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Chapter

Role of Vitamin E in Boosting the Immunity from Neonates to Elderly

Mariyappan Kowsalya, Mohan Prasanna Rajeshkumar, Thangavel Velmurugan, Kattakgounder Govindaraj Sudha and Saheb Ali

Abstract

The vitamin E is a fat-soluble vitamin which occurs as a tocopherol component abundant in humans. The vitamin E supplements in humans and animals have provided numerous health benefits. The vitamin E is rich in antioxidants which slow the aging process and reduce the free radical damage. Vitamin E isoforms play an important role in respiratory health. It is also important in health and well-being of preterm neonates. Vitamin E deficiency in new born includes hemolytic anemia, disease of retina, bronchopulmonary dysplasia. Further, in vitro studies, vitamin E has increased the oxidative resistance and prevents the atherosclerotic plaque. The consumption of vitamin E rich foods reduces coronary heart diseases. This chapter focuses on the treatment of vitamin E deficiency in preterm babies and the role of vitamin E in preventing coronary heart diseases.

Keywords: Vitamin E, neonates, immunity, preterm infants, α-tocopherol

1. Introduction

Vitamins are defined as "organic compounds required in diet in little quantity to execute specific biological functions for normal protection of ideal growth and health of the organism" [1]. In 1922, vitamin E was discovered by Evans and Bishop named it as "X-factor" and got its name after the classification of other vitamins [2]. Vitamin E is generally used as a common word for four tocopherols (α, β, γ and δ) and tocotrienols (α, β, γ and δ) present in food. The main component of the group of compounds in vitamin-E is α-tocopherols. The tocopherols are products of 6-hydroxy chromane (tocol) ring with isoprenoid side chain. Vitamin E with the aid of selenium prevents the non-enzymatic oxidation of cellular components and free radical formation. Vitamin is lipophilic in nature and present on association with derivatives of lipids and cell membranes [1]. The synthetic α- tocopherol is called as *all-rac-* α-tocopherol and naturally available form is RRR- α-tocopherol [3]. The key characteristics of vitamin-E was identified as scavenger of free radical and it is the foremost fat-soluble vitamin responsible for protecting cell membranes against peroxidation [4]. In early stages of life, vitamins are extremely important. Vitamin -E supplies the essential antioxidant protection and stimulates the development of the

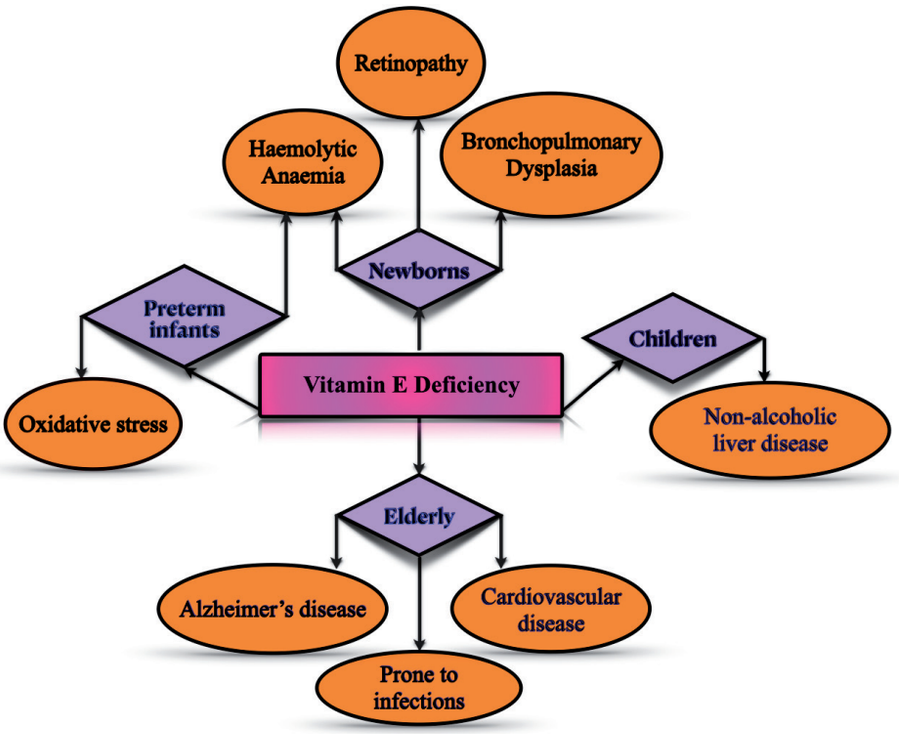


Figure 1.
The low level of serum α-tocopherols was observed in certain disease was mentioned which cause high rate of morbidity in neonates. And also, elderly patients have diseases associated with low level of vitamin E and other micronutrients in their diet.

immune system in new-borns [5]. Our human system does not synthesize Vitamin E and it is obtained through dietary intake. Vitamin E rich foods are wheat germ oil, sunflower oils, soybean oil, sunflower seeds, cotton seed, walnut, hazel nuts, peanut butter, corn, palm, spinach, broccoli, kiwi fruit, mango, raspberries, blackberries, blackcurrant, avocado and tomato [6–8]. The vitamin E deficiency was known as the cause of foetal death. Early high dose of vitamin E either through intravenous or intramuscular route decreases the chance of hemorrhage, bronchopulmonary dysplasia, haemolytic anemia, retrolental fibroplasia and retinopathy of prematurity [9]. The low level of vitamin E in serum was observed in certain diseases which was depicted in **Figure 1**.

The antioxidant potential of vitamin E could protect the polyunsaturated fatty acids in the membrane from oxidation, regulating the production of reactive oxygen species, reactive nitrogen species and modulates signal transduction [10]. The effect of antioxidant activity of vitamin E was based on the number of methyl group in its chromane ring. The α-tocopherol have three methyl group whereas the δ- tocopherol has only one methyl group in it [2]. Vitamin E also has anti-cancer potential by stimulating the p^{53} gene, down regulation of mutant p^{53} gene and activates the heat shock proteins. Production of PKC and collagenase was inhibited by α-tocopherol. In milieu, γ- tocopherol has effective anti-cancer activity than the α-tocopherol [5]. Intrauterine growth restriction (IUGR) is one of the major causes of neonatal morbidity and mortality. Some studies shows that α-tocopherol aids in the intrauterine development of foetus. 15 million babies are born premature every year and they need special care just to stay alive [11]. During gestational period, the maternal oral intake of vitamin E increases the weight of foetus [12]. The oral administration of vitamin E was given to children to combat malabsorption disorders. Some of the compounds used as vitamin E therapy in newborn and preterm infants are α-tocopherol, tocofersolan, dl- α-tocopherol, dl-α-tocopheryl acetate [13]. In 2000, the institute of medicine (IOM) chose the hydrogen peroxide induced

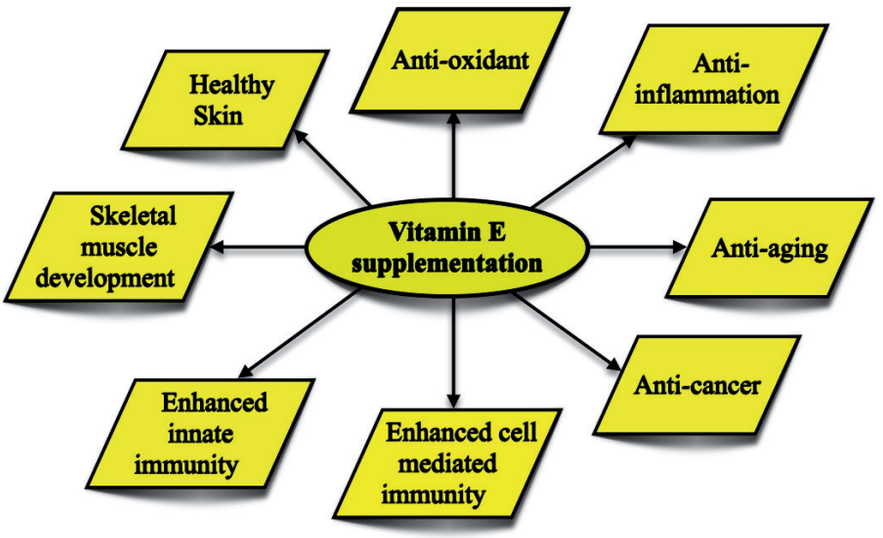


Figure 2.
Vitamin E supplementation has many biological activities and it enhances the immune response.

erythrocyte haemolysis test as a marker to determine the vitamin E status. Because, erythrocyte fragility and anemia with higher erythrocyte was observed in children. In adults, vitamin E deficiency occurs due to genetic disorders in α-tocopherol transfer protein (TTP) which causes ataxia. Further, fat malabsorption also leads to vitamin E deficiency due to genetic disorder in TG transfer protein [14]. The people with ataxia are provided with 800-1200 mg of vitamin E as a supplement to prevent the progression of disease [6]. Orally, vitamin E was given in the form of dl-*α*-tocopherol acetate. Supplementation of *α*-tocopherol increases insulin sensitivity and decreases the oxidative stress [15]. Oxidative stress was due to the disturbance in balance between generation of free radicals and their exclusion by free radical scavenging activity of the system [16]. Vitamin E supplementation has enhanced the host defense system by heightening the humoral and cell mediated immune system. In elderly people, vitamin E has boosted the resistance against viral diseases and also stimulates immune response to distinctive antigen [5]. Immunostimulatory property of Vitamin E provides enhanced resistance to many pathogens [9]. Earlier studies show that vitamin E possess neuroprotective activity in both foetus and adult rats [17]. The vitamin E supplementation has numerous biological activity which was depicted in the **Figure 2**.

2. Immunological functions of vitamin E in different stages of life

2.1 Preterm infants

Preterm birth was defined as parturition prior to 37 weeks of gestation, the leading cause of mortality and morbidity in neonates. The rate of prematurity complications increases with decreased gestational age and birth weight [10]. Newborns are one of the risk groups of vitamin E deficiency. The limited transfer of *α*-tocopherol through the placenta which results in low level of vitamin-E in tissues and serum at the time of birth in premature infants than in full term infants [18]. The preterm infants' blood vessels are exposed to high oxygen tension due to the deficient amount of vitamin E [19]. Preterm infants are born with low body weight and have less stored fat-soluble vitamins. The level of *α*-tocopherol is low at their time of birth was shown by the elevated erythrocyte haemolysis in the presence

of hydrogen peroxide. The enteral dose of vitamin E is given at 50 IU/kg within 4 hours of birth and it increases the serum α-tocopherol level [20]. The preterm infants those less than 1000 g in NICU were given 1.5 ml of vitamin E per day through infuvite pediatric as a portion of parental nutrition. And infants in 1000 g to 3000 g obtain 3.5 ml of vitamin E per day. Each vial (1 ml) of infuvite encompasses 7 mg of α-tocopheryl acetate [3].

The preterm infants administering the oral dose of vitamin E helps in treating the vitamin E deficiency syndromes like anemia, retinopathy, thrombocytosis and congenital malformation [21]. The retrolental fibroplasia occurs often in preterm infants because the last portion of the retinal blood vessel continues to develop till the end of eight month of gestation. The blood vessels of the preterm infants might not be developed well and they need an appropriate environment with arterial oxygen tension, blood supply, nutrient, disposal of wastes and exposure to visible light [18]. The haemolytic anemia was frequently observed in preterm infants, where their intake of fortified iron is higher along with linolenic acids. Nowadays, the formula for preterm babies had increased the vitamin E and reduces their iron content so that this helps to prevent the development of haemolytic anemia [22]. The vitamin E supplements in preterm infants increases the hemoglobin level after 8–10 weeks of birth [23]. Previous studies reported that preterm infants born below 2000 g, when supplemented with 16.5 mg of α-tocopherol acetate per day for about ten days has improved the hemoglobin level and decreases the reticulocyte count. Supplementing 16.5 mg concentration of vitamin E is higher in their study compared to regular dose of 1.5 mg/day but it shows betterment of disease condition, however their consequences have to be studied [24].

The bronchopulmonary dysplasia (BPD) was observed among preterm infants due to free radicals which injures the lung cells. It was generally noticed in preterm infants particularly born before 28 weeks of gestation. Oral supplementation of vitamin E is tolerable in pregnancy and infancy. They are present routinely in the total parenteral nutrition (TPN) which is used in the treatment of BPD. And also, the α-tocopherol plays a key role as anti-inflammatory factor in neonatal lungs [15]. A study with 133 preterm infants were grouped into 68 preterm infants with confirmed case of BPD, 65 preterm infants without BDP. It was observed that as the condition of BPD increases with vitamin E deficiency. The involvement of vitamin E in BDP was confirmed and their supplementation would become a therapy to BPD [25].

2.2 Neonates

The adequate intake of Vitamin E is essential in neonates as they are born with low stores of it. The routine recommended intake of vitamin E is 2.8 IU/kg per day (Maximum 7 IU/kg per day) [8]. The term babies gestational age was between 37 and 41 weeks and their weight at the time of birth was 2500 g -3700 g [26]. It was observed that very low birth weight in infants were deficient in Vitamin E. Hence, vitamin E supplementation is required to enhance the weight gain in infants [27]. The yellow coloration of the skin and sclera of new born babies are referred to as neonatal jaundice which is the result of bilirubin deposition. Vitamin -E is supplemented along with phototherapy of the full-term neonates [28]. In an extrauterine environment, vitamin E acts as defense against oxygen toxicity and their placental transfer to the foetus is limited during gestational period. Hence, maternal milk is important to supply this vitamin to the neonates in their initial period and during lactation, thus, protecting it from haemolytic anemia, bronchopulmonary dysplasia, neurological dysfunction and increased neonatal mortality. The studies show that vitamin E in maternal milk decreases with increase in lactation period i.e., colostrum (40.5 ± 15 μmol/L) provides the highest content of vitamin E to infants.

Whereas it gradually decreases in transitional (13.9 ± 5.2 μmol/L) and mature (8.0 ± 3.8 μmol/L) milk of lactation. The higher concentration of alpha-tocopherol in colostrum acts as complementary mechanism [29]. Hyperbilirubinemia was observed in neonates which was treated with phototherapy and vitamin E supplementation [30]. The world health organization WHO has issued a global public health recommendation that infants should exclusively breastfed for 6 months to attain optimal growth and development as the maternal milk was the infant's best source of nutrients. The average amount of vitamin E in maternal milk is 2.5–2.9 mg it contributes to prevention of free radical propagation in numerous lipid structures within the system [31]. The Dietary Reference Intake (DRI) recommends the intake of 4 mg/day of vitamin E for children between 0 and 6 months. The vitamin E supplementation in children is essential to the development of the immune system, lungs, extracellular matrix of the vascular system and mental development [29].

2.3 Children

Vitamin E enhances the immune responses of the children. Cardiomyopathy was observed as a symptom in children with critical deficiency of vitamin E. The prescribed amount of vitamin E supplementation in children is 1000 mg/d [13]. Low level of maternal plasma α-tocopherol increase the chance of asthma in children within their first ten years [32]. The antioxidant intake of vitamin E during pregnancy and their effect on development of wheezing and eczema in children is needed to be confirmed with the follow up investigation on the children's growth and their dietary intake [33]. In previous report, the association of vitamin E intake during pregnancy and chance of asthma in children was observed in 2000 pregnant women. The α-tocopherol level in plasma was examined during gestation and cord blood after delivery. Their intake of anti-oxidant vitamins are also examined. Then follow up studies was performed up to five-year age of children. The symptoms of asthma, wheezing and dietary intake was collected for 1253 children and 797 children were participated in hospital evaluation. They have concluded that low level of serum vitamin E during pregnancy was observed among the children with phenotypic symptoms of asthma. Though, vitamin E does not directly improve the conditions of asthma patients their deficiency in early stage of life was perceived in children be inflicted with asthma [34].

The children suffering from chronic kidney disease are at high risk of micronutrient deficiency. The concentration of vitamin A and vitamin B12 was within the range of reference while vitamin E shows major changes as the kidney disease worsens hence advance studies are essential to determine the required concentration of vitamin supplements in infants and children with this disease [35]. In children, respiratory tract infection is common cause of the morbidity. The vitamin E supplementation helps to treat this disease. A substantial amount of plasma vitamin E improves the hemolytic uremic syndrome in children. Which was due to the defect in production of prostacyclin and thus preventing the mortality and morbidity rate [36]. Supplementation of vitamin E (100 IU/ day) has increased the glutathione level and decreased the lipid peroxidation and concentration of HBA1C in the erythrocytes of type 1 diabetics children [37]. The childhood obesity was growing and it may be due to imbalance in the oxidant and antioxidant level. The obese children were observed with increased level of oxidants like isoprostanes and decreased level of antioxidant like vitamin E. Oxidative stress markers were decreased by vitamin E supplementation in obesed children with liver steatosis. Hence, early implementation of vitamin E will reduce the risk of cardiovascular and metabolic changes connected with non-alcoholic fatty liver disease in children and adolescence [38].

2.4 Adults

The reactive oxygen species include (ROS) like hydrogen peroxide, hydroxyl radicals, and superoxide were studied exclusively. The formation of ROS during electron transport chain was presumed due to increased ingestion of oxygen by mitochondria in the cell. Some recent studies reported that exercises increased the ROS production. The studies revealed that vitamin-E supplementation in athlete improved the muscle performance and protects the cell membrane from damage through oxidative stress. This study augment that vitamin E would strengthen the skeletal muscle of the older people [39].

In the previous research, Women with the possibility of pre-eclampsia during pregnancy was provided with 400 IU of vitamin E and 1 g of vitamin C per day. As a result, very low birth weight infants were born to supplemented group compared to placebo group. Hence, the vitamin E concentration should not be exceeded above the required dietary allowances [40]. Furthermore, the greater the concentration of serum vitamin E during pregnancy then there is a chance of macrosomia [41]. Recently, a study with 897 girls in their adolescence found that vitamin E aids in the inflammatory response and oxidative stress during menstrual cycle [42].

Cystic fibrosis was one the genetic disorder which leads to deterioration of pulmonary functions in children and adults, partially due to oxidative stress. The vitamin E supplementation greater than required dietary allowances has enhanced the serum α-tocopherol [43]. In USA, the higher acceptable level of vitamin E per day was 1000 mg/day [44].

2.5 Elderly

Vitamin E group has tocopherol and tocotrienol groups each with identical isomers but with alteration in hydrophobic tridecyl chain saturation point. The tocotrienol was recently discovered to be more effective than tocopherol in the treatment of age-related cardiovascular diseases [45]. The low intake of vitamin E in childhood and adulthood leads possibly to hypertension than those who have taken an adequate amount of vitamin E. The cardiovascular disease risk can be decreased by - α-tocopherol which inhibits LDL oxidation and reduces the inflammatory responses [46]. The intake of antioxidants could prevent the lipid peroxidation [47]. The epidemiological study with 27271 men who were smokers and by no records of myocardial infraction in the age group 50–69 was divided into group and supplemented with vitamin E, placebo and beta-carotene. The groups were keenly monitored to detect the possible effect of vitamin E supplementation in cardiovascular disorder. The results revealed that 50 mg/day supplementation of vitamin E has prevented the occurrence of nonfatal myocardial infraction by 4% and fatal coronary heart disease by 8%. The vitamin E (α-tocopherol) supplemented group has lessened the chance of coronary heart disorder in human trails followed up to six years related to the placebo group. The beta-carotene supplementation has no effect on non-fatal myocardial infraction disease [48].

Immunological function especially cell-mediated immune response will decrease with age and hence elders are prone to infectious diseases. The 200-800 mg supplementation of vitamin E enhances the production of antibody to a primary immunization [49]. In the in vivo study, healthy elderly people in the age group greater than 60 years are supplemented with 800 mg of vitamin E per day and the fasting blood sample was collected for the duration of 6 months and this study has evidenced the increase of α-tocopherol level in serum and increase in delayed

type hypersensitivity was observed [50]. In four month of clinical trials, vitamin E supplementation greater than RDA in elderly people had enhanced production of antibodies against various diseases like tetanus, hepatitis B and DTH vaccines [51].

The oxidative stress was one of the reasons for neurodegenerative diseases like Alzheimer's disease, Parkinson's disease and processes in cells related to aging. The brain cells were easily damaged by free radicals due to its consumption of high amount of oxygen along with certainly peroxidable lipid membranes and comparatively lesser enzymes with antioxidant potential. The vitamin E and vitamin C were the antioxidant rich supplements which will scavenge the reactive oxygen species and helps in regeneration of neurons [52]. Vitamin E also protects the nervous system with aging [13]. Neurological abnormalities are observed in children and adults when the serum α-tocopherol level is less than 0.5 mg. Vitamin E deficiency manifests as neuropathic and myopathic disorders. Spinocerebellar syndrome, ataxia, hyporeflexia, vibratory sensation was commonly observed clinically. Moreover, skeletal myopathy and pigmented retinopathy also occurs due to the vitamin E deficiency [6]. Further, Vitamin E supplementation has upgraded the cognitive function and vascular dementia in elderly [53]. The higher level of α-tocopherol in the brain generates an anti-inflammatory milieu to decrease the density of microglial cells. It also protects from the Alzheimer's disease [54]. A study group involved 39,876 women in US, in which 6377 women were greater than 65 years. It was evidenced that vitamin E supplementation in 600 IU alternative days with the follow up for 4 years had enhanced cognitive development. Because the oxidative stress was the major cause for dementia pathogenesis and numerous reports proved that vitamin E has decreased the lipid peroxidation in brain and also prevent the occurrence of Alzheimer's disease [55].

Previous studies reported that intervention of Vitamin E improves the lymphocyte proliferation and delayed type hypersensitivity was enhanced with higher production of Il-2 and lesser production of Il-6 [9]. An intervention of 200 mg of vitamin E has enhanced immune response of elderly people [56]. When the older mice supplemented with vitamin E has enhanced the cell mediated immune response, production of IL-2 and delayed type hyper sensitivity. In elder human subjects also vitamin E supplementation progresses both the innate and adaptive immunity. The phagocytic capability of leucocyte was improved but declined the bactericidal activity which might be due to the antioxidant potential of vitamin and lesser production of hydrogen peroxide. Further, the optimal concentration of vitamin E supplementation is 200 IU per day than the 60 and 800 IU per day of vitamin E supplementation has increased the T-cell proliferation in elder people [57].

In vivo studies of both animals and human have evident that immunity decreases with aging process. It was observed by decreased antibody response, delayed-type hypersensitivity, proliferation of T cell in response to mitogens. Research has proved that antioxidants have helped to improve the immunity in aging process [50]. Aging is a gradual and typical loss of the physiological system along with its immune response. The elderly people are prone to infections and other diseases like cancer due to the age related decrease of immunity. One of the widely consented reason for aging was oxidative stress. The previous study suggested that supplementation of both vitamin C (500 mg/day) and vitamin E (200 mg/day) to the elderly people has improved their immune function by enhancing the humoral and cell- mediated immune response. The α-tocopherol acts as immunomodulator and enhances the cytokine levels in older population of group. Level of INF- γ has increased in tested groups of older people supplemented with vitamin E [58].

S. No	Groups	No. of Participants	Age	Disease Condition	Dosage form of Vitamin E	Quantity	Outcome	Reference
1	Preterm Infants	12	28–30 week gestation	Very low Birth weight	dl-alpha-tocopheryl-acetate	3.5 mg/dl	Reduce the risk of Retinopathy	[62]
2		215	28–30 week gestation	Very low Birth weight	Soybean oil-based lipid emulsion	—	Reduce cholestasis	[63]
3		34	≤ 35 week gestation	Very Low Birth Weight	alpha-tocopheryl acetate	16.5 mg/ day	Increases Hemoglobin concentration	[64]
4		168	≤ 30 week gestation	Very Low Birth Weight	Vitamin E	3.3 mg/day	Prevent retrolental fibroplasia	[65]
5		25	< 30 week gestation	Very Low Birth Weight	dl-alpha-tocopheryl acetate	25 mg Ephynal	Enhances serum alpha-tocopherol	[66]
6		36	25.5 week gestation	Very Low Birth Weight	Mixed vitamins in parenteral solution	3.17 mg/ day	Increased serum alpha-tocopherol	[67]
7		151	< 35	Very Low Birth Weight	alpha- tocopherol	50 mg/kg	Decreases the bilirubin level	[33]
8	Neonates	77	37–42 week gestation	—	RRR-alpha- tocopheryl acetate; *all*-rac-alpha-tocopheryl acetate	20 IU; 13.5 IU	Infants discriminates natural and synthetic vitamin E	[15]
9		80	—	Hyperbilirubinemia	Phototherapy & Vitamin E	4 mg/day	Faster Recovery	[23]

Table 1.
Role of vitamin E in improving immune system in various disease condition of preterm infants and neonates.

S. No	Groups	No. of participants	Age	Disease Condition	Dosage form of Vitamin E	Quantity	Outcome	Reference
1	Children	2372	≤ 5 years	Kwashiorkor	Vitamin E, riboflavin, Se	—	No data on morbidity	[68]
2		16	—	Chronic Cholestasis	d- alpha -tocopheryl polyethylene glycol 1000 succinate (TPGS)	20–25 IU	Improves neurological development	[69]
3		61	≤10 years	Acute pyelonephritis	Vitamin E	—	Reduces Renal scarring	[70]
4		141	≤ 14.5 years	Cystic fibrosis	Vitamin E	—	Enhances vitamin E level	[71]
5	Adults	716	Gestation period	HIV infected	alpha -tocopherol acetate	30 mg/ day	Improves vitamin status in infants	[72]
6		23	—	Oxidative stress	Vitamin E	400 IU	Prevents exercise induced oxidative stress	[73]
7	Elders	184	—	Cardiovascular disease	alpha -tocopheryl acetate	400 IU	Reduces lipid per oxidation	[74]
8		29133	50–69	Pneumoniae	alpha -tocopherol	50 mg/ day	Decrease the risk	[75]

Table 2.
Role of vitamin E in improving immune system in various disease conditions of children, infants and elderly.

3. Immunological functions of vitamin E in infections

3.1 Pneumoniae

The in vivo studies on older mice affected with pneumonia was supplemented with vitamin E at the concentration of 500 mg per kg for four weeks and found that it has help to improve the lung functions. It was observed that migration of neutrophil and production of inflammatory cytokines was reduced with the intake of vitamin E. In human subjects, the older people supplemented with 200 IU of vitamin E per day has subsided the necessary to re-hospitalization of older people with pneumoniae up to 63% and it aids in faster recovery [57].

3.2 Human immunodeficiency virus

The vitamin E possess the anti-inflammatory property and people infected with HIV was found be lack of it and weakened immune system. Vitamin E supplementation in 400 IU per day has reinstate the delayed type hypersensitivity, production of IL-2 and T_H cells. The higher level of α-tocopherol in serum had blocked the advancement of infection. The murine model with HIV infection supplemented with increase in fifteen-fold of dietary vitamin E regularize the distorted immune system caused by infection to normal state [5]. Further, there was greater incidence of non-alcoholic steatohepatitis in HIV infected patients. The previous studies with 27 HIV patients with NASH reported that vitamin E supplementation was a most effective treatment as it has enhanced the ALT level, ck-18 and CAP score. Moreover, it does not cause any adverse effects in participated individuals [59].

3.3 Influenza virus

Influenza virus cause severe damage to lungs and also inflammation leads to greater oxidative stress. The vitamin E acts as an effective antioxidant therapy in influenza diseases. Thus, vitamin E supplementation protects the respiratory system and prevents the occurrence of oxidative damage due to influenza [60].

3.4 Others

The mouse models were infected with coxsackievirus which induces myocarditis. And in vitamin E deficient group the virulence of this virus is greater. In human studies, the coxsackie virus was isolated from infected individual, which was called as keshan an endemic disease commonly observed among children and women. The affected individuals were deficient in vitamin E and Se hence their supplementation in diet can prevent the viral infection [61]. The role of vitamin E in boosting immune system in various diseases in infants, children and elderly are depicted in **Tables 1** and **2**.

4. Discussion

The vitamin E was present in many natural foods which should be taken in adequate amount because the fortified or supplementation of vitamin E does not provide greater health benefits. The natural form of vitamin E rich foods should be incorporated into the diet. The healthy foods should be added to the diet for the efficient action of antioxidants in the human system [47]. The mother's milk

especially colostrum contains higher concentration of vitamin E which prevents the infants from oxidative damage and develops their immune system. Since, very less amount of vitamin E is transferred through the placenta, maternal milk plays a crucial role in enhancing the serum α-tocopherol level in new born [76]. The babies born with lesser gestational age was highly prone to oxidative stress and the maternal milk is the best source of antioxidants than the formulas to protect the new born infants [77]. Still today, α-tocopherol level in the serum was frequently measured through HPLC analysis. A novel method should be developed for their measurements.

The preterm infants were susceptible to oxygen radical disease and it can treat with antioxidant therapy in which the well-known antioxidant nutrient vitamin E can be used to treat this condition in preterm infants [78]. The formula fed preterm infants have the risk of developing high oxidative stress but in the study with 31 healthy preterm infants shows that long chain poly unsaturated fatty acid supplemented group does not affect the solubility of α and γ- tocopherol [79]. Another research also suggest that both the breast fed and formula fed preterm infants possess the ability to tolerate oxidative stress. It was confirmed by the presence of malonaldehyde (MDA) in the urine which was measured by HPLC analysis [80]. The vitamin E supplementation is required in preterm infants to improve certain disease conditions like haemolytic anemia, retrolental fibroplasia, bronchopulmonary dysplasia but their long-term high dosage leads to sepsis, necro colitis and in some cases even death of premature infants. Hence the ideal dosage of vitamin E is prerequisite to treat the disease in preterm infants on the other hand to ensure the safety and longer healthy life to the preterm babies [81].

In children, vitamin E deficiency results in the development of chronic cholestasis. In this case, the children have normal serum α-tocopherol level but decreased ratio to the total lipid content [82]. The vitamin E deficiency could be combated by intaking fortified foods can enhance the vitamin E and it was one of the best methods to reach daily requirements of vitamin E [83]. Vitamin E supplementation along with other micronutrients and trace elements increases our defense barrier system and prevents the development of infection [84].

The oxidative stress in the human body was mainly originated from the free radicals produced by mitochondria and other cellular components. The external factor for oxidative stress includes UV light rays from sun, ozone, pollutants, smoke from cigarette and smog. These factors contribute to the aging process. The antioxidant rich foods would help to balance the oxidant- antioxidant level in human body. The foods enriched with vitamin E are a good choice to delay the aging process and to have healthy and youthful glowing skin in later stages of life. [85].

Further, vitamin E supplementation also improves the cognitive function when their dietary intake is higher at the earlier stage of Alzheimer's disease. And also in the later stages of this disease their admission to centre is greatly reduced but it does not improve any cognitive functions [52]. The vitamin E is an effective antioxidant which shows beneficial report in preventing the progression of Alzheimer's disease, Parkinson's disease and dementia [55]. Though, there was no significant cognitive improvement in healthy individuals supplemented with vitamin E, it helped in the diseased condition We suggest that vitamin E has positive impact in improving the brain disorders associated with oxidative damage of brain cells.

Vitamin E was one of the efficacious nutrients which could modulate the immune system. The concentration of vitamin E is higher in immune cells than other cells in the blood. It has been observed that deficiency of vitamin E worsens the immune system in both animals and humans. Thus, vitamin E supplementation exceeding the required dietary recommendation has contributed to enhance the immune system. It has intensifies the differentiation and proliferation of T cell,

production of IL2, activity of T_H cells, macrophages and phagocytic cells [57]. The vitamin E supplementation in elderly has improved their immune response towards improved antibody response, delayed type hypersensitivity and also T-cell was proliferated was stimulated in response to mitogens. And Vitamin E in combination with vitamin C has also shows an enhanced immune response in elderly group than with the study group administered with vitamin E alone [50]. The higher level of vitamin E (α-tocopherol) in serum the greater the ability to resist viral infection in elder population [5]. Furthermore, the dietary intake of vitamin E enhances the immunity in elders and immunocompromised persons [86].

The vitamin E supplementation has modulated the immune system in both direct and indirect way. Directly it has maintained the cellular integrity and protected the cells from damage caused by oxidative stress. While indirectly it has aid the modulation of inflammatory intermediaries like proinflammatory cytokines and prostaglandin E2. The studies in mice suggests that inflammatory lung disease can be treated with the combination of probiotic strain *Bifidobacterium lactis* and vitamin E, C to lessen the lung inflammation due to air polluting agents [87]. In animal models, the α-tocopherol possess the anti-inflammatory and γ- tocopherol with pro-inflammatory property it could be used in the treatment of asthma [88].

The elderly people in the age group of 65 years and above was investigated for the association of vitamin E supplementation and respiratory tract infection. The study results shows that the vitamin E supplantation does not show any statistical difference among the lower respiratory infection among the supplemented and placebo group. However, the vitamin E supplementation group has a remarkable result in preventing the upper respiratory tract infection and against common cold [89]. Acute and chronic lung injuries was observed in new-borns due to oxidative damage. Usually, surfactant lipids protect the type II alveolar cells of lungs from air-borne pathogens. The vitamin E supplementation enhance surfactants and prevent the development of lung diseases like bronchopulmonary dysplasia [90]. Thus, based on these results vitamin E supplementation in our diet would prevent the upper respiratory tract infection and strengthens the lungs alveolar cells which might help us to combat the Covid-19 infection and help us to build a stronger immunity in current pandemic situation.

5. Conclusion

In past decades, vitamin E deficiency was frequently observed in preterm infants and neonates leading to various diseases like bronchopulmonary dysplasia, retrolental fibroplasia, hyperbilirubinemia, haemolytic anemia. Most often, the very low birth weight infants are at the high risk of developing vitamin E deficiency. The adequate amount of vitamin E supplementation has prevented the development of these disease conditions. The alpha tocopherol and alpha tocopheryl acetate are the most common form of vitamin E supplemented to preterm infants and new born infants. Vitamin E supplementation has prevented the development of asthma in children but not in patients with chronic severe asthma. Hence, the mechanism of vitamin E involved in preventing the disease in juvenile stage in children is need to be investigated. Vitamin E also possess numerous health benefits along with its antioxidant property. The aging process decreases the immunological response and increases the chances of infection in elder population. Thus, vitamin E supplementation has improved the T-cell mediated immune response and prevented the progression of Parkinson's disease and dementia in older people. Further, vitamin E is an important micronutrient which plays a crucial role in the early stage of our life to lead a healthy life. Many reports proved that vitamin E supplementation

has enhanced the immunity and prevented many diseases in infants. However, the optimal dosage amount, isoform and duration of vitamin E supplementation in each disease conditions in preterm infants and newborn is still need to be validated. Indeed, the mechanism behind the vitamin E in curing the infectious diseases and improving the immune response is little-known and future research will bring to light the unknown mechanism of vitamin E in boosting immune response in infants.

Conflict of interest

The authors declare no conflict of interest.

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