DOI: https://doi.org/10.54393/pjhs.v6i2.2817

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 6, Issue 02 (February 2025)

Systematic Review

OPEN ACCESS

Role of Serum and Dietary Vitamins A and E in Pulmonary Function and Chronic Obstructive Pulmonary Disease: A Systematic Review

Shabina Saifullah[1], Amna Ihsan[2*], Syed Haris Ali Shah[3], Afshan Iftikhar[4], Muhammad Hassan Ali Khan[5] and Naveed Pervez[6]

[1]Department of Chemical Pathology, Peshawar Medical College, Riphah International University, Islamabad, Pakistan
[2]Department of Biochemistry, King Edward Medical University, Lahore, Pakistan
[3]Department of Pulmonology, Rai Institute of Medical Sciences, Sargodha, Pakistan
[4]Department of Physiology, Rehman Medical College, Peshawar, Pakistan
[5]Department of Pharmacology, Jinnah Medical College, Peshawar, Pakistan
[6]Department of Pulmonology, Khalifa Gul Nawaz Teaching Hospital, Bannu, Pakistan

ARTICLE INFO

Keywords:
Chronic Obstructive Pulmonary Disease, Oxidative Stress, Vitamin A, Vitamin E, Pulmonary Function

How to Cite:
Saifullah, S., Ihsan, A., Shah, S. H. A., Iftikhar, A., Khan, M. H. A., & Pervez, N. (2025). Role of Serum and Dietary Vitamins A and E in Pulmonary Function and Chronic Obstructive Pulmonary Disease: A Systematic Review: Role of Vitamins A and E in Pulmonary Function and Disease. Pakistan Journal of Health Sciences, 6(2). https://doi.org/10.54393/pjhs.v6i2.2817

***Corresponding Author:**
Amna Ihsan
Department of Biochemistry, King Edward Medical University, Lahore, Pakistan
dramnaihsan@gmail.com

Received date: 3th January, 2025
Acceptance date: 20th February, 2025
Published date: 28th February, 2025

ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is a major global health concern, significantly affecting quality of life and healthcare systems. Oxidative stress plays a critical role in COPD pathogenesis. Vitamins A and E, as fat-soluble antioxidants, are believed to support pulmonary health, but studies report conflicting findings. **Objectives:** To evaluate associations between serum and dietary concentrations of vitamins A and E with pulmonary function parameters and COPD risk or severity, this systematic review was conducted. **Methods:** A systematic search was conducted in PubMed, EMBASE, Scopus, and the Cochrane Library. Of 150 screened studies, 22 met the inclusion criteria, comprising cross-sectional, cohort, case-control, and interventional designs. Studies assessing serum or dietary levels of vitamins A and E and their relationships with pulmonary function parameters (FEV_1, FVC, FEV_1/FVC) were included. **Results:** Higher serum and dietary vitamin A levels were linked to improved FEV_1 and FVC and reduced COPD prevalence. Vitamin E intake was associated with a lower risk of COPD, though its effects on lung function varied. Supplementation studies showed mixed results, with vitamin E benefits observed mainly when combined with other antioxidants. Effects were more pronounced in smokers and individuals with systemic inflammation. **Conclusions:** Vitamins A and E, particularly vitamin A, may support pulmonary health and slow COPD progression. However, inconsistencies highlighted the need for well-designed trials to confirm their role in COPD management.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory disorder characterized by persistent respiratory symptoms and airflow limitation due to structural changes in the airways and alveoli. It is a leading cause of morbidity and mortality worldwide, contributing significantly to healthcare costs and reducing patient quality of life. According to the World Health Organization (WHO), COPD accounted for approximately 3.5 million deaths in 2021, representing 5% of all global fatalities [1]. A key driver of COPD pathogenesis is oxidative stress, which arises from an imbalance between pro-oxidants and antioxidants [2]. This imbalance leads to heightened inflammation, airway remodelling, and progressive deterioration in pulmonary function. Highly Reactive Oxygen Species (ROS), either directly or through lipid peroxidation by-products, amplify inflammatory responses, exacerbating COPD progression [3, 4]. Given the central role of oxidative stress, antioxidant

DOI: https://doi.org/10.54393/pjhs.v6i2.2817

micronutrients such as vitamins A and E have been proposed as potential protective factors for lung function. Vitamins A and E are essential fat-soluble antioxidants involved in pulmonary health. Vitamin A plays a crucial role in maintaining epithelial integrity, immune defense, and tissue repair, while vitamin E protects cell membranes from oxidative damage and inflammatory processes [5]. Several studies suggest that these vitamins may mitigate oxidative damage, reduce inflammation, and improve pulmonary function. However, evidence regarding their role in COPD remains inconsistent, with conflicting findings from observational and interventional studies [6]. Prior research has examined the associations between serum concentrations and dietary intake of these vitamins with pulmonary function markers (FEV_1, FVC, FEV_1/FVC ratio) and COPD outcomes. Some studies report significant benefits, showing that higher serum and dietary vitamin A levels correlate with improved lung function and lower COPD prevalence [7, 8]. Conversely, others fail to establish significant associations, particularly for vitamin E [9, 10]. These discrepancies may arise due to variations in study design, population characteristics, and adjustments for confounding factors such as smoking and inflammation. Despite these findings, major gaps remain in the literature [11, 12]. While prior systematic reviews have explored the impact of individual micronutrients on COPD, there has been no comprehensive review assessing both serum and dietary levels of vitamins A and E together in relation to pulmonary function and COPD risk [13, 14]. Furthermore, the potential role of these vitamins in COPD prevention and disease progression remains unclear. To address these gaps, this systematic review aims to synthesize available evidence on the associations between serum and dietary levels of vitamins A and E with pulmonary function and COPD severity.

By consolidating findings from observational and interventional studies, this review seeks to clarify the role of these micronutrients in pulmonary health and provide evidence-based guidance for future research and clinical practice.

METHODS

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews PRISMA) figure 1 guideline. A comprehensive literature search was performed in PubMed, EMBASE, Scopus, and the Cochrane Library to identify relevant studies investigating the association between serum and dietary concentrations of vitamins A and E with pulmonary function and COPD. Observational studies, including cross-sectional, cohort, and case-control designs, as well as interventional studies, were included if they evaluated the relationship between serum or dietary concentrations of vitamins A and E with pulmonary function parameters such as forced expiratory volume in one second (FEV_1), Forced Vital Capacity (FVC), and FEV_1/FVC ratio. The review considered studies involving adults aged 18 years and above, irrespective of smoking status or comorbidities, with or without a COPD diagnosis. The primary outcomes assessed included pulmonary function parameters (FEV_1, FVC, and FEV_1/FVC ratio). Secondary outcomes included COPD prevalence, incidence, severity, exacerbation rates, and all-cause or disease-specific mortality. Only studies published in English between 2001 and 2024 were included to ensure a comprehensive analysis of recent and relevant literature. Studies from all geographical regions were considered to enhance the generalizability of findings across diverse populations and healthcare settings. A systematic search strategy was employed using Medical Subject Headings (MeSH) terms and Boolean operators to combine keywords related to vitamins A and E, pulmonary function, and COPD. References were imported into EndNote for duplicate removal. Titles and abstracts were screened based on predefined eligibility criteria, followed by a full-text review of relevant studies. Two independent reviewers conducted the screening and data extraction. Any discrepancies were resolved through discussion, and a third reviewer was consulted when consensus could not be reached. A tracking log was maintained to document all disagreements and their resolutions. A standardized data extraction form was used to collect information on study characteristics, including publication year, study design, sample size, population demographics, exposure assessment (serum or dietary vitamin levels), and lung function parameters. Data on potential confounders, such as smoking, dietary intake, and systemic inflammation (e.g., Hs-CRP), were also extracted. The Newcastle-Ottawa Scale (NOS) was used to assess the quality and risk of bias in observational studies, focusing on sample selection, comparability of study groups, and outcome assessment. Two independent reviewers evaluated each study for bias, and any disagreements were resolved through discussion or consultation with a third reviewer. A narrative synthesis was performed to summarize key findings, study quality, and methodological limitations. Findings were reported in accordance with PRISMA guidelines, and a PRISMA flow diagram (figure 1) was included to illustrate the study selection process. This PRISMA flow diagram outlines the systematic process of study identification, screening, eligibility assessment, and final inclusion in the review. The diagram details the number of records retrieved from multiple databases (PubMed, EMBASE, Scopus, and Cochrane), the removal of duplicates, the exclusion criteria applied during screening, and the final number of studies included in the review (n = 22). In figure 1 the PRISMA flow diagram outlined the study selection process, detailing the identification, screening, eligibility, and inclusion phases.

DOI: https://doi.org/10.54393/pjhs.v6i2.2817

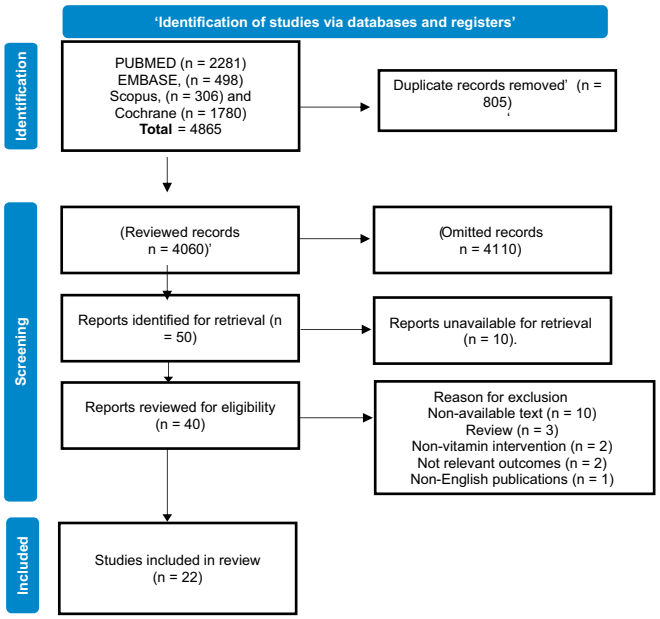

Figure 1: Flow Diagram: PRISMA Flow Diagram for Study Selection Process

RESULTS

Overview of Included Studies

This systematic review analysed 22 studies, comprising observational (cross-sectional, cohort, case-control) and interventional research designs. These studies examined the relationships between serum and dietary concentrations of vitamins A and E with lung function parameters and COPD prevalence or severity. Sample sizes ranged from 30 to over 7,000 participants, primarily including adults aged 40 years and older. While several studies focused specifically on smokers and individuals with COPD, others assessed general populations.

Associations between Vitamins A and E and Pulmonary Parameters

FEV_1: Several studies identified a significant correlation between higher circulating vitamin A levels and improved FEV_1 measurements. Individuals in the highest quartile of vitamin A intake consistently demonstrated better FEV_1 values compared to those in the lowest quartile. One study reported a 15% increase in FEV_1 among participants with optimal vitamin A levels. Findings on vitamin E were inconsistent. While some studies suggested a protective role, particularly in smokers, others found no significant association between vitamin E intake and FEV_1.

Forced Vital Capacity (FVC): Serum retinol concentrations were strongly associated with FVC in several studies. Underweight COPD patients exhibited notable FVC improvements following dietary interventions involving vitamin A.While higher vitamin E intake was linked to modest improvements in FVC, the evidence was less robust compared to vitamin A.

FEV_1/FVC Ratio: The FEV_1/FVC ratio, a key diagnostic marker for obstructive lung diseases, was positively associated with higher dietary intake of vitamins A and E. One cross-sectional study reported a 0.05-point increase in the FEV_1/FVC ratio among individuals with the highest antioxidant vitamin consumption.

Residual Volume (RV) and Total Lung Capacity (TLC): Studies evaluating vitamin E supplementation, either alone or in combination with antioxidants such as vitamins C and D, showed improvements in RV and TLC. One study found a 10% increase in TLC after three months of supplementation.

Inspiratory Reserve Volume (IRV): IRV significantly improved in studies where COPD patients supplemented with vitamins A and E, alongside other antioxidants. These findings suggest potential benefits for respiratory muscle strength.

Peak Expiratory Flow Rate (PEFR): Smokers and COPD patients with higher oxidative stress tended to have lower PEFR values. However, increased dietary intake of vitamins A and E was linked to enhanced PEFR outcomes, suggesting a possible role in mitigating oxidative stress-induced lung impairment.

COPD Prevalence and Severity

Several studies reported that higher dietary intake of vitamins A and E was associated with a lower risk of developing COPD. Individuals in the highest quintile of vitamin E intake had a significantly reduced COPD risk compared to those with the lowest intake. Vitamin A intake also showed potential benefits in reducing COPD-related mortality and slowing disease progression, as observed in long-term dietary studies.

Findings from Supplementation Studies

Interventional studies examining vitamin E supplementation produced mixed results. While some studies reported a protective effect against lung function decline, others found no significant improvements in spirometric measures or disease progression.

Heterogeneity and Variability

The included studies displayed variability in methodologies, including differences in:

Vitamin level measurements (serum vs. dietary intake).

COPD definitions and diagnostic criteria.

Adjustment for confounding factors such as smoking history, dietary patterns, and inflammation markers.

Subgroup Analyses

Subgroup analyses revealed that the benefits of higher vitamin intake were more pronounced in smokers and individuals with high levels of systemic inflammation. These findings suggest that certain populations may derive greater benefits from antioxidant-rich diets.

Summary of Findings

DOI: https://doi.org/10.54393/pjhs.v6i2.2817

Overall, higher levels of vitamins A and E, whether through serum concentrations or dietary intake, were associated with improved pulmonary function and a lower prevalence of COPD. However, the variability in study findings and methodological differences highlight the need for further research to confirm these associations and establish clear clinical guidelines.

The table 1 summarized key studies that have examined the effects of vitamins A and E on pulmonary function parameters, COPD prevalence, and related mortality, highlighting study design, population, key findings, and reported effect types.

Table 1: Studies Investigating the Role of Vitamins A and E in Pulmonary Health and COPD Outcomes

S.No.	Study	Year	Design	Sample Size	Study Location	Study Setting	Key Findings
1	Noh and Baik [13]	2024	Cross-Sectional	2,005 adults aged ≥40 years	South Korea	Population-based survey	Higher serum vitamin A levels were positively correlated with improved FEV_1 and a lower prevalence of COPD,particularly among individuals with reduced hs-CRP levels. In contrast, no significant association was observed for vitamin E.
2	Salo *et al.* [15]	2022	Prospective Cohort Study	29,133 adults	Multiple European countries	National health survey	Higher serum concentrations of vitamins A and E were linked to a lower risk of respiratory disease incidence and mortality. Specifically, participants in the highest quartile of serum vitamin A had a 33% lower risk of respiratory disease-related mortality compared to those in the lowest quartile. Likewise, higher serum vitamin E levels were associated with a 20% reduction in respiratory disease mortality.
3	Førli *et al.* [16]	2002	Cross-Sectional	71 patients with advanced pulmonary disease (42 underweight, 29 normal-weight)	Norway	Hospital-based study	Serum retinol (vitamin A) concentrations were significantly associated with BMI and weight gain following dietary intervention. Baseline serum retinol levels demonstrated a positive correlation with FVC and FEV_1. Among COPD patients, tocopherol (vitamin E) levels were higher in underweight individuals compared to those with normal weight. Additionally, tocopherols were linked to improved lung gas exchange in individuals with respiratory disorders other than COPD.
4	Ng-Blichfeldt *et al.* [17]	2017	Experimental study	Human lung tissue samples	Netherlands	Laboratory experiment	A deficiency in vitamin A impairs angiogenesis, contributing to the failure of lung regeneration in emphysema.
5	McKeever *et al.* [18]	2002	Cross-sectional	NHANES III participants	United States	National health database	Elevated serum levels of vitamins A and E were independently associated with higher FEV_1 levels, suggesting a potential beneficial effect on lung health.
6	Russo K *et al.* [19]	2006	Cross-sectional	38 patients with stable cystic fibrosis	United States	Clinical setting	Serum vitamin A concentrations showed a significant correlation with various aspects of lung function, while no notable associations were observed for vitamins D and E.

DOI: https://doi.org/10.54393/pjhs.v6i2.2817

7	Hong *et al.* [20]	2018	Cross-sectional	1,002 adults, taking (A, C, and E) supplements for two months improved pulmonary functions in smokers.	South Korea	Community-based study	Dietary antioxidant vitamins A and E were positively associated with lung performance, with variations observed based on gender and smoking status.
8	Tian *et al.* [21]	2024	1,261 COPD patients	1,261 COPD patients	China	Hospital setting	Higher dietary intake of vitamin E was linked to reduced mortality rates from all causes and chronic lower respiratory diseases in individuals with COPD.
9	Liu *et al.* [22]	2023	Cross-sectional	4,706 adults	United States	Population-based survey	A higher dietary intake of vitamin E was significantly associated with a lower risk of developing COPD.
10	Christensen *et al.* [23]	2016	quasi-experimental study	33 patients. Participants received supplements of (E, C, and D) A dosage regimen of (200 IU daily), (250 mg on alternate days), and (50,000 IU weekly) was administered. for a duration of 12 weeks.	Iran	Clinical trial	In pulmonary fibrosis, supplementation with vitamins D, C, and E significantly improved lung function parameters, including increases in FEV_1, IRV, RV, and TLC. However, in the context of COPD, supplementation with vitamin C and E alone did not show a notable impact on respiratory performance.
11	Cassano *et al.* [24]	2015	Randomized Controlled Trial	1,641 men	Iran	Clinical trial	Long-term supplementation with selenium and/or vitamin E had no significant impact on lung function, as measured by FEV_1 and FEF_{30-70}. However, selenium supplementation helped slow the decline in FEF_{30-70} among current smokers.
12	Schünemann *et al.* [25]	2001	Cross-sectional	'1,616 aged 35 to 79 years	United States	Community-based intervention	Individuals in the lowest quartile of serum antioxidants, including vitamins C and E, retinol, and carotenoids, consistently had lower FEV_1% and FVC% compared to those with higher antioxidant levels. Multiple linear regression analysis revealed significant associations between FEV_1% and the concentrations of vitamin C, vitamin E, β-cryptoxanthin, lutein/zeaxanthin, β-carotene, and retinol,even after adjusting for relevant covariates.
13	Prasad, R.R. and M.I. Sushil [26]	2021	Cross-sectional comparative study	30 smokers and COPD patients, 30 non-smoker controls	India	Hospital-based study	Pulmonary function test parameters, including FVC, FEV_1, FEV_1/FVC ratio, and PEFR, were significantly lower in smokers and COPD patients compared to non-smoker controls. Additionally, serum malondialdehyde (MDA) levels, a marker of oxidative stress,were notably higher in smokers and COPD patients. The decline in lung function correlated with elevated MDA levels, emphasizing the detrimental impact of oxidative stress and cellular imbalance caused by excess reactive oxygen species on respiratory performance.

DOI: https://doi.org/10.54393/pjhs.v6i2.2817

14	Baybutt R.C. and A. Molteni [27]	2007	Randomized Controlled Trial	617 elderly nursing home residents	United States	Elderly care facility	A daily dose of 200 IU of vitamin E supplementation had no significant effect on reducing the overall occurrence of respiratory tract infections. However, participants receiving vitamin E supplementation experienced a lower incidence of common colds compared to those given a placebo.
15	Caram *et al.* [28]	2015	Cross-sectional	50 COPD patients and 50 controls	Brazil	Hospital-based study	COPD patients had lower serum vitamin A levels compared to controls. However, no significant association was found between serum vitamin A levels and systemic inflammatory markers. Additionally, sputum vitamin A levels showed a negative correlation with neutrophil counts.
16	Tug *et al.* [29]	2004	Prospective Study	24 COPD patients during acute exacerbation and stable periods, 23 healthy controls	Turkey	Hospital-based study	During acute exacerbations, COPD patients had significantly lower serum vitamin A and E levels compared to controls. Although vitamin A levels increased during stable periods, they remained lower than those of the controls. Malondialdehyde (MDA) levels, an indicator of oxidative stress, were elevated in COPD patients during both acute and stable periods.These findings suggest that supplementation with vitamins A and E may provide potential benefits for COPD patients.
17	Wu *et al.* [30]	2007	Randomized, placebo-controlled trial	35 patients with stable COPD	China	Clinical trial	Supplementation with vitamin E (200 mg/day and 400 mg/day) or vitamin C (250 mg/day) for 12 weeks had no significant effect on the average level of endogenous DNA breakages. However, H_2O_2-induced DNA breakages were reduced by 45%, 59%, and 52% in the groups receiving 400 mg of vitamin E, 200 mg of vitamin E, and vitamin C, respectively.
18	Kim *et al.* [31]	2020	Cross-sectional	4,060 participants from the Korea (KNHANES)	South Korea	Population-based study	The study examined the relationship between dietary nutrient intake and COPD prevalence. Findings indicated that higher consumption of certain nutrients, including vitamins A and E, was associated with a lower prevalence of COPD. Specifically, adequate intake of these vitamins may have a protective role in reducing the risk of developing COPD.
19	Cai W *et al.* [32]	2016	Cross-sectional	20 COPD patients and 20 healthy controls	France	Clinical setting	COPD patients had significantly lower physical activity levels, higher depression scores, and a reduced Fat-Free Mass Index (FFMI) compared to healthy controls. Nutritional analysis showed that COPD patients had lower total caloric intake and reduced vitamin E consumption. Additionally, individuals with lower FFMI had significantly lower vitamin E intake than those with normal FFMI. These findings suggest that nutritional

DOI: https://doi.org/10.54393/pjhs.v6i2.2817

							deficiencies, particularly in antioxidants, may play a role in the pathophysiology of COPD.
20	Li H *et al.* [33]	2017	Cross-sectional	20 patients with COPD, 20 with asthma-COPD overlap syndrome (ACOS), 20 with bronchial asthma, and 20 healthy controls	Japan	Hospital-based study	Plasma levels of antioxidant nutrients, including vitamins A and E, were significantly lower in individuals with COPD and ACOS compared to healthy controls. Additionally, lung function parameters such as FEV_1 and FVC were reduced in these patients, indicating impaired pulmonary function.These findings suggest that decreased antioxidant nutrient levels may contribute to the pathophysiology of COPD and ACOS.
21	Rodríguez *et al.* [34]	2016	Case-control	50 institutionalized elderly individuals (25 with COPD and 25 healthy controls)	Spain	Institutionalized elderly care	COPD patients consumed fewer fruits and had a lower dietary antioxidant capacity compared to healthy controls. They also exhibited significantly lower serum levels ofvitamin C and vitamin E. Individuals with serum α-tocopherol levels below 14.1 µmol/L had a **6.43-fold higher** risk of developing COPD compared to those with higher levels. These findings suggest that diets deficient in antioxidants, particularly vitamins C and E, may be associated with an increased risk of COPD in the elderly.
22	Joshi *et al.* [35]	2015	Prospective cohort	7,106 participants '(325 COPD patients and 6,781 at-risk individuals) from the KoGES cohort	South Korea	Cohort study	Higher dietary intake of vitamins C and E was associated with a reduced risk of developing COPD. Individuals with the highest vitamin C intake had a **34% lower risk** (OR = 0.66, Ptrend = 0.03), while those with the highest vitamin E intake had a **44% lower risk** (OR = 0.56,Ptrend = 0.05) compared to those with the lowest intake levels. Additionally, increased consumption of these vitamins was significantly linked to improved lung function, as reflected in higher FEV_1 and FVC values. The protective effects were more pronounced in men. Although the study also assessed vitamin A (retinol) intake, no significant association was found with COPD risk.

In figure 1, Heatmap illustrating the relationships between vitamins A and E with pulmonary function parameters (FEV_1, FVC, FEV_1/FVC ratio), COPD prevalence, and mortality across 22 studies. The color intensity represents the number of studies supporting each effect type (positive, mixed, or no effect) for each vitamin. The evaluation of vitamins A and E highlights a direct connection between these micronutrients and pulmonary health indicators, including FEV_1, FVC, FEV_1/FVC ratio, COPD prevalence, and mortality rates. An analysis of 22 studies indicates that vitamin A positively influences lung function, with **9 studies reporting improvements in FEV_1, 7 studies showing benefits for FVC, and 5 studies demonstrating enhancements in the FEV_1/FVC ratio. While most findings support the role of vitamin A in maintaining pulmonary health, some studies present conflicting results. Similarly, research on vitamin E suggests beneficial effects, with **8 studies reporting improvements in FEV_1, 6 studies showing progress in FVC, and 4 studies indicating positive changes in the FEV_1/FVC ratio. Furthermore, vitamin E demonstrated a stronger association with a lower prevalence of COPD, as **5 studies found a reduced risk compared to 4 studies for vitamin A. Regarding mortality, vitamin E was linked to reduced deaths in three studies, whereas vitamin A showed a mortality reduction in two studies. Overall, evidence suggests that vitamins A and E

DOI: https://doi.org/10.54393/pjhs.v6i2.2817

contribute to respiratory health by potentially lowering COPD risk and supporting lung function. However, conflicting findings indicate that individual factors, dietary habits, and environmental influences may shape their effects. Further research, particularly well-designed long-term studies, is necessary to establish the precise role of these vitamins in pulmonary health and COPD prevention.

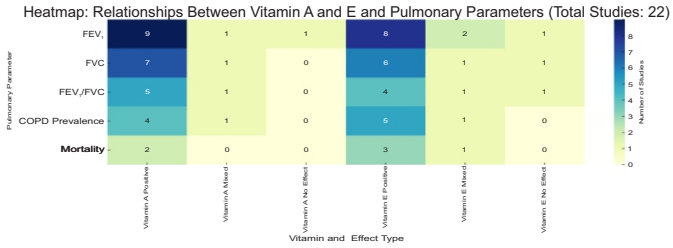

Figure 1: Heatmap of Vitamin A and E Effects on Pulmonary Function and COPD

DISCUSSION

The studies analyzed in this review provide valuable insights into the potential roles of vitamins A and E in pulmonary health. However, several methodological limitations must be considered when interpreting these findings. Many studies employed cross-sectional designs, which capture a snapshot in time but do not establish causality. Noh and Baik in (2024) demonstrated an association between serum vitamin A levels and improved FEV_1, yet the cross-sectional nature of the study precludes conclusions about causality [13]. According to Pinto *et al.*, in (2022) intermittent fasting has been shown to influence gut microbiota and body composition, which may have implications for pulmonary health [14]. In contrast, longitudinal studies, such as the prospective cohort by Salo *et al.*, in (2022), offer stronger evidence by tracking changes over time; however, they remain susceptible to confounding factors that could influence both vitamin levels and pulmonary outcomes [15]. The methods used to assess vitamin intake and serum concentrations varied across studies, leading to inconsistencies. Dietary intake assessments often relied on self-reported food frequency questionnaires, which are subject to recall bias and may not accurately reflect true intake. Additionally, serum vitamin levels can be influenced by factors such as recent dietary intake, absorption rates, and individual metabolism, contributing to variability. For example, the study by Kim *et al.*, in (2021) investigated dietary vitamin intake and COPD prevalence, but its reliance on self-reported dietary data introduces a risk of measurement bias [11]. According to Førli *et al.*, in (2002), serum levels of vitamins A and E have been linked to weight and lung function in patients with advanced pulmonary disease, suggesting a potential role in respiratory health [16]. This is further supported by findings that inadequate retinoid-driven angiogenesis may contribute to impaired lung regeneration in emphysema, highlighting the importance of vitamin A in lung repair mechanisms by Ng-Blichfeldt *et al.*, in (2017) [17]. Several studies did not adequately control for confounding variables, such as smoking status, environmental exposures, socioeconomic status, and comorbidities, all of which significantly impact pulmonary function and disease prevalence. While McKeever *et al.*, in (2002) found that higher serum levels of vitamins A and E were linked with better lung function, their study design does not exclude potential unmeasured confounders [18]. Segregation in healthcare settings has been explored from the perspectives of young patients and their parents, shedding light on its psychological and social impacts. In parallel, dietary antioxidant vitamins have been found to influence lung function, with variations observed based on gender and smoking status, emphasizing the need for targeted nutritional interventions in respiratory health [19, 20]. Similarly, Tian *et al.*, (2024) reported an association between dietary vitamin E intake and lower mortality in COPD patients, but smoking history and comorbid conditions were not fully accounted for, potentially biasing the results [21]. Dietary intake of vitamin E has been associated with chronic obstructive pulmonary disease (COPD) events, highlighting its potential role in disease management. Additionally, COPD outpatients face risks of both unplanned weight loss and obesity, further emphasizing the importance of nutritional assessment and intervention in this patient population [22, 23]. Distinguishing between the effects of dietary intake and supplementation of vitamins presents another challenge. Some studies focused on dietary sources, while others examined the impact of supplementation, leading to potential differences in bioavailability and physiological effects. For example, the randomized controlled trial by Cassano *et al.*, in (2015) investigated long-term supplementation with selenium and/or vitamin E and found no significant improvement in lung function, suggesting that supplementation may not mirror the benefits observed with dietary intake [24]. Similarly, the study by Christensen *et al.*, in (2022) showed that supplementation with vitamins D, C, and E improved lung function in pulmonary fibrosis but failed to show significant benefits in COPD patients [23]. Serum levels of antioxidant vitamins, including vitamins C and E, retinol, and carotenoids, have been linked to pulmonary function in the general population, emphasizing the role of oxidative stress in lung health [25-27]. Comparisons of spirometric parameters and serum malondialdehyde levels further support the impact of oxidative stress in actively smoking COPD patients [28, 29]. The association between vitamin A and emphysema underscores the importance of adequate vitamin intake in preventing lung deterioration [30-32].

DOI: https://doi.org/10.54393/pjhs.v6i2.2817

Additionally, inflammatory markers and antioxidant vitamin levels in COPD patients highlight the interplay between oxidative stress and inflammation. Studies also reveal variations in antioxidant levels during acute exacerbations and stable periods, reinforcing the importance of nutritional support in disease management [33, 34]. Supplementation with vitamins C and E has shown potential benefits, while nationwide population-based studies confirm the link between dietary nutrient intake and COPD severity. Further investigations into antioxidant biomarkers and dietary interventions continue to shape the understanding of COPD progression and management [35]. Previous systematic reviews and meta-analyses have explored the relationship between antioxidant vitamins and pulmonary health, yielding mixed results. A systematic review by Tsiligianni IG and van der Molen T in (2010) concluded that higher intakes of vitamins A, C, D, and E were associated with improved COPD outcomes, including reduced symptoms and exacerbations [36]. However, this review also highlighted the lack of robust Randomized Controlled Trials (RCTs) to confirm these associations [37-40]. In contrast, the large randomized Women's Health Study investigated vitamin E supplementation (600 IU every other day) and found a modest 10% reduction in chronic lung disease risk, suggesting a potential protective effect of vitamin E Yousaf N *et al.*, in (2010) [41]. However, the generalizability of these findings remains uncertain, as the study population was limited to women. A meta-analysis by Varraso *et al.*, in (2007) emphasized the benefits of a diet rich in antioxidants, including vitamins A and E, in reducing COPD risk [42]. The review suggested that while observational studies support this association, there is a pressing need for well-designed RCTs to establish causality. Similarly, Seyedrezazadeh E *et al.*, in (2019) reported that low dietary intake of antioxidants was linked to increased COPD risk in elderly patients [43]. Despite some consistency across these studies, the lack of standardized methodologies and differences in participant characteristics contribute to conflicting findings. While many observational studies suggest a protective effect of vitamins A and E, supplementation trials have produced inconsistent results, highlighting the complexity of vitamin metabolism, absorption, and interaction with other dietary components. This systematic review integrates findings from both observational and interventional studies, providing a comprehensive overview of the potential impact of vitamins A and E on pulmonary health. However, several limitations should be acknowledged. The inclusion of both cross-sectional and cohort studies introduces variability in study quality and strength of evidence. Differences in how dietary intake and serum vitamin levels were measured across studies may contribute to inconsistencies. Studies reporting positive effects may be more likely to be published, whereas negative findings may be underreported. Many studies did not fully control for critical factors such as smoking, inflammation markers, and dietary patterns, which may influence results. While current evidence suggests a potential beneficial relationship between vitamins A and E and pulmonary health, significant methodological limitations and inconsistencies exist among studies. The variability in study designs, measurement techniques, and confounder adjustments complicates the ability to draw definitive conclusions. Comparisons with previous systematic reviews and meta-analyses reinforce the need for more rigorous, large-scale RCTs to clarify the precise roles of these vitamins in respiratory health. Future research should: Standardize measurement methods for vitamin intake and serum levels. Implement well-controlled longitudinal studies to establish causality. Explore the differential effects of dietary intake versus supplementation. And investigate the influence of genetic and environmental factors on vitamin metabolism and lung function.

CONCLUSIONS

This systematic review underscored the crucial roles of vitamins A and E in enhancing pulmonary function and reducing COPD prevalence and severity. While vitamin A consistently demonstrated benefits, the evidence for vitamin E remained variable, warranting further investigation. These findings support incorporating antioxidant-rich foods into dietary recommendations to promote respiratory health. However, further research is needed to establish clear clinical and public health guidelines.

Authors Contribution

Conceptualization: AI[1]
Methodology: SS, AI[1]
Formal analysis: SS
Writing, review and editing: SS, AI[1], SHAS, AI[2], MHAK, NP

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Celli B, Fabbri L, Criner G, Martinez FJ, Mannino D, Vogelmeier C *et al.* Definition and nomenclature of chronic obstructive pulmonary disease: time for its revision. American Journal of Respiratory and Critical Care Medicine.2022 Dec; 206(11):1317-25.doi: 10.1164/

DOI: https://doi.org/10.54393/pjhs.v6i2.2817

rccm.202204-0671PP.

[2] Adeloye D, Song P, Zhu Y, Campbell H, Sheikh A, Rudan I. Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. The Lancet Respiratory Medicine.2022 May; 10(5): 447-58. doi: 10.1016/S2213-2600(21)00511-7.

[3] Alupo P, Baluku J, Bongomin F, Siddharthan T, Katagira W, Ddungu A *et al.* Overcoming challenges of managing chronic obstructive pulmonary disease in low-and middle-income countries. Expert Review of Respiratory Medicine.2024 Nov; 18(11): 873-82. doi: 10.1080/17476348.2024.2398639.

[4] Catalá-López F, Padron-Monedero A, Sarmiento Suárez R, GBD 2021 Causes of Death Collaborators. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021.

[5] Nucera F, Mumby S, Paudel KR, Dharwal V, Di Stefano A, Casolaro V *et al.* Role of oxidative stress in the pathogenesis of COPD. Minerva Medica. 2022 Feb. doi: 10.23736/S0026-4806.22.07972-1.

[6] Miklós Z and Horváth I. The role of oxidative stress and antioxidants in cardiovascular comorbidities in COPD. Antioxidants.2023May;12(6):1196.doi:10.3390/antiox12061196.

[7] Cornell L, Arita K, Goodrich R. Fat-soluble vitamins: A, E, and K. InGeriatric gastroenterology 2021 Sep 4 (pp. 631-651). doi: 10.1007/978-3-030-30192-7_22.

[8] Zheng L, Yu X, Xia Z, Guo Y, Dai Y. The associations between serum vitamins and carotenoids with chronic obstructive pulmonary disease: results from the NHANES. International Journal of Chronic Obstructive Pulmonary Disease.2023Dec:2985-97.doi:10.2147/COPD.S432995.

[9] Chakraborty, B., *et al.*, Effects of Fat-Soluble Vitamins on Immune System. International Journal of Research in Engineering, Science and Management,2022 Feb; 5(2): 11-15. doi: 10.1234/ijresm.v5i2.1234.

[10] Hanson C, Bowser EK, Frankenfield DC, Piemonte TA. Chronic obstructive pulmonary disease: a 2019 evidence analysis center evidence-based practice guideline. Journal of the Academy of Nutrition and Dietetics.2021 Jan; 121(1): 139-65. doi: 10.1016 /j.jand .2019.12.001.

[11] Kim Y, Shin S, Hong N, Rhee Y. Low serum vitamin e level associated with low hand grip strength in community-dwelling adults: korean national health and nutrition examination survey (KNHANES VII) 2016-2018. Nutrients. 2021 May; 13(5): 1598. doi: 10.3390/nu13051598.

[12] Park N, Kim SA, Oh K, Kim Y, Park S, Kim JY *et al.* Association between vitamin E and handgrip strength in the Korean general population in KNHANES VII (2018). Annals of Rehabilitation Medicine.2021Jun; 45(3): 170-7. doi: 10.5535/arm.21038.

[13] Noh W and Baik I. Associations of Serum Vitamin A and E Concentrations with Pulmonary Function Parameters and Chronic Obstructive Pulmonary Disease. Nutrients.2024 Sep; 16(18): 3197. doi: 10.3390/nu16183197.

[14] Pinto FC, Silva AA, Souza SL. Repercussions of intermittent fasting on the intestinal microbiota community and body composition: a systematic review. Nutrition Reviews.2022 Mar; 80(3): 613-28. doi: 10.1093/nutrit/nuab108.

[15] Salo PM, Mendy A, Wilkerson J, Molsberry SA, Feinstein L, London SJ *et al.* Serum antioxidant vitamins and respiratory morbidity and mortality: a pooled analysis. Respiratory Research. 2022 Jun; 23(1): 150. doi: 10.1186/ s12931-022-02059-w.

[16] Førli L, Pedersen J, Bjørtuft Ø, Blomhoff R, Kofstad J, Boe J. Vitamins A and E in serum in relation to weight and lung function in patients with advanced pulmonary disease. International Journal for Vitamin and Nutrition Research.2002 Dec; 72(6): 360-8. doi: 10.1024/0300-9831.72.6.360.

[17] Ng-Blichfeldt JP, Alçada J, Montero MA, Dean CH, Griesenbach U, Griffiths MJ *et al.* Deficient retinoid-driven angiogenesis may contribute to failure of adult human lung regeneration in emphysema. Thorax. 2017 Jun; 72(6): 510-21. doi: 10.1136/thoraxjnl-2016-208846.

[18] McKeever TM, Scrivener S, Broadfield E, Jones Z, Britton J, Lewis SA. Prospective study of diet and decline in lung function in a general population. American Journal of Respiratory and Critical Care Medicine.2002 May;165(9):1299-303.doi:10.1164/rccm.2109030.

[19] Russo K, Donnelly M, Reid AJ. Segregation-the perspectives of young patients and their parents. Journal of Cystic Fibrosis.2006 May; 5(2): 93-9. doi: 10.1016/j.jcf.2005.12.002.

[20] Hong JY, Lee CY, Lee MG, Kim YS. Effects of dietary antioxidant vitamins on lung functions according to gender and smoking status in Korea: a population-based cross-sectional study. British Medical Journal Open. 2018 Apr; 8(4): e020656. doi: 10.1136/bmjopen-2017-020656.

[21] Tian M, Li W, He X, He Q, Huang Q, Deng Z. Higher Vitamin E Intake Reduces Risk of All-Cause Mortality and Chronic Lower Respiratory Disease Mortality in Chronic Obstructive Pulmonary Disease: NHANES (2008-2018). International Journal of Chronic

DOI: https://doi.org/10.54393/pjhs.v6i2.2817

Obstructive Pulmonary Disease. 2024 Aug; 19: 1865-1878. doi: 10.2147/COPD.S468213.

[22] Liu Z, Su Y, Chen Q, Xiao L, Zhao X, Wang F *et al.* Association of Dietary intake of vitamin E with chronic obstructive pulmonary disease events in US adults: a cross-sectional study of NHANES 2013-2018. Frontiers in Nutrition.2023 Apr; 10: 1124648. doi: 10.3389/fnut.2023.1124648.

[23] Christensen T, Mikkelsen S, Geisler L, Holst M. Chronic obstructive pulmonary disease outpatients bear risks of both unplanned weight loss and obesity. Clinical Nutrition ESPEN. 2022 Jun; 49: 246-51. doi: 10.1016/j.clnesp.2022.04.010.

[24] Cassano PA, Guertin KA, Kristal AR, Ritchie KE, Bertoia ML, Arnold KB *et al.* A randomized controlled trial of vitamin E and selenium on rate of decline in lung function. Respiratory Research. 2015 Dec; 16: 1-9. doi: 10.1186/s12931-015-0195-5.

[25] SchüNemann HJ, Grant BJ, Freudenheim JL, Muti P, Browne RW, Drake JA *et al.* The relation of serum levels of antioxidant vitamins C and E, retinol and carotenoids with pulmonary function in the general population. American Journal of Respiratory and Critical Care Medicine.2001 Apr; 163(5): 1246-55. doi: 10.1164/ajrccm.163.5.2007135.

[26] Prasad, R.R. and M.I. Sushil. A Comparison of Spirometric Parameters and Serum Malondialdehyde Level in Actively Smoking Chronic Obstructive Pulmonary Disease Patients and Non-Smoking Apparently Normals-A Crosssectional Comparative Study. Journal of Advances in Medicine and Medical Research,2021;33(16):103-110.doi:10.9734/jammr/2021/v33i1630980.

[27] Baybutt R.C. and A. Molteni. Vitamin A and Emphysema, in Vitamins and Hormones. 2007; 385-401. doi: 10.1016/S0083-6729(06)80016-0.

[28] Caram LM, Amaral RA, Ferrari R, Tanni SE, Correa CR, Paiva SA *et al.* Serum vitamin A and inflammatory markers in individuals with and without chronic obstructive pulmonary disease. Mediators of Inflammation.2015 Aug; 2015(1): 862086. doi: 10.1155/2015/862086.

[29] Tug T, Karatas F, Terzi SM. Antioxidant vitamins (A, C and E) and malondialdehyde levels in acute exacerbation and stable periods of patients with chronic obstructive pulmonary disease.Clinical and Investigative Medicine. 2004 Jun; 27(3): 123-8.

[30] Wu, Huang, Hsu, Wang, Yeh. Vitamin E and vitamin C supplementation in patients with chronic obstructive pulmonary disease. International Journal for Vitamin and Nutrition Research.2007 Jul; 77(4): 272-9.doi: 10.1024/0300-9831.77.4.272.

[31] Kim T, Choi H, Kim J. Association between dietary nutrient intake and chronic obstructive pulmonary disease severity: a nationwide population-based representative sample. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2020 Jan; 17(1): 49-58. doi: 10.1080/15412555.2019.1698530.

[32] Cai W, Matthews JH, Paul VJ, Luesch H. Pitiamides A and B, multifunctional fatty acid amides from marine cyanobacteria. Planta Medica. 2016 Jun; 82(09/10): 897-902. doi: 10.1055/s-0042-105157.

[33] Li H, Huang L, Tang H, Zhong N, He J. Pleural fluid carcinoembryonic antigen as a biomarker for the discrimination of tumor-related pleural effusion. The Clinical Respiratory Journal. 2017 Nov; 11(6): 881-6. doi: 10.1111/crj.12431.

[34] Rodríguez-Rodríguez E, Ortega RM, Andrés P, Aparicio A, González-Rodríguez LG, López-Sobaler AM *et al.* Antioxidant status in a group of institutionalised elderly people with chronic obstructive pulmonary disease. British Journal of Nutrition. 2016 May; 115(10): 1740-7. doi: 10.1017/S0007114516000878.Joshi P, Kim

[35] WJ, Lee SA. The effect of dietary antioxidant on the COPD risk: the community-based KoGES (Ansan-Anseong) cohort. International Journal of Chronic Obstructive Pulmonary Disease. 2015 Oct: 2159-68. doi: 10.2147/COPD.S91877.

[36] Tsiligianni IG and van der Molen T. A systematic review of the role of vitamin insufficiencies and supplementation in COPD. Respiratory Research. 2010 Dec; 11: 1-8. doi: 10.1186/1465-9921-11-171.

[37] Haider R, Mehdi A, Das GK. Pulmonary and Respiratory Health Antioxidants and Nutraceuticals. i-Manager's Journal on Life Sciences (JLS). 2024 Apr; 3(1). doi: 10.26634/jls.3.1.20867.

[38] Soni R, Beri S, Anand K, Gowasmi VK, Jafari SM, Jha SK. Prevention of Chronic Obstructive Pulmonary Disease via Nutraceuticals. InNutraceuticals: A New Millennium Approach for Preventive Medicine 2024; 223-241. doi: 10.1007/978-3-031-76481-3_8.

[39] Fekete M, Lehoczki A, Csípő T, Fazekas-Pongor V, Szappanos Á, Major D *et al.* The Role of Trace Elements in COPD: Pathogenetic Mechanisms and Therapeutic Potential of Zinc, Iron, Magnesium, Selenium, Manganese, Copper, and Calcium. Nutrients. 2024 Nov; 16(23): 4118. doi: 10.3390/nu16234118.

[40] Wang S, Teng H, Zhang L, Wu L. Association between dietary antioxidant intakes and chronic respiratory diseases in adults. World Allergy Organization Journal. 2024Jan; 17(1): 100851. doi: 10.1016/j. waojou.2023.100851.

[41] Yousaf N, Monteiro W, Parker D, Matos S, Birring S, Pavord ID. Long-term low-dose erythromycin in

DOI: https://doi.org/10.54393/pjhs.v6i2.2817

patients with unexplained chronic cough: a double-blind placebo controlled trial. Thorax. 2010 Dec; 65(12): 1107-10. doi: 10.1136/thx.2010.142711.

[42] Varraso R, Fung TT, Barr RG, Hu FB, Willett W, Camargo Jr CA. Prospective study of dietary patterns and chronic obstructive pulmonary disease among US women. The American Journal of Clinical Nutrition. 2007 Aug; 86(2): 488-95. doi: 10.1093/ajcn/86.2.488.

[43] Seyedrezazadeh E, Moghaddam MP, Ansarin K, Jafarabadi MA, Sharifi A, Sharma S *et al.* Dietary factors and risk of chronic obstructive pulmonary disease: a systemic review and meta-analysis. Tanaffos. 2019 Apr; 18(4): 294.