. Case records with detailed descriptions of the illness, diagnosis, and a complete investigation sheet attached were included in the study. Patients who lost to follow-up and those



who were deceased while under treatment were excluded from the study. Those medical records with missing pages and incomplete data were excluded from the study.

Data extraction: After scrutinizing the case records for diagnosis, the treatment undergone, and supplementations prescribed, and laboratory investigations, data extracted from the medical records include age, gender, diagnoses falling into any of the ICD-10 codes, blood parameters measured before and after therapy. A personal interview with the patient at every follow-up session was conducted to assess quality of life, such as physical and mental efficacy.⁸ Case sheets were kept on each patient. Before and after therapy, pain relief, anxiety, sleep patterns, limited movements, depression, and appetite were analyzed as dichotomous data to determine whether the quality of life has improved or not.

Statistical Analysis: Statistical analyses were carried out using SPSS 27.0 software. The survey data will be collected, identified, and organized. Descriptive statistics were used to analyze the data. Frequency distribution was used to determine whether the integrated therapy improved the patient's symptoms (dichotomous outcome measure) among different systemic disorders. A Chi square test was used to analyze the relationship between age, gender, and response to treatment for the various chronic diseases mentioned above. Data was tested for normality using Kolmogorov-Smirnov and Shapiro-Wilk test and found to be normally distributed. One-way ANOVA was used to determine the effect of integrated therapy in normalizing the blood parameters.

RESULTS:

Descriptive statistics:

A total of 47 case records of patients suffering from different systemic illnesses were identified during 5 year period from 2019 to 2023. Of the 47 patients, males were 53.1% (n=25) and females were 46.8% (n=22). The majority were old aged people between age 50-64 years (46.8%) followed by middle-aged people of years 35-49 (34%). The mean age of the population was 47 years old. Most of the people who came to the wellness centre were to get treated for joint pain, bloating and distension of the abdomen, adrenal insufficiency, and depression. Characteristics and demographic data of the case records are presented in Table 1.



Table 1: Characteristics of the case records - Demographic data

Demographic data	Total	Disorders				
		Cardio-vascular and Respiratory disorder	Central Nervous System and Neuromuscular disorders	Gastro-intestinal and excretory system disorders	Blood and Infectious disorders	Endocrinal system disorders
Gender						
Male	25	5	5	10	4	1
Female	22	1	8	2	3	8
Total	47	6	13	12	7	9
Age						
<18	2		1	1		
18-34	3			1	1	1
35-49	16	3	4	3	3	3
50-64	22	2	8	6	3	3
>65	4	1		1		2
Blood parameters						
TC	20	3	5	3	6	3
Platelet	20	3	5	3	6	3
ESR	12	1	3	2	5	1
RBC	18	3	5	3	6	1
HbA1c	8	1	1	-	4	2
Urea	10	3	1	3	4	-
hsCRP	6	-	1	1	3	1
25-OHD	12	1	3	3	4	1
Hb	22	3	7	3	6	3
Creatinine	12	3	1	3	5	-
Homocysteine	4	-	1	-	2	1
SGOT	10	1	2	1	4	2
SGPT	5	-	2	1	2	-
Ferritin	15	1	6	1	4	3
LDH	3		-	1	1	1
T. Cholesterol	8	1	2	-	3	2
Cortisol AM	5	1	1	-	2	1
TSH	8	1	3	-	3	1
Uric acid	6	1	1	-	4	-
Albumin	4	-	2	-	2	-
Vitamin B12	3	-	1	-	2	-
CEA	3	-	-	-	2	1
FBS	1	-	-	1	-	-
PPBS	1	-	-	1	-	-
PCV	18	3	5	3	6	1



CRP	4	1	1	-	1	1
SAP	9	1	2	-	4	2
GGT	7	1	2	-	2	2
Anti-CCP	1	-	1	-	-	-
T. Bilirubin	5	-	2	-	3	-
T. Protein	5	-	2	-	3	-
D-Dimer	2	-	-	-	2	-
CA 19-9	1	-	-	-	1	-
DHEA-S	2	-	-	-	2	-
Quality of Life						
Pain	32	4	7	7	8	6
Mobility	4	3	-	-	1	-
Sleep	8	-	3	2	2	1
Amnesia	1	-	-	-	-	1
Depression	5	-	3	1	-	1
Appetite	5	-	2	3	-	-
Bowel movements	14	3	3	7	-	1
General Health	9	2	-	3	2	2

Despite differences in age, gender, and disorders, the response to therapy there is no statistically significant difference (Table 2).

Table 2: Association between socio-demographic variables, systemic disorders, and response to integrated therapies

Variables		N (%)	Value	df	p-value
Gender	Male	16 (66.7)	0.013	1	0.908
	Female	13 (65)			
Age	<18 years	1 (50)	2.141	4	0.710
	18-35 years	2 (66.7)			
	36-49 years	11 (73.3)			
	50-64 years	13 (68.4)			
	>65 years	2 (40)			
Disorders	GIT	9 (75)	4.446	4	0.349
	CVS	2 (40)			
	CNS	11(68.8)			
	Endocrinal	4 (50)			
	Blood	3(100)			

Chi-square test performed; $p < 0.05$ considered statistical significance

Abbr: GIT- Gastrointestinal Tract; CVS-Cardiovascular system; CNS-Central Nervous System.

Self-reported Quality of Life:



The study has found multiple sessions of ozone therapy, Vitamin C infusions, natural forms of antioxidant, and multivitamin/multimineral therapy have significantly reduced pain in 21 of 33 reported patients (63.8%). 11 among 14 patients showed improvement in their bowel habits (78.6%). 7 in 9 case records (77.6%) reported that the general health has been restored. Although there are only a few case records that mention the quality of life, more than 60% of them have reports of improved symptoms as shown in Table 3.

Table 3: Frequency distribution table representing an improvement in quality of life

Quality of Life	N	No. of case records showed improvement	Percent (%)
Pain	33	21	63.6
Mobility	5	3	60
Sleep	8	5	62.5
Amnesia	1	1	100
Depression	5	4	80
Appetite	5	5	100
Bowel movements	14	11	73.3
General Health	9	7	77.8

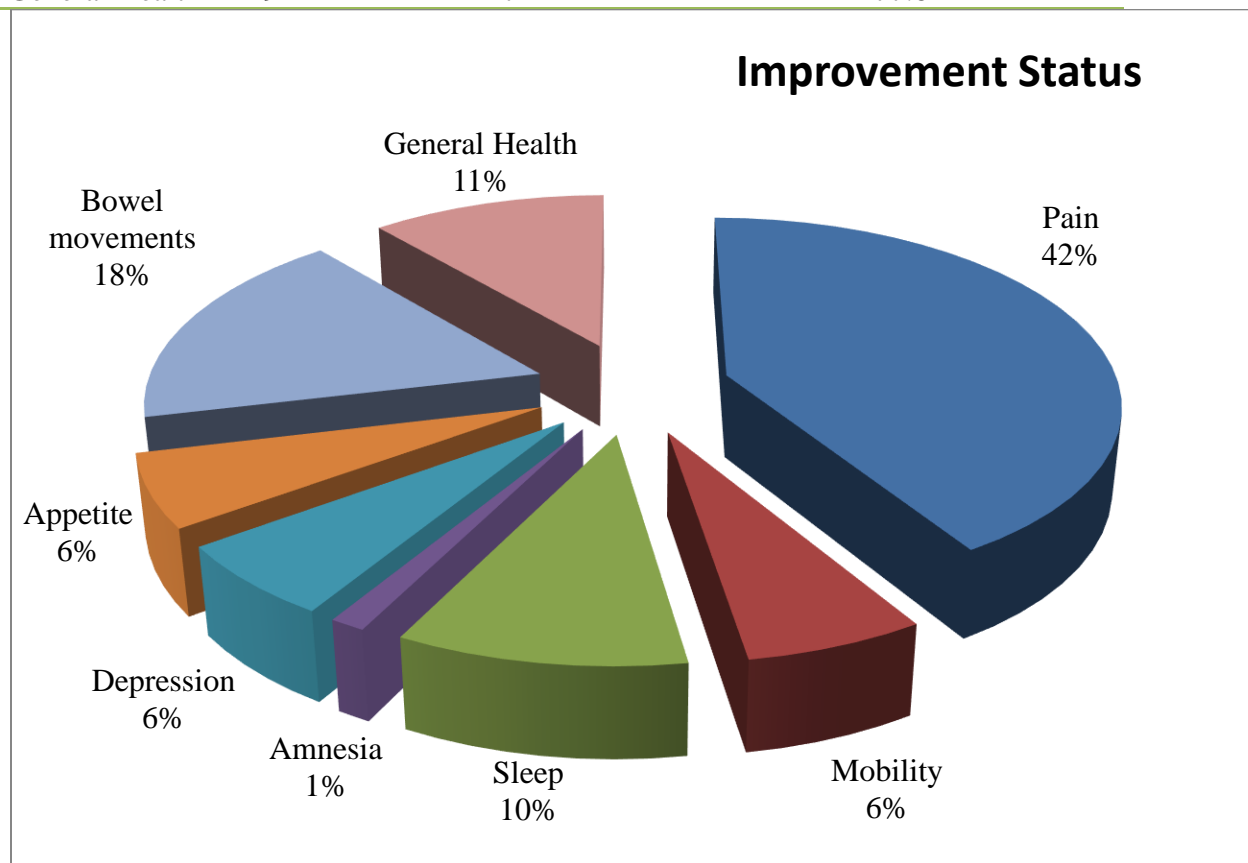




Fig. 1: Graph representing percentages of improved quality of life among chronically ill patients after wellness therapy

Blood parameter:

Mean ESR levels before intervention among 12 patients were found to be 32.96 ± 9.8 (95% CI, 20.9 - 45.11) which was reduced to 23.3 ± 12.77 (95% CI, 7.44 - 39.45) after intervention. Critically low level of Vitamin D before intervention 10.97 ± 3.54 (95% CI, 5.32 – 16.32) was improved to 40.82 ± 16.72 (95% CI, 14.44 – 67.43). Homocysteine level was reduced from 15.24 ± 3.08 (95% CI, 7.57 – 22.90) to 10.31 ± 4.48 (95% CI, -0.84 – 21.46). Also, there is a statistically significant difference between and within groups ($p < 0.001$) before and after intervention, as represented in Table 4.

Table 4: Analysis of Variance in blood parameter before and post-intervention

Sources of variation		SS	df	MS	F	p-value
Baseline	Between Groups	270393519.267	33	8193743.008	17.564	<.001***
	Within Groups	23792255.159	51	466514.807		
	Total	294185774.426	84			
Post Intervention	Between Groups	273866594.756	33	8298987.720	25.521	<.001***
	Within Groups	16584271.521	51	325181.795		
	Total	290450866.277	84			

One-way ANOVA performed; *** $p < 0.001$ considered statistical significance.

DISCUSSION

To the best extent of our knowledge, this is the first study to investigate the effectiveness of holistic, integrated medicine in treating various chronic illness conditions, including communicable and non-communicable disorders, among the Indian population. Various works of literature focus either on Complementary and Alternative Medicine (CAM) therapy or specific



adjunct therapy such as ozone therapy or vitamin C therapy in majorly treating cancer patients, diabetic foot ulcers, renal clearance, and dermatological conditions³. Integrated therapies include ozone therapy like Extracorporeal Blood Oxygenation and Ozonation (EBOO) and Major Auto Haemotherapy (MAHT), Vitamin C IV infusion, Chelation therapy, detox therapy, Correction of electrolyte imbalance, De-worming in some patients, Multivitamin, multi-mineral supplementations, and Phytochemical supplementation.² Research on holistic, integrated therapies is still a wide area to explore.

Common diseases encountered include joint pain, fatigue, Coronary Artery Disease, Irritable Bowel Syndrome, depression, dysmenorrhea, adrenal dysfunction, lymphoma, and cancer. The pain was improved in 21 patients out of 33 (63.8%), bowel movements were improved in 77%, and nearly 78% admitted that their overall health improved after therapy. The study also revealed a statistically significant ($p < 0.001$) improvement in normalizing blood parameters before and after treatment.

Andressa Urbano Machado et al. reviewed around 18 randomized clinical trials on the effectiveness of ozone therapy for dermatological disorders. Out of 18 studies, 12 showed the superiority of ozone therapy compared to the control group, and almost 15 studies showed equal effectiveness of ozone therapy in treating diabetic foot ulcers, chronic venous leg ulcers, wound healing, mycoses, atopic dermatitis, and skin burns. The authors also suggest it could be the best alternative to conventional treatment modalities.⁹ In contrast to the present study, Kadir et al. did not exhibit any significant difference between the experiment and control (conventional therapy) group among diabetic foot ulcer patients in wound healing.¹⁰ The current study demonstrates a considerable reduction in pain and general health improvement, despite little improvement in blood parameters among patients infected with cytomegalovirus and psoriasis. Ozone therapy remains a controversial treatment modality as it has a potential for toxicity demands more clinical trials in different ethnic groups in order to provide cost-effective treatment option to people in need.

Massimiliano Berreta et al. 2020, reviewed the most recent studies on ascorbic acid infusion in critically ill patients such as cancer, infectious diseases, and cardiovascular disorders.¹¹ Among cancer patients, various studies showed improvement in quality of life,¹² increased survival rate¹³ and safe.¹⁴⁻¹⁶ IV Ascorbic acid also increases the antioxidant status in Post-Covid 19 patients,¹⁷



Human Immunodeficiency Virus (HIV) patients,¹⁸ and hepatitis.¹⁹ At the same time, Makinde O. et al. study did not show any effect on HIV patients.²⁰ Oral ascorbic acid reduces blood pressure, reduces the risk of cardiovascular diseases, and has a beneficial effect on vascular endothelial function.²¹⁻²³ Our research reveals a symptomatic improvement in coagulation function, general health, and alleviation of pain among patients with coronary artery diseases and post-covid complications. Additionally, there has been a noticeable improvement in their ESR, Eosinophils, HbA1c, and creatinine levels.

Various studies have shown the link between multivitamin/multi-mineral supplements and cancer risk, among which one study published in August 2010 analyzed eight cohort and case-control studies. The study showed that women who took multivitamin/multi-mineral supplements daily for at least ten years still faced the same risk of breast cancer as those who did not take those.²⁴ In contrast to the previously mentioned meta-analysis, the Women's Health Initiative has conducted several studies on the association between multivitamin/multimineral supplementation and cancer-related deaths, including one that tracked 7,728 women diagnosed with invasive breast cancer for an average of 7.1 years after they were diagnosed. Compared to non-users, multivitamin/multi-mineral supplementation users had a 30% lower mortality rate from breast cancer.²⁵ In another large prospective study, 489,640 men and women over 50–71 years of age were followed for 16 years to examine the association between multivitamin/multimineral supplementation and cancer risk. According to the study, women and men taking more than one multivitamin/multimineral supplement every day had an 18% lower risk of developing breast cancer than non-users.²⁶ The present study shows that patients with Non-Hodgkin lymphoma, lung, and breast cancer have improved overall health and experienced less pain, also patients with cervix cancer have experienced less bleeding; and there is a significant improvement in sleep, appetite, bowel movements, and a reduction of pain in stomach cancer patients. CRP, hsCRP, and ESR are improved in NHL, cervical, and lung cancer patients. A decrease in CEA levels has been observed in cervical cancer patients.

Meta-analysis on multivitamin/ multi-mineral supplementation and cardiovascular risk association, including myocardial infarction and stroke, did not lower the incidence between users and non-users significantly.^{27,28} A well-known trial, The French Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) study, examined the impact of multivitamin



and multi-mineral supplementation on chronic disease risk and mortality. A total of 13,017 adults aged 35-60 were randomly assigned to receive a placebo or a daily supplement containing vitamins C, E, beta-carotene, selenium, or zinc. 7.5 years after the supplements were administered, men had a 31% lower total cancer incidence rate and 37% lower all-cause mortality rate, but women did not.²⁹

Bethan L. Richards et al. reviewed the effectiveness of conventional medicines like diazepam, triazolam, zopiclone, and short-term muscle relaxants on patients affected with inflammatory arthritis.³⁰ They found that the treatment did not reduce pain in 24 hours, one week (95% CI – 1.02 to 0.58) and two weeks (95% CI –0.59 to 0.18). The study also mentioned its association with significant adverse effects of dizziness and drowsiness (95% CI 2 to 7). In contrast, Aidan G Cashin et al. study in 2021 showed a reduction in pain intensity in less than two weeks among the case group who had non-benzodiazepines antispasmodics compared to controls (95% CI, –12.1 to –3.3). Yet, no improvement in the reduction of disability was evidenced.³¹ Dario Gregori et al. study conducted a systematic review and meta-analysis based on 47 randomized controlled trials among knee osteoarthritis patients. Multiple therapeutic modalities like analgesics, antioxidants, bisphosphonates, Strontium Ranelate, NSAIDs, Intra-articular injection medications such as hyaluronic acid and corticosteroids, symptomatic slow-acting drugs like Glucosamine and Chondroitin sulfate and putative disease-modifying agents like Cindunistat Sprifermin were intervened and found Glucosamine significantly reduced pain also showed improvement in physical function.³² Similarly, Luis Ceballos-Laita et al. assessed non-pharmacological methods to relieve pain among hip osteoarthritis patients and found that a combination of manual therapy, physical therapy, and patient education significantly reduced pain and improved physical function.³³ Three out of four patients with chronic joint pain conditions had reduced pain and improved bowel habits and appetite in the current study. A significant decrease in hs-CRP levels has also been observed among them.

LIMITATIONS

In light of the study's reliance on secondary data, more precise studies of each treatment modality are needed. Its major limitation is the lack of few data, where not all case records include information about pain aggravation or subsidence. Even though the study has some



limitations, we were able to find a significant improvement in patient symptoms and general health.

CONCLUSION

In the study, it is evident that patients with chronic illnesses have benefited significantly from integrated therapy. The emergence of a holistic approach to treating patients that includes both conventional medicine and integrated therapy is also welcomed in the future as it will create a breakthrough in patient care. Because so many integrated therapies aren't approved officially, many clear studies will serve as a key for us to advance in healthcare management.

SOURCES OF SUPPORT: Authors didn't receive any source of funding or grants.

CONFLICTING INTEREST: Authors have no conflict of interest.

ABBREVIATIONS:

CAM: Complementary and Alternative Medicine, TCIM: Traditional, Complementary, and Integrative Medicine, ICD-10: International Classification of Diseases – 10th revision, EBOO: Extracorporeal Blood Oxygenation and Ozonation, MAHT: Major Auto Haemotherapy, QoL: Quality of Life, IHD: Ischemic Heart Disease, COPD: Chronic Obstructive Pulmonary Disease, DM: Diabetes Mellitus.

ACKNOWLEDGEMENTS: Nil

ETHICS APPROVAL: Nil

AUTHOR CONTRIBUTIONS:

Conceptualization and Intellectual content: Sujitha S, Rajmohan M, Sindhu R, Prabu D and Sowndarya Madugula. **Design:** Rajmohan M, Arul K, Prabu D and Dinesh Dhamodhar.

Literature search: Sujitha S, Arul K, Sindhu R, Lubna Fathima and Sowndarya Madugula.

Data Collection and Data Entry: Sujitha S, Rajmohan M, Sindhu R, Prabu D, Lubna Fathima and Sowndarya Madugula. **Statistical Analysis:** Sujitha S, Lubna Fathima and Sowndarya Madugula.

Manuscript writing and editing: Sujitha S, Rajmohan M, Arul K, Sindhu R, Prabu D, Dinesh Dhamodhar, Lubna Fathima and Sowndarya Madugula. **Manuscript Review:**

Rajmohan M, Arul K, Sindhu R and Prabu D. **Plagiarism Check:** Rajmohan M, Dinesh Dhamodhar and Prabu D.

REFERENCES



1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L. et al. (2024). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: <https://gco.iarc.who.int/today> [Cited on April 24, 2024]
2. David Rakel MD, Andrew Weil MD. (2007). Philosophy of Integrative Medicine. *Integrative Medicine*. 2nd ed.
3. World Health Organization.: Global partners commit to advance evidence-based traditional, complementary and integrative medicine. c2023-08. <https://www.who.int/news/item/19-08-2023-global-partners-commit-to-advance-evidence-based-traditional--complementary-and-integrative-medicine> [Cited on August 19, 2024].
4. David Rakel MD, Andrew Weil MD. (2018). Philosophy of Integrative Medicine. *Integrative Medicine*. 2nd ed.
5. Aishwarya, Rajmohan, Suganya.P, Prabu D, Bharathwaj, Prashanthi MR. (2021). A Comparative Analysis of Misery Index and Its Impact on Health Indicators Across The Globe. *Indian Journal of Forensic Medicine & Toxicology*, 5(4): 35-40.
6. Prabu D, Gousalya V, Rajmohan M, Dinesh MD, Bharathwaj VV, Sindhu R, Sathiyapriya. (2023). Need Analysis of Indian Critical Health Care Delivery in Government Sectors and its Impact on the General Public: A Time to Revamp Public Health Care Infrastructure. *Indian J Crit Care Med*, 27(4): 237–245.
7. International Classification of Diseases, Tenth Revision, Clinical Modification (ICD – 10 – CM) Classification of Diseases, Functioning and Disability. Centers for Disease Control and Prevention. <https://www.cdc.gov/nchs/icd/icd-10-cm.htm> [Cited on April 24, 2024].
8. Jalili S, Ghasemi Shayan R. (2022). A Comprehensive Evaluation of Health-Related Life Quality Assessment Through Head and Neck, Prostate, Breast, Lung, and Skin Cancer in Adults. *Front. Public Health*, 10: 789456.
9. Andressa Urbano Machado, Renata Vidor Contri. (2022). Effectiveness and Safety of Ozone Therapy for Dermatological Disorders: A Literature Review of Clinical Trials. *Indian J Dermatol.*, 67(4): 479.
10. Kadir K, Syam Y, Yusuf S, Zainuddin M. (2020). Ozone therapy on reduction of bacterial colonies and acceleration of diabetic foot ulcer healing. *Home Healthc Now*, 38: 215–20.
11. Berretta M, Rinaldi L, Taibi R, Tralongo P, Fulvi A, Montesarchio V, Madeddu G, Magistri P, Bimonte S, Trovò M, Gnagnarella P, Cuomo A, Cascella M, Lleshi A, Nasti G, Facchini S, Fiorica F, Di Francia R, Nunnari G, Pellicanò GF, Guglielmino A, Danova M, Rossetti S, Amore A, Crispo A, Facchini G. (2020). Physician Attitudes and Perceptions of Complementary and Alternative Medicine (CAM): A Multicentre Italian Study. *Front Oncol*, 10: 594.
12. Vollbracht C, Schneider B, Leendert V, Weiss G, Auerbach L, Beuth, J. (2011). Intravenous ASC administration improves quality of life in breast cancer patients during chemo-/radiotherapy and aftercare: Results of a retrospective, multicentre, epidemiological cohort study in Germany. *In Vivo*, 25: 983–990.



13. Polireddy K, Dong R, Reed G, Yu J, Chen P, Williamson S, Violet PC, Pessetto Z, Godwin AK, Fan F, Levine M, Drisko JA, Chen Q. (2017). High Dose Parenteral Ascorbate Inhibited Pancreatic Cancer Growth and Metastasis: Mechanisms and a Phase I/IIa study. *Sci. Rep*, 7: 17188.
14. Wang F, He MM, Wang ZX, Li S, Jin Y, Ren C, Shi SM, Bi BT, Chen SZ, Lv ZD, Hu JJ, Wang ZQ, Wang FH, Wang DS, Li YH, Xu RH. (2019). Phase I study of high-dose ascorbic acid with mFOLFOX6 or FOLFIRI in patients with metastatic colorectal cancer or gastric cancer. *BMC Cancer*, 19: 460.
15. Fritz H, Flower G, Weeks L, Cooley K, Callachan M, McGowan J, Skidmore B, Kirchner L, Seely D. (2014). Intravenous ASC and Cancer. *Integr Cancer Ther*, 13: 280–300.
16. Hoffer LJ, Robitaille L, Zakarian R, Melnychuk D, Kavan P, Agulnik J, Cohen V, Small D, Miller WH Jr. (2015). High-Dose Intravenous ASC Combined with Cytotoxic Chemotherapy in Patients with Advanced Cancer: A Phase I-II Clinical Trial. *PLoS One*, 10: e0120228.
17. Tan SHS, Hong CC, Saha S, Murphy D, Hui, JH. Medications in COVID-19 patients: (2020). Summarizing the current literature from an orthopaedic perspective. *Int Orthop.*, 12: e7560.
18. Musisi E, Matovu DK, Bukenya A, Kaswabuli S, Zawedde J, Andama A, Byanyima P, Sanyu I, Sessolo A, Seremba E, Davis JL, Worodria W, Huang L, Walter ND, Mayanja-Kizza H. (2018). Effect of anti-retroviral therapy on oxidative stress in hospitalized HIV-infected adults with and without TB. *Afr Health Sci.*, 18: 512–522.
19. Madill J, Arendt BM, Aghdassi E, Therapondos G, Lilly L, Chow CW, Guindi M, Allard JP. (2009). Hepatic Lipid Peroxidation and Antioxidant Micronutrients in Hepatitis Virus C Liver Recipients with and Without Disease Recurrence. *Transplant Proc.*, 41: 3800–3805.
20. Makinde O, Rotimi K, Ikumawoyi V, Adeyemo T, Olayemi S. (2017). Effect of vitamin A and ASC supplementation on oxidative stress in HIV and HIV-TB co-infection at Lagos University Teaching Hospital (LUTH) Nigeria. *Afr Health Sci.*, 17: 308–314.
21. Ashor AW, Lara J, Mathers JC, Siervo M. (2014). Effect of ASC on endothelial function in health and disease: A systematic review and meta-analysis of randomised controlled trials. *Atherosclerosis*, 235: 9–20.
22. Martín-Calvo N, Martínez-González M.Á. (2017). ASC Intake is Inversely Associated with Cardiovascular Mortality in a Cohort of Spanish Graduates: The SUN Project. *Nutrients*, 9: 954.
23. Sabri M, Ghaffari G, Hashemipour M, Mostofizadeh N, Koushki AM. (2016). Effect of long-term ASC intake on vascular endothelial function in diabetic children and adolescents: A pilot study. *J Res Med Sci.*, 21: 119.
24. Chan ALF, Leung HWC, Wang SF. (2011). Multivitamin supplement use and risk of breast cancer: A meta-analysis. *Ann Pharmacother.*, 45: 476-84.



25. Larsson SC, Åkesson A, Bergkvist L, Wolk A. (2010). Multivitamin use and breast cancer incidence in a prospective cohort of Swedish women. *Am J Clin Nutr.*, 91: 1268-1272.
26. Wassertheil-Smoller S, McGinn AP, Budrys N, Chlebowski R, Ho GY, Johnson KC, Lane DS, Li W, Neuhouster ML, Saquib J, Shikany JM, Song Y, Thomson C. (2013). Multivitamin and mineral use and breast cancer mortality in older women with invasive breast cancer in the women's health initiative. *Breast Cancer Res Treat.*, 141: 495-505.
27. Lim J, Weinstein SJ, Liao LM, Sinha R, Huang J, Albanes D. (2021). Multivitamin use and overall and site-specific cancer risks in the National Institutes of Health-AARP Diet and Health Study. *J Nutr.*, Published online ahead of print.
28. Macpherson H, Pipingas A, Pase MP. (2013). Multivitamin-multimineral supplementation and mortality: A meta-analysis of randomized controlled trials. *Am J Clin Nutr.*, 97: 437-44.
29. Hercberg S, Galan P, Preziosi P, Bertrais S, Mennen L, Malvy D, Roussel AM, Favier A, Briançon S. (2004). The SU.VI.MAX study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals. *Arch Intern Med.*, 164: 2335-42.
30. Bethan L Richards, Samuel L Whittle, Désirée M Van der Heijde, Rachelle Buchbinder. (2012). The Efficacy and Safety of Muscle Relaxants in Inflammatory Arthritis: A Cochrane Systematic Review. *The Journal of Rheumatology Supple.*, 90: 34-39.
31. Cashin AG, Folly T, Bagg MK, Wewege MA, Jones MD, Ferraro MC, Leake HB, Rizzo RRN, Schabrun SM, Gustin SM, Day R, Williams CM, McAuley JH. (2021). Efficacy, acceptability, and safety of muscle relaxants for adults with non-specific low back pain: systematic review and meta-analysis. *BMJ*, 374: n1446
32. Gregori D, Giacobelli G, Minto C, Barbetta B, Gualtieri F, Azzolina D, Vaghi P, Rovati LC. (2018). Association of Pharmacological Treatments with Long-term Pain Control in Patients With Knee Osteoarthritis A Systematic Review and Meta-analysis. *AMA*, 320(24): 2564–2579.
33. Luis Ceballos-Laita, Elena Estébanez-de-Miguel, Gadea Martín-Nieto, Elena Bueno-Gracia, María Fortún-Agú, Sandra Jiménez-Del-Barrio. (2019). Effects of non-pharmacological conservative treatment on pain, range of motion and physical function in patients with mild to moderate hip osteoarthritis. A systematic review. *Complement Ther Med.*, 42: 214-222.