

Review Article

An insight to Vitamin A: A neglected vitamin

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Abstract: Fat soluble vitamins consists of many vitamins in which vitamin A is major fat soluble vitamins, Vitamin A actually an assembly of unsaturated and double bonded organic compounds in which carbon is major element of its structure, it is known as retinol, retinal and retinoic acid (because of their structure and position of its atoms). Vitamin A has been showed its importance by the fact that it cannot be manufactured in the human body and must be taken from the outside of body through diet. Pro-active form of fat soluble vitamin A are carotenoids as it is formed in plants also considered as important and major alimentary source of Vitamin A when it has been passed through the process of break down by enzymes (which are actually protein in nature). It has been considered that lack of Vitamin A is primary cause of worldwide load of ailments that specifically effect the states of shortage of Vitamin A sources. Vitamin A act as immunomodulator and enhance erythropoietic activity thereby improving iron (ferritin) levels and reducing anemic condition in vulnerable groups.

Keywords: vitamin, Fat soluble, Vitamin A, immunomodulator

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INTRODUCTION:

Fat soluble vitamins consists of many vitamins in which vitamin A is major fat soluble vitamins, Vitamin A actually an assembly of unsaturated and double bonded organic compounds in which carbon is major element of its structure, it is known as retinol, retinal and retinoic acid (because of their structure and position of its atoms), (Figure 1). Vitamin A has been showed its importance by the fact that it cannot be manufactured in the human body and must be taken from the outside of body through diet. Pro-active form of fat soluble vitamin A are carotenoids as it is formed in plants also considered as important and major alimentary source of Vitamin A when it has been passed through the process of break down by enzymes (which are actually protein in nature). It has been considered

that lack of Vitamin A is primary cause of worldwide load of ailments that specifically effect the states of shortage of Vitamin A sources (WHO, 2009).

Vitamin A is actually present in many forms, in which chief alimentary forms of Vitamin A has its own structure. Animal source derived vitamin A is known as Preformed Vitamin A (retinol) is chiefly found as retinly palmitate in the major of supplements of Vitamins, fortified foods and in the livers of animals. Proformed is actually the inactive form of vitamin A that are present in plants, approximately fifty Provitamin A is carotenoids that are actually alpha-carotene, beta-carotene and beta-cryptoxanthin. Plant derived Pro-vitamin A carotenoids and it's shapes are mostly measured through human serum.

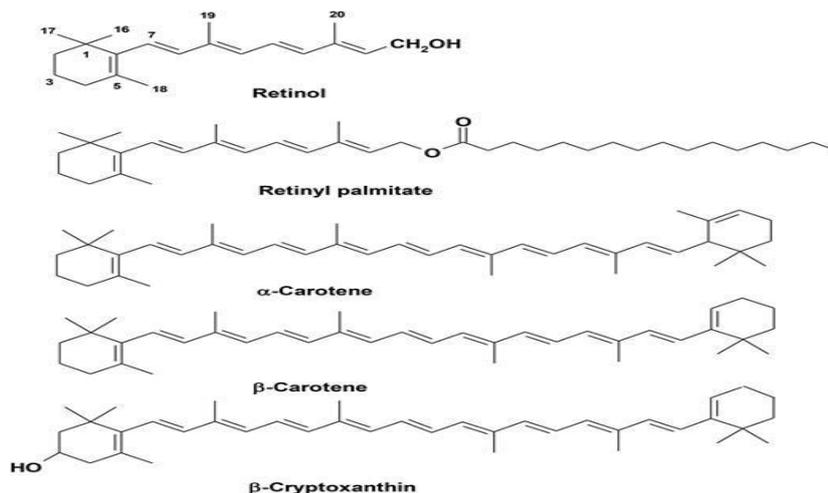


Figure 1: Structure of Vitamin A

Sources:

Vitamin A is present in 2 major forms. First is Preformed Vitamin A which is considered as retinol and the plants derived Vitamin A is Pro-vitamin A that is actually originators of carotenoids that are known as

retinol when they exert direct effect on humans. Preformed Vitamin are actually retinol that are only present in animals while proformed Vitamin A are carotenoids that are present in plants and plant derived foods, Figure 2.

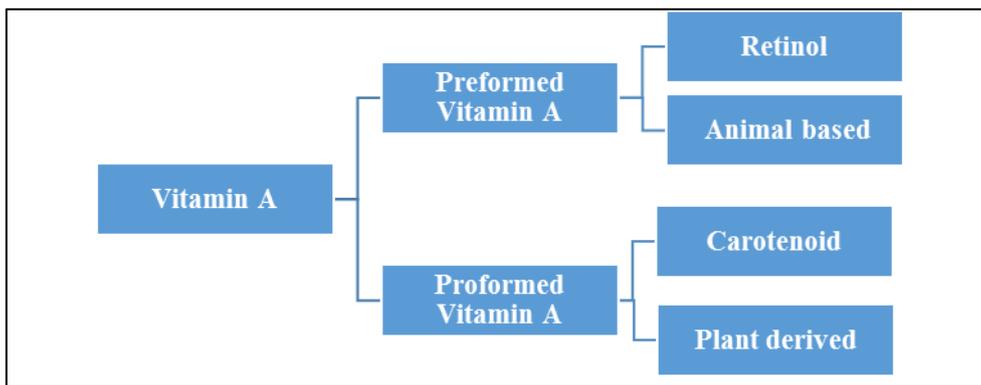


Figure 2: Types of Vitamin A

Presence of Carotenoids in animal foods are actually depends on alimentary source (Chndrika *et al.*, 2006). it is shown that average alimentary consumption of vitamin A in the United States is actually comprised of almost twenty five percent Provitamin A and seventy five percent is preformed vitamin A (Zheng *et al.*, 2014) in which milk and milk products as well as in the fortified products are a major causative alimentary /nutritional /food items. Whereas it has been shown through the researches that almost eighty percent of vitamin A is fulfill from carotenoids and pro-vitamin A items (Chandrika *et al.*, 2006) It has been revealed through studies that shortage of preformed vitamin A food sources and its high priced is counted in these states in which blindness of eyes is obvious health ailment (Ross *et al.*, 2000).

Major and preliminary compound of Vitamin A is actually exist in all-trans retinol that are actually in structure of isoprenoids compounds which are animal in origin (Chandrika *et al.*, 2006, Zheng *et al.*, 2016).

All types of bet-ionine derived compounds are generally known as Vitamin A except carotenoids. Vitamin A is present in retinly palmitate which is the primary deposit form of vitamin A is mainly an ester of a fatty acid chain almost ninety percent of it deposit in liver. Pigmented compounds which emits the colors are known as carotenoids which are actually group of four hundred pigments are present in some fruits. Oils of vegetable origin, and items originated from animals that are eaten such as egg yolk and shrimp. In these foodstuffs almost fifty percent are recognized biologically as biologically active Vitamin A (Jin *et al.*, 2003, Beatty *et al.*, 2004). Proformed vitamin A carotenoids in which Beta-carotene (Figure 3) is recognized to be have greater vitamin A activity could be transferred into active form of Vitamin A by the breakdown through oxidation (Topuz and Ozdemir, 2007). Sometimes, pigmented compounds of plants origin are captivated whole and then stored in the different parts of body tissues of humans as well as in

fat stores, skin, shells, eggs and milk (Beatty *et al.*, 2004).



Figure 3: Expression units of Vitamin A

RDA of vitamin A

The inability of human body to produce vitamin A forces us to have a balanced diet in order to intake the recommend supply of this nutrient. Children aged between 1 and 8 years should receive 400-600 µg/d and with more than 8 years should receive about 600-800 µg/d of vitamin A. On the other hand, adult men and adult women should intakes 900 µg/d and 800 µg/d, respectively. However, during pregnancy women should only consume 700 µg/d due to potential teratogenic effects. Vitamin A can be provided in form of carotenoids (provitamin A) and retinol or retinyl esters (preformed vitamin A) (Chapman 2012).

Food sources

Vitamin A is compulsory throughout the whole life and at different stages of life cycle. At the time of birth to 1 years of age, first milk excreted through mammary glands called colostrum and mothers milk are major source of combined forms of vitamin A (preformed & proformed) specifically when a mother nourish herself with appropriate alimentary sources of vitamin A (Latham, 2010) as suggested through dietary guidelines (Madatuwa *et al.*, 2007). After the age of one year fat soluble vitamin A is fulfilled through food through preformed vitamin A of animal origin as a retinyl esters, predominantly retinyl palmitate (Figure 1). It can also be availed through pigmented compounds known as (Figure 1), extracted from plant sources just as beta-carotene and beta-cryptoxanthin (Mahawithanage *et al.*, 2007, UN, 2019). In the world, fortified or enriched foods are major sources of preformed vitamin A (active form of Vitamin A) in both the states (developed and developing). When we talk about developed states of world(at first in progress) vitamin A fortified foods are present in the state of ready-to-eat cereals, snacks foods, drinks (beverages), trans fat products (margarine) and processed dairy products (Imdad *et al.*, 2017). In the developing state of world vitamin A enriched foods are less but they are typically found in cereals flours, sugar, and eatable oils (Imdad *et al.*, 2017, Haider and Bhutta, 2015) margarine (Kapil, 2011), and noodles (Akhtar *et al.*, 2009). It has been revealed that the strategies are planned for the enrichment of food with vitamin and minerals by the working strategy of World Health Organization (Akhtar, 2009).

Another strategy was included to meet the requirements of vitamin A other than dietary supplies of vitamin A is delivering the Vitamin A only or just as part of multivitamin nutritional supplements. In the manufacturing of nutritional supplements of that are available in market, both retinly acetate or retinly palmitate (preformed Vitamin A) and beta-carotene (Provitamin A) are usable (Souganidis *et al.*, 2013). From the viewpoints of intakes of vitamin A, intake of preformed retinol is greater in the developed states of world rather than in undeveloped states in whom Provitamin A (carotenoids) signify the higher food suppliers of Vitamin A. In the US the ratio of children and adolescents that rely on preformed vitamin A and originate it from the preformed food suppliers of vitamin A is eighty percent while usual full grown persons are expected its consumption are greater than sixty five percent (Samad, 2011). While the preschoolers of Uganda state take 5-25% of preformed vitamin A and full grown man eat five to twenty percent of preformed vitamin A (Akhtar *et al.*, 2013). While people in china state consume approximately fifty percent of food from retinol or preformed vitamin A supplies (for the contrasting aims of retinol to other states: when repeatedly measure a bioconversion feature of six to twelve microgram is equals to one microgram retinol/preformed vitamin A) (Akhtar *et al.*, 2010). There are many sources of proformed Vitamin A in which beta-cyptoxanthin are primarily present in orange color citrus fruits, maize or corn of yellowish or orange in color and in few pumpkins. There is also another Provitamin A (carotenoid) that has availability and absorbability equivalent to beta-carotene in animal (Souganidis *et al.*, 2013) as well as in humans (Akhtar *et al.*, 2013). Alternative Provitamin A carotenoids that usually present in human serum is actually alpha-carotene, primarily present in carrots that mainly orange in color and also in few types of pumpkins (Souganidis *et al.*, 2013). As the structural composition (Figure 1), of alpha carotene is different with respect to beta carotene so alpha carotene hypothetically produces ½ the retinol than beta-carotene as such, that has been verified with the help of gerbil procedure (A) (Akhtar *et al.*, 2011).

Retinol (preformed vitamin A) exists in animal tissues, particularly liver and liver oil (cod liver oil), dairy products, and eggs; β-carotene and its precursor

are derived from plant-based foods. Economic and sociocultural determinants lead the world community to rely on plant sources for meeting vitamin A requirements in the form of pro-vitamin, β -carotene, which is subsequently converted into retinol in the gut, and its activity is expressed in retinol activity equivalents (RAE): (1 RAE=1 μ g retinol, 12 μ g β -carotene) (Akhtar *et al.*, 2013). Vitamin A primarily known is present in greater amount in palm oils. red palm oil is that type of oil which has greatest absorption of Provitamin A. These red palm oils are usually used as edible oil in food in West African region (Farombi, 2003). Though, it has been revealed through the latest study that vitamin A activity is 10 times higher in concentrations in buriti palm oil than in red palm oil (Barbosa-Filho *et al.*, 2008). Irrespective of all food sources, preformed vitamin A activity is greater in concentration in animal source of food just like fish livers and fish oils (Zile, 2004). Other food sources of provitamin A includes, dark leafy vegetables, algae, red and yellow vegetables and tubers, red and orange fruits, flowers, and juices, red palm oil. Sources of vitamin A includes milk and milk products, eggs, fish and associated oils, shellfish, liver and organ meats, chicken. We generally divide the food into groups as variety is present in between and also with in the subgroup for both Provitamin A as well as preformed vitamin A because two known supplies of vitamin A

preformed and Provitamin A are very huge and wide. it has been considered that provision of blindness of eyes is greater in regions where rice consumption is greater at the start of introduction of solid foods because white roots and tubers and whole grains are deliberately less in Provitamin A concentration (Bushamuka *et al.*, 2005). It has been observed that strengthening of color does not matter, certainly it is actually not a consistent sign for carotenoids that are biologically active. Just like green leafy vegetables is known as best suppliers of Provitamin A but actually the chlorophyll a compound present in these plants hidden the presence of pigmented carotenoids (Chandrika *et al.*, 2006). Furthermore, such as procedures to explain about shape and structure of carotenoids and its chemical structure in plants are cleared and well known with the help of HPLC for the examination of knowledge about the carotenoids foods, other earlier hypothesis about the Provitamin A food supplies is known to be reviewed. It doesn't clearly described about the equal deposition of preformed vitamin A, it is excellently deposits in liver and kidneys (Zile, 2004). Preformed vitamin A is deposited in the guts walls of fish, in the fatty tissues of eels and in the eyes of specific sub groups shrimp. With the exclusion of bird meat goods consists of beef and pork doesn't consist of important amounts of preformed vitamin A (Chandrika *et al.*, 2006), Table 1.

Table 1: Food sources of Vitamin A

Sr No.	Food item (100g)	Retinol equivalent	β -carotene equivalents	Vitamin A activity
1.	Apple	---	43	7
2.	Apricot (fresh)	---	450-3,500	75-583
3.	Apricot (dried)	---	1,260-6,540	210-1,090
4.	Avocado	---	60-532	10-88
5.	Beef (flesh)	24	5	25
6.	Beef (Kidney)	300	0	300
7.	Beef (liver)	810	180	840
8.	Banana	---	60-130	10-21
9.	Beet	---	2,927	487
10.	Bitter gourd (cooked)	---	13.260	2,210
11.	Blueberry	---	60-170	10-28
12.	Buffalo milk	64	0	64
13.	Cabbage (green)	---	60	10
14.	Carrot	---	7,200	1,200
15.	Cashew	---	760	127
16.	Cassava	---	3,000	500
17.	Chicken (flesh)	10-74	0	10-74
18.	Chicken	6-20	0	6-20
19.	Chikori	---	600-2,1600	100-360
20.	Chile pepper	---	459	77
21.	Cocount oil	---	0	0
22.	Cow milk	27-34	14-22	29-38
23.	Cow pea	---	4,500	4750
24.	Egg (chicken)	260	0	260
25.	Egg (duck)	540	1,200	740
26.	Ghee (cow milk)	270	230	308
27.	Goat (flesh)	0	0	0
28.	Goat (liver)	13,500	2,800	13,967

29.	Goat milk	19-71	0	19-71
30.	Guava	---	80-400	13-67
31.	Kale	---	900-7,580	150-1,263
32.	Lettuce	---	1,950	325
33.	Loquat	---	1,580	263
34.	Mango (unripe)	---	60	10
35.	Mango (ripe)	---	708-2,400	118-400 1
36.	Maize (raw)	---	360	60
37.	Muskmelon	---	620	103
38.	Okra	---	730	121
39.	Olive oil	---	25	4
40.	Oyster raw	90-96	0	90-96
41.	Palm oil	---	304.000	50,667
42.	Papaya	---	300-2.500	50-417
43.	Persimmon	---	3,000	500
44.	Potato	---	2-20	0-3
45.	Pumpkin	---	1000	160
46.	Raspberry	---	60	10
47.	Rice	---	0	0
48.	Sheep flesh	0-45	0	0-45
49.	Sweet potato (raw)	---	1,100-2,700	183-450
50.	Sweet potato (boiled)	---	1.745 291	1.745 291
51.	Tuna	90-96	0	90-96
52.	Turnip yellow (raw)	---	1,620	270
53.	Turnip yellow (cooked)	---	1,320	220
54.	Watermelon	---	50-350	8-58
55.	Yoghurt	23	23	23

Absorption and bioavailability of provitamin A carotenoids:

Approximately 70–90% of preformed vitamin A esters are absorbed and utilized or stored (Blomhoff and Blomhoff, 2006), though the array for the absorption of carotenoids (provitamin A) is wider than other Carotenoids (Provitamin A) is present in both form either in cis form or Trans form. Among thirty five percent and eighty eight percent of engrossed all-*trans* beta-carotene is oxidatively break down by beta-carotene 15, fifteen-dioxygenase one (BCO1) into two molecules all-trans retinal in the inner cells (dela Seña *et al.*, 2014), that can be break down oxidatively permanently to retinoic acid by one to three with the help of retinal dehydrogenases or less converted to retinol by the help of retinal reductase enzyme (Duester *et al.*, 2003, Lietz *et al.*, 2010). Before break down is completed. The cis isomers of vitamin A is changed shape to all-trans shape before BCO1 consequently lessening the effectively conversions of this isomers in human body (Bresnahan *et al.*, 2014). Retinoic acid is also made by the clear procedures of break down that are arbitrated by enzyme beta carotene nine, ten oxygenase (BCO2). This, though, signifies a slight passageway for breakdown of beta-carotene (Keifer *et al.*, 201).

Fat soluble Vitamin A and carotenoids (Provitamin A) are actually fat-soluble vitamins. It is best absorbed in fats and lipids. When it is consumed, then retinly esters are break and dissolved by the general hydrolases and amalgam with fats and salts of

bile for the cells called micelles parallel to the Provitamin a carotenoids. Just as micelles are absorbed into the enterocytes, carotenoids (Provitamin A) is converted into the retinol through beta carotene fifteen, fifteen dioxygenase. Preformed vitamin a which is retinol is than mixed with and form esters with fatty acids then adding into chylomicra parallel to the Provitamin A (carotenoids) that are not break. After that it is passed through lymph and reached into the blood streams and lessens their few of retinly esters and Provitamin A t o the tissues when they are in the movement throughout the body. Eventually, precursor of retinly esters and Provitamin A are given to the hepatic as chylomicrons parts. There are variety of researches that measure the presence of beta carotene in fruits and vegetables in developing states. Presence of beta carotene and its conversion in human body is lessened in (West *et al.*, 2002) and it is good from oranges (Tang *et al.*, 2009). The causal features of accessibility in humans secret from plants manipulating the presence of availability in living organism as well as place of carotenoids (Provitamin A) within the chromolplast as opposite to the chloroplast It has been noted that cooking methods and fire also effect on the absorption and bioavailability of vitamin A in plants , and these procedures generally consequently greater in availability in human beings (Tanumihardjo *et al.*, 2010). As a result of this multifaceted and different absorption pathway, considerenses have been higher with respect to people whom are actually reliant highly on vegetables sources (Jiménez-Monreal *et al.*, 2009),

and fruit to fulfill the recommended amount of vitamin A (Tanumihardjo *et al.*, 2010).

It has been revealed through the present studies about the procedures to consider the changing and eventual deposition of vitamin A from the plant sources that are questionable now. For example, with the help of latest dilution technology of sensitive isotopes that are stable in environment, greenish and yellowish color vegetables are capable of fulfill the total body vitamin deposits in ten weeks of intervention (Jiménez-Monreal *et al.*, 2009). Also, procedures and strategies used with isotopes have a long range of stable isotope for Provitamin A convert from varied supplies of plant (Tanumihardjo *et al.*, 2010). The bioconversion mass ratio of β -carotene equivalents in various food matrices to yield 1 μg vitamin A ranged from high values of 21:1 in spinach and 15:1 in carrots (Tang *et al.*, 2005), moderate values of 13:1 for sweet potatoes, and 10:1 for pureed spinach (Haskell *et al.*, 2004) and low values of ~2:1 in genetically engineered Golden rice (Tang *et al.*, 2010). Actually, these varieties is because of reason of different amount of statuses of vitamin A in study participants for example in Vitamin A shortage persons may break Provitamin A at greater degree consequently higher efficiency of absorption in living organism (Gannon *et al.*, 2014).

Because green vegetables that are leafy in appearance, poor carotenoids (Provitamin A) is proposed through green and other varied vegetables so it's can be improved by through diet which include the approaches to enriched and fortified sources of vitamin A (Chandrika *et al.*, 2006 West *et al.*, 2008, Johns *et al.*, 204, Faber *et al.*, 2002) consist of approaches of:

- Elevation of dietary supplies of preformed vitamin A (for example ; animal and enriched foods),
- Advancement of a broader selection of larger Provitamin A carotenoid-comprising dietary items, including bio-fortified wheat and staple food, and
- Food productions procedures that boost Provitamin A (carotenoid) captivation.

Separately or mixture, of these strategies suggesting the applied schemes for boosting vitamin A degree (West *et al.*, 2009).

Physiology of Vitamin A:

Fat soluble vitamin A is compulsory for the normal functioning and working of variety of the procedures that is carry on with in the human body as well as it help us to prevent from the night blindness and the maintenance of outer layer of body, strong the body defense and immune system for human body security, growth and development of body, and the increase the size and weight of fetus with in the womb of mother. Preformed Vitamin A (retinol) is basically the precursors for two or more naturally fundamental moveable parts of elements: it has been seen that all particles of trans retinoic acids are acting as undermining as well as make the substance or mixture formation of particle receptors just like retinoic acid receptors (Blomhoff and Blomhoff, 2006; Herforth, 2010), and eleven-cis preformed (vitamin A) retinal is essential in the pathway of optic (Ahmed *et al.*, 2012; Von-Lintig, 2010).

Vision

Eleventh -cis preformed vitamin A which is compulsory for the pathway of optic connect to the protein opsin (that forms the part of visual pigment rhodopsin by the action of light) with optic pigment known as rhodopsin (present in the rods of retina) thus it makes light with in the normal limit ad gives the clear image of everything. When the eleven-cis preformed vitamin A retinal join with a light emitting particle photon: it modify into all tarns preformed Retinal and it emit and released from the protein opsin after it. The alteration of eleventh cis retinal is comprises of a new thing discovered in optical pathway, Figure 4. A thrilled internal part of the rod of visual pigment rhodopsin greatly strengthen the ignition and provoke of light by changing the membrane potential pf the pole film thus it causative factor of stage of the movement of power for nerves that is helpful in normal vision (Kam *et al.*, 2012).

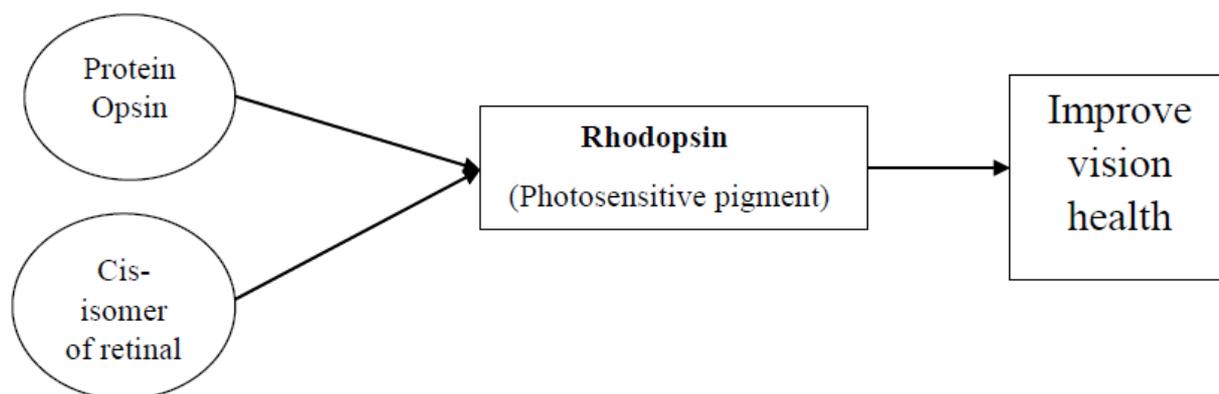


Figure4. Retinal for vision health

Nuclear receptors/gene regulation

It has been seen that essential and organic and pertinent part of vitamin A is all trans retinoic corrosive. In Eyes Irritation/ Eyes damage adhered and triggers with some particle that respond to some compounds just like retinoic acid receptors, retinoid X stimulants and Peroxisome-proliferator-activated receptors (Kiser *et al.*, 2013). When element combine and adhere and form ligand and do it imposing their act in pathway, retinoic acid receptors attach and form dimers with a retinoid X receptor to form a new structure of a different composition heterodimer, that it interfere the quality at that stage by the basic retinoic acid induced eyes irritation which is the part in advocating zone of greater than five hundred genes that are at target (Blomhoff and Blomhoff, 2006).

Vitamin A Absorption:

Some alimentary form of retinol ester that eventually form retinol that necessarily break down at the adjacent and earlier part of inside of small intestine, when it move to engrossed in cells of large intestine (Von-Lintig, 2010). Few food enhancement are done in the new formed structure of acetic acid and hypothesized that it's not present with in the body secretion and absorbed untarnished in the absence of water break down in the intestines previously (Kam *et al.*, 2012). When retinol is break down in the intestine and grasp through the cells of mucosa, preformed vitamin A again form the ester with large shape composed structure with the help of previously engrossed fatty acids just like palmitate with the help of enzyme (catalysis) lecithin: retinol acyltransferase (Kiser *et al.*, 2013). Finally the resulting retinyl esters are combined with other neutral fat formed esters into lipoprotein formed in gut and released through the ways of lymphatic channel with in the universal circulation. It has been seen that large components of lipoproteins formed in gut (chylomicrons triglycerides is break down with the help of lipoprotein lipase enzyme in liver cells that is present outside of the liver. Few ester that is formed by the retinyl are released into outer tissue of liver from the lipoprotein chylomicrons (129), especially in the pulmonary region and spleen (Al Tanoury *et al.*, 2013), although its larger portion is deposit in the hepatic region (Harrison, 2005; Penniston *et al.*, 2006).

Vitamin A in the liver

The remaining metabolites of lipoprotein (chylomicrons) that composed of greater proportion of newly formed esters/ large chains of ester of retinyl, which is grasped into hepatic portion at that place esters of retinyl is break down in the presence of water into the retinol which is preformed vitamin where it is either capable of bonding with retinol restricting protein or form esters again with the help of fatty acids with the help of Lecithin Retinol Acyltransferase (human enzyme) LRAT (Kiser *et al.*, 2013). When fat soluble vitamin A is in appropriate amount, hepatic is the

region where the vitamin A is deposited with greater than ninety five percent of all preformed vitamin A (retinol) form ester with the help of fatty acids generally forms retinyl stearate and palmitate in the person which has appropriate amount of vitamin A. little amount of retinyl esters are extracted and given from the alimentary system and renal organ. (Penniston *et al.*, 2006, D'Ambrosio *et al.*, 2011). Adipose tissues is of the great importance for the deposit and storing site for fat soluble vitamins (Riabroy and Tanumihardjo, 2014), mainly persons of adequate vitamin A. Before it is stimulated form hepatic organ, retinyl esters are broken down in the presence of water and arbitrary retinol is formed compound and mixture with retinol binding protein for the release from the hepatic region into blood (Kiser *et al.*, 2013). Retinol binding protein form mixture with retinol is further equals with the help of imposing transthyretin in blood part (plasma) (Senoo *et al.*, 2013).

In two thousand seven, stimulated and maintained the level by retinoic corrosive six stimulants was perceived as separate as superficial layer of stimulants for retinol binding protein to released retinol or preformed vitamin A (Yang *et al.*, 2005). STRA6, notwithstanding, isn't communicated in all cell types, and concentrates in Stra6-lacking mice propose that there are different pathways that encourage retinol take-up into cells (Zanotti and Berni, 2004). As these cell lines that take part sufficiently and with proper proportion from within the lipoproteins of gut (chylomicrons) or varieties of these lipoproteins are most probably those that distribute alpha-retinol that don't connect the retinol binding proteins. (Ruiz *et al.*, 2012, Dever *et al.*, 2010). Alpha retinol which is form of preformed vitamin A has been originated from the structure of alpha carotene and provisions of growth in vitamin A insufficient animals like rodents (Paik *et al.*, 2004).

Vitamin A homeostasis and storage

Complete vitamin A deposition maintains the vitamin A balance (Ouchi *et al.*, 2011). Nutrient A status additionally by implication directs bioconversion of provitamin A carotenoids to retinol (Riabroy *et al.*, 2014). Alteration with in the human body is done with in the alimentary canal and is engaged with the help of consumption practice stimulants supervisory mechanism (Jang *et al.*, 2000). The declaration of gastrointestinal zone categorical compartment in body clarification feature (ISX) is triggered by retinoic corrosive with the help of retinoic acid receptors to this type of difficulty in a specific retinoic damage response constituent present with in the interpretation feature six advocator. When triggered, clarification feature six suffocates the alimentary freeloader of class B of degree one and Beta-carotene Oxygenase one (BCO1) show their expression, representing that alimentary provitamin A involved and dietary A group are below undesirable involvement regulator with the help of

armament of Interference factor six expression (Ribaya-Mercado *et al.*, 2000).

It cannot be described yet that at what extent storage and deposition as well as alteration in body of Provitamin A is under the effect of hepatic vitamin A storage. (Jang *et al.*, 2000). In any situation, like wise children of Zambian region with the toxicity of vitamin A is examined by usage of maintain isotope flagging (Gannon *et al.*, 2014), it also had been scene of larger carotenoids deposited in serum (Leitz *et al.*, 2010) and greater number of persons have high level of carotenoids in their blood in the middle of mango weather, the season of larger carotenoids production (because of yellow and orange colored fruits and vegetables) (Lobo *et al.*, 2010). It had been seen that at the degree of average assessed hepatic dietary factor and emphasis at or above the current ratio of high level of vitamin A) greater than one micromole per gram of hepatic ratio thus Provitamin A eating cannot truly obstructed. In an animal model like rodents that have reduced vitamin A balance, vitamin A utilization is disappeared after equivalence (Dever *et al.*, 2010). As a model of gerbil display it has been noted that alteration of Provitamin A carotenoid with in the human body at the moderate in hepatic organ secure alteration of zero point four micromole per gram (Tanumihardjo *et al.*, 2010; Mondloch *et al.*, 2015), suggesting that in any place are in the degree of zero point one to zero point four micromole per gram the human body is in the balanced state (Al Tanoury *et al.*, 2013). When the range cross the limit of zero point four micromole per gram of hepatic region then disappeared plant source Provitamin A carotenoid alteration and modification most probably is the determinants of Provitamin A deposition in serum in the persons that are more rely on plant food sources in their diet as has been shown in Zambian children. (Gannon *et al.*, 2014; Leitz *et al.*, 2010; Jang *et al.*, 2000).

Vitamin A interactions with other nutrients

Relationship of dietary components as an adjunction has been shown among the retinol or carotenoids and both of energy giving components and variety of small components of diet.

Iodine

It has been described that Nutrient A degree and level maintains and normalize the level of thyroid glands and proteins that triggers an action of absorption and production of the protein of thyroid: thyrotropin from the anterior part of pituitary glands. Vitamin A shortage is seen to associate with the with the shortage of vitamin A mediated the stoppage the expression or response of pituitary thyroid animating hormone(protein) beta genetic factor and its expression as well as associated raising thyroid stimulating hormone and abnormal enlargement of eyes (Tanumihardjo, *et al.*, 2015). A study was conducted on the kids of Moroccan that has been suffered from

concurrent deficiencies of food components just like of vitamin a and Iodine. Those persons that take both the salt enriched with Iodine and vitamin A adjunct provoke the feasibility in these health ailments because of shortage of Iodine (Tanumihardjo, 2008). An insufficiency may not reduce the presence of Iodine present in food to report the problems of shortage of iodine and greater amount of Vitamin A enrichment may decreases the excessive excretion of thyroid and threat of enlargement of thyroid gland (Tanumihardjo, *et al.*, 2015).

Iron

Maintaining the vitamin A status in human body provoke and improve the hemoglobin response to the enhancement of iron during the puberty state and child giving state (Tanumihardjo, 2008; Zimmermann, 2007). A study was conducted on the population of Indonesian conceived ladies (Zimmermann *et al.*, 2004), in which a small group is taken as experimental subject, degree and level of vitamin A when measured is provoke and upgraded in their values in blood specifically when we use mixture and amalgam of iron as well as vitamin A rather than tablets use of these nutrient separately, when they bring the modification and alteration in vitamin A amount through corresponding amount reaction test (Ahmed *et al.*, 2001). In newly birth infants of human, enhancement of iron nutrient is the main determinant of sufficient concentration of retinol in its plasma state although it also provoked and enhanced the deposition of vitamin A in hepatic organ (Muslimatun *et al.*, 2001). A study was conducted on the Ethiopian children in which separate and one large amount of vitamin A nutrient is given to them, the results is the enhanced status of hemoglobin as well as iron in these kids (Tanumihardjo, 2002).

Zinc

Micronutrient as vitamin A and Zinc work in a team and associate with each other to perform some essential roles and physiology in the human body. Consequently, deficiency of mineral Zinc and its shortage in the human body act as a causative agent to effect on the level of fat soluble vitamin A in the human body. It had been described in an article on human that stated that Zinc mineral is actually a job of supporting the enzymes in a chemical reaction and improved that reaction known as co-factor in the reaction of beta-carotene Oxygenase one (BCO1) (Wieringa *et al.*, 2003) although, exact function or role has not be clearly showed. Indeed , vitamin a is a fat soluble vitamin , alimentary fat and fat in foodstuff take some time for the understanding of effect of absorption of bothe plant source of vitamin A (Provitamin A-carotenoids) and animal source Preformed vitamin A (retinol. Retinal) (Gebremedhin, 2014). It has been showed through the studies of that impact and outcome of fat in the human body to the plant source provided Provitamin A as in carotenoids deposition and storage as well as its

absorption in human body explanatory this procedure and consist of the following hypothesis: varieties of studies have done the investigation on this procedure and showed that plant source Provitamin A which comprises of carotenoids has enhanced its own ingestion and digestion as well its deposition in the human through inclusion of enhanced fats in our food that further provoke the inclusion of it in to micelles (specific cells for the digestion of fat) (Jang, 2000).

In a study when we give categorized and classified quantity of fat given to the animals in their diet then the effectiveness of absorption of beta carotene present in yams was enhanced with the larger quantity of dietary fats (Lederberg, 2003). Only when we include three to five grams of fat per consumption time then it actually carry the impact on the digestion and absorption of beta carotene in variety of persons (Dijkhuizen *et al.*, 2004). Just 3– 5 g fat/meal guarantees effective ingestion of β -carotene in people (WHO, 2011; Mills *et al.*, 2008). It has been in many experimental subjects like animals that carotenoids convert its full active form of retinol in the human body when the animals consume the diet higher in amount of medium chain unsaturated fatty acids as well as poly unsaturated fatty acids of omega three and omega six in their consumption. It has been seen that energy producing components of food (protein) also gives influence on the impact of modification. When we consume appropriate amount of protein (which is an essential in the production of Beta carotene oxygenase one in body) in eating time then the optimum effect is achieved (Jang *et al.*, 2000).

Implications for Public Health:

Vitamin a is helpful in the regulations of variety of function in the human body, it is only include in the normal and own functioning of human body but its also helpful in the differentiation of current and fresh causative agents for specific diseases which is beneficial in hospital based studies as well as in individuals based studies. there are variety of people which are more vulnerable to the insufficiency and toxicity of fat soluble vitamin A .

Vulnerable Groups for Deficiency and Excess

Risk of vitamin A deficiency

- Premature new born that are at the risk of shortage of storage as the result of reduced deposition of vitamin A during the growth time in womb of mothers.
- Specifically mothers of new born infants kids, whom are actually have shortage of vitamin A during the period of milk production and giving to their kids.
- Persons who have been suffered from variety of diseases just like malabsorption of bile production genetically and ailments of respiratory tracts.

- Persons spent lives in the severe shortage of resources of food
- persons which are more rely on alcohol consumption

Risk of vitamin A excess:

Persons that are more include the vitamin A enhanced foodstuffs and consume animals meat as well as overconsumption of adjunctive form of Vitamin A in retinol shape are at the vulnerable state of vitamin A toxicity.

Regulatory Roles of Vitamin A in Immune Function:

Exact function of vitamin A is shown in animals of birth giving age and concluded that vitamin A has a role of regulation of leaving of outer layer of body and strong immune system of body. (Ribaya-Mercado, 2002). It has been seen through the experimental study conducted on animals and concluded that fat soluble vitamin A has a role of maintenance of proper defense function inside of the body by the rescue of hindrances with in the pathway of mucosal cells and these hindrances is causative factor of damage that is shown in through the infection in kids as well as it provokes the physiology of white blood cells like macrophages (engulfing substances), neutrophils and Nuclear factor K- beta cells (biomarkers of inflammation in body) (Ribaya-Mercado, 2002). Vitamin A is compulsory for the enhancement of ability of defense system and perform the function of increases the upgradation of helper T cells, maintenance of T cells and lymphocyte B cells of although there is a need of greater research is required in this area (Ribaya-Mercado *et al.*, 2007). Its generation by cells of the immune system is managed during an immune reaction in a manner that is as yet being explained (Stephensen, 2001). All trans preformed vitamin A (retinoic acid) stopped the manufacturing of chemicals they secrete and which promote the manufacturing of helper t cells of type one which is the sub types of Helper T cells and provoke the manufacturing of chemicals that secreted by these cells for the regulation of helper t cells of type two as seen in T lymphocytes of individuals (Pino-Lagos *et al.*, 2008).

REGULATORY ROLES OF VITAMIN A:

Anemia:

Iron level is greatly effected through the fat soluble vitamin A level in body. Fortification of fat soluble vitamin A with Hemoglobin producing adjuncts provoke the iron production than the use of fortification in tablets in separately used (Zimmermann, 2007).

Cancer

Preformed vitamin A (few retinoid) has a role of stoppage of growth and proliferation of variety of begins cancers like tumors (abnormal growth of cells that are localized) and they helpful in the treatment of cancer through the chemically treated and prevented methods (Wu *et al.*, 2015; Altucci and Gronemeyer,

2011). All-trans retinoic corrosive is utilized as a chemotherapeutic specialist to treat intense promyelocytic leukemia, and in most by far of these

patients this treatment prompts a total abatement (Niles, 2000).

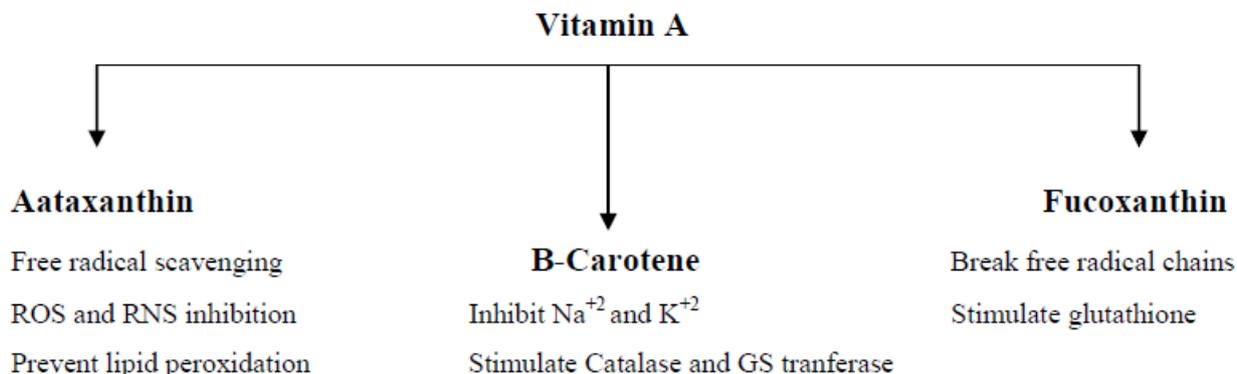


Figure 5: Antioxidant activity of vitamin A

DIABETES

It has been seen in the infected persons of class one diabetes mellitus, and show that Preformed vitamin A is linked with the reduced amount of preformed vitamin A(retinol) and it’s carrier enzymes (proteins) like retinol binding proteins and other proteins (Siddikuzzaman and Berlin Grace, 2011). It has been ambiguously bonded seen among the preformed vitamin A and (retinol) and its carriers enzymes, deep research described that vitamin A has no function in the treatment and preventive function of class two Diabetes (Wang and Chen, 2008). It has been described that insufficiency and overproduction of vitamin A have fluctuating and discordant effect on the energy producing chemicals and its absorption in variety of tissues as well as in various cells (Xu and Venge, 2000; Iqbal, 2015). It has been seen that it is involved in upraded and provoke of islets of Langerhans and its ability: inappropriateness is the causative factor of beta cells mass reduction in the infants with in the womb of mother (Xu and Venge, 2000) As well as it disappeared the secretion of islets of Langerhans from its alpha and beta cells individually (Xu and Venge, 2000; Iqbal, 2015). When retinol binding protein is released from the adipose tissues have been included as a bonded between the insulin firmness and hindrances of insulin through the inquisitive of insulin movements in tissues and larger the liver production of insulin. Preformed vitamin A binding protein: retinol binding protein is risk factor of antagonist of insulin secretion by inclusion of fats cells production irascibility with the help of secretion of chemicals of immune system before inflammatory reaction and the gadget is retinol-and other components independently (Chen and Chen, 2014).

Energy Metabolism and Obesity

It has been seen in animal models like in live mouse and working with protein manufacturing of C and this shows that preformed vitamin A fortification is supporting compound of enzymes known as co-factor in

metabolism reaction and actually included in the maintenance of power usage of mitochondria (Norseen *et al.*, 2012).

HIV and Pregnancy

There has been no confirmed evidence of usage of fortified vitamin A impact on Human immunodeficiency virus conduction is present in an erect manner. In this manner world Health Organization doesn’t include the promotion of fortification and adjunction of Vitamin A in birth giving women of Human immunodeficiency virus active women to reduces the complication as well as its further impact on the health of ladies that dives the birth to new born and has the alarm of conduction of this virus to the new born infant (Ziouzenkova *et al.*, 2007). A known as Cochrane reviews described that separately use of fat soluble vitamin A (Shabrova *et al.*, 2015) and as well as fortification of vitamin and minerals (Awasthi *et al.*, 2013) could not bees used as an alternative recommended for anti HIV in recommendation.

Measles

It has been researched relied upon the Based on an arbitrary, false management organized medical earliest in adolescents and children with ailments, parallel to different experimental study, it has been demonstrated though the recommendations of World Health Organization that amount of fat soluble vitamin A that is appropriate for age is set as 2 times in twenty four hour , alienated for the infants and children suffered from ailments (measles) in public at where vitamin A inadequacy may be present to disappear the hazard of expiry form the health ailments(measles) (Siegfried *et al.*, 2012). Replacement of food greater in the amount of animals derived food sources than the products fortification of vitamin A in the form of capsules of vitamin A as an adjunctive at the area of vitamin A inadequacy is actually a common clinical matter disappeared the issues of existence and epidemic

of health ailments (measles) in the infants and children of six to fifty nine months of age (Kuhn *et al.*, 2006).

Fortification efforts with preformed vitamin A.

There have been showed that enhanced and enriched fundamental food that has been eaten on daily basis are eaten by large group of people and are more preferable to consumed by ladies and females at the household level opposite of the branded and high priced food stuff that are typically eaten by the men of household level. However, to remove and reduce the level of hemoglobin in the females and kids, 2 types of enrichment inventive of staple food like wheat that is consumed daily, obviously purposeful for the reduction of hemoglobin deficiency. Micronutrient enterprise specifically take the task of upgraded and provoke the health of mothers than their previous status of health but it cannot seen in working condition like they cannot In touch with brand that are in the race of selling their food items just like the enterprises of utility stores corporation of eatable fats and oil (WHO, 2016).

Food fortification with preformed vitamin A is a viable option that can be 2–4 times more cost-effective in providing vitamin A than either capsule distribution with preformed retinyl palmitate or dietary diversification efforts (Mayo-Wilson *et al.*, 2011). Fortification with vitamin A has been used successfully in the developed world for >80 y, and its potential was recognized in the developing world 40 y ago. In general, food fortification with vitamin A has the advantages of being socially acceptable and requiring minimal changes in food habits.

Provision of fat soluble Vitamin A can be used in the form of enrichment of food that available in market is most appropriate option for two to four degree greatly suitable for budget than vitamin A is provided in the form of capsules to fulfill their requirement of vitamin A in body. (Gazdar and Zuberi, 2015). Enrichment of eating things with fat soluble micronutrient (vitamin A) is advantageous for its consumption for greater than eighty years in the variety of states, and it is helpful to working as forty years in the progressive states (Dary and Hurrell, 2006). Enrichment of food has been influential and essential at the country state to fulfill the few conditions of fulfillment of food. It has been seen that its crucial task for the government and decision making persons of a country to reach to certain styles that are essential for the assets with the help of profitable funds and it also seem to the beneficial for the risky group of a state to reach these styles and methodologies (Dary and Mora, 2002). There are variety of enrichment of eating stuff that are present in the market just like it is necessary option for the organization named as west Pakistan of application of pure food rules to enriched fats and oils with micronutrients especially with vitamin A in nineteen hundred and sixty five and this option is

considered vital for all the cities of Pakistan (Fiedler and Lividini, 2014).

Risk Factors

Populations affected by VAD imperiled to poor housing conditions, presence of comorbidities and depletion of serum retinol level out of these infections are ones that enforces the need or encourage endogenous losses of vitamin A, and protein-energy malnutrition (PEM), affecting the formation of retinol binding protein (RBP), thus lowering retinol availability (de Cássia Ribeiro-Silva *et al.*, 2014). Decreased dietary intake of preformed vitamin A and its precursors, together with a high prevalence of infectious diseases, like diarrhea, measles, and respiratory tract infections are commonly linked with VAD. An insufficient dietary vitamin A bring about lowered serum vitamin A levels, causing several physiological implications, especially tissue development, metabolism, and infection resistance (Chopra *et al.*, 2009).

Factors Affecting Vitamin A Deficiency in School Going Children

Various factors are leading to vitamin A deficiency in school going children. These factors include dietary factors such as low ingestion of dark green leafy vegetables, low consumption of dairy products and the low intake of energy and other nutrients. Other than dietary factors the risk factors for vitamin A deficiency include low socioeconomic status, the number of family members living together, the number of working members of a family, education of parents including both mother and father. The nutritional status of the children as malnourishment in terms of under nutrition and over nutrition (WHO, 2009). Diet is the most important risk factor that should not be neglected. A poor dietary habit and lack of vitamin A in diet can directly lead to the deficiency of vitamin A. In school going children, the intake of vitamin A rich food including both plant and animal sources leads to poor status of vitamin A in children of school going age (Sachdeva *et al.*, 2011). Lack of the consumption of dairy products including milk, liver of animals, cod liver oil, eggs and beta carotene from the plant based products also contribute to vitamin A deficiency (Singh and West, 2004). Less consumption of dark green leafy vegetables growing wild in the country side is also a factor involve in the prevalence of vitamin A deficiency (120). Diets poor in vitamin A results in decreased serum vitamin A levels, causing numerous physiological implications, specifically tissue development, metabolism, and resistance to infections. Severe VAD is the most common cause of preventable blindness among children as it leads to xerophthalmia, (Ramakrishnan and Darnton-Hill, 2002).

Leaves of many cole, root, and bulb crops such as cauliflower, cabbage, beets, and radish are also sources of vitamin A. the leaves of these vegetables are not utilized by our children. These leaves are usually

discarded after the use of these vegetables by our mothers. This is also one of the main reason that contribute to vitamin A deficiency (Thurnham *et al.*, 2003). Various religious and economic factors are also a leading cause of vitamin A deficiency. In some religions dairy products are restricted. Low consumption of dairy products always be a case because the school going children have low consumption of vegetables which are the source of beta carotene (WHO, 2009) The most important factor that leads to vitamin A deficiency in school going children is child's nutritional status and co morbidities other than distal socio-demographic factors (Akhtar *et al.*, 2014). The other factors that indirectly related to vitamin A deficiency impaired mechanisms of host resistance, increased severity of infection, anemia, poor growth and mortality. Gestational and postpartum vitamin A deficiency might also increase the risk of deficiencies in the age of school going in children (Ahmed *et al.*, 2012). Vitamin A deficiencies in mothers, repeated pregnancies of vitamin A deficiency in mothers can be chronic which leads to deficiencies in children in early age, school going and even in adolescent period (Ramakrishnan and Darnton-Hill, 2002). Maternal Night Blindness is also a risk factor for both mothers and children (Samba 2010). Age can also be a risk factor because the school age children have lower health and nutritional status in the developing countries. This lower risk profile is also a risk factor for vitamin A deficiency and its disorders (Chauhan *et al.*, 2011). The infants who are not breast fed and who take little or no milk in their early life are deficient in vitamin A including the infants who did not receive colostrum are more likely to suffer from vitamin A in their school going age (Mahmood *et al.*, 2008).

Poor bioavailability is another factor that fulfills a chief function in the development of VAD in those who rely only on plant sources to meet their nutritional deficiencies (Swati and Esam, 2012). Economic crisis of the countries and the socioeconomic status of the population living in the country are also the factors that are indirectly contributing to the poor nutritional status primary vitamin A deficiency in children (FAO, 2009). Availability of vitamin A rich foods, is also important in contributing vitamin A deficiency. We have less production of green leafy vegetables in our home gardens and the countries facing economic crisis are also producing less fruits and vegetables. The population face unavailability of these products leads to vitamin A deficiency (Faber, 2011). Education of parents including both mothers and fathers are important to prevent their children from vitamin A deficiency because the educated parents can understand the beneficial effects of consuming fruits and vegetables. They also better understand the earlier signs of vitamin A deficiencies which help them to prevent their children from these deficiencies. Different studies shows that improvement in better knowledge and understanding of mothers related to health issues and

vitamin A deficiency leads to better health status of their children (Demissie *et al.*, 2009).

Intestinal parasites infections also contribute to vitamin deficiency. Almost 4.5 billion people are people are affected by vitamin A deficiency due to these infections all around the world. Round worms, usually known as *Ascaris lumbricoides*, causing many intestinal parasitic diseases in the developing countries. The Trichuriasis is linked with the low vitamin A status in the teenage school girls living a poor life in Sri Lanka. Illness caused by contaminated food clearly had a bad effect on the people's health and economics status living in the developing countries. There are food safety issues due to high temperature and humidity in these countries. The high temperature and humidity might cause Mould proliferation in the stored food. In South Asian developing counties VAD risk can be reduced by environmental sanitation, proper hygiene safe water supply, and food safety, regular deforming and immunization against diphtheria, tetanus, typhoid, pertussis and cholera. The proper hygiene and sanitation may help to remove their poorer economic status, in addition with the antihelminthic therapy (Sinha *et al.*, 2011). Due to the absence of many basic facilities such as safe drinking water, proper housing, drainage and disposal of wastage makes the population in the city more affected by the infectious diseases. This may also have effect on the health of those which are living in those cities. There is less research on school going children and its effect on vitamin A deficiency due to poor water and sanitary system. There is research in the urban area of Bareilly which is, basically on the school children having age from 3-12 years, on the effect of vitamin A deficiency. This research also contains material to identify the connected biosocial factors and it suggests the preventive measures for the xerophthalmia among them (Arlappa, 2013).

Not only insufficient dietary vitamin A results in xerophthalmia but it also linked with ignorance, poverty, false dietary habits of the society but especially among young children (van Jaarsveld *et al.*, 2005) Other than the entire population the young people including school going children are most likely to be effected by the vitamin A deficiency. This might be because they have poor eating habits, mostly avoid food containing Vitamin A. The basic cause is poor intake of Vitamin A rich food due to poor wealth. Ignorance of vitamin A rich foods and faulty eating habits may also leads to vitamin A deficiency in population (Faber and Laurie, 2011). In Bangladesh more than 20 million children women are suffering from micronutrient deficiency including vitamin A deficiency due to poor consumption of fruits and vegetables in their diet, lack of awareness and education (Muhit *et al.*, 2007) In African countries the causes of VAD are poor dietary habits, poor maternal education and low economic status. School going children are more prevalent to VAD due to their less consumption of vitamin A rich

foods (Jingxiong *et al.*, 2006). In China the main cause of vitamin A deficiency is poor education and the more children are suffering from vitamin D deficiency in western provinces of China because of poor education as compared with eastern areas of China (NNS, 2011). In Pakistan poor health of pregnant and breast feeding mothers, lack of education and awareness among population, unhygienic conditions in rural areas, low consumption of fruits and vegetables in school going children are the factors that lead to vitamin A deficiency (Thompson and Amoroso, 2014).

Vitamin A Deficiency:

Approximately one-third of the world's population is affected by micronutrient deficiencies as vitamins and minerals collectively pronounced as "Hidden Hunger" (Stevens *et al.*, 2015). Globally tetrad micronutrient as Iodine, iron, vitamin A and Zinc deficiencies and its associated health outcomes are among the highest prevailing public health issues. In low- and middle income countries approximately one third of children less than 5 years of age get afflicted with vitamin A deficiency (VAD) (Thompson and Amoroso, 2014). Improvement in vitamin A rank can remarkably create difference in overall child health, ocular manifestation and wellbeing (Akhtar *et al.*, 2013). Measles sufferer children were likely to develop VAD and Pakistan is considered as a country with "severe subclinical deficiency of vitamin A" (143). The data has shown that every year approx. 250,000 to 500,000 children suffer childhood blindness due to insufficient intake of vitamin A is linked with childhood blindness in approximately 250,000 to 500,000 children every year leading to compromised immune system (State of the World Report 2015). Low socioeconomic countries and women of child bearing age are more susceptible to Vitamin A deficiency (VAD) (144). Vulnerable group is categorized as preschool age children, women of child bearing age as expectant and lactating females. Children and adolescents are among the vulnerable group for the onset of vitamin A deficiency. Vitamin A is important in these phases for proper physical development and growth (Gaffey *et al.*, 2014).

Food deficiencies with reference to imbalanced micronutrient intake has directly or indirectly due to disease burden, has shown huge impact on the economy of a country during the current scenario and in future it is expected to continue if not properly taken care. The accumulated economic consequences (Lost workforce, lost future productivity, lost current productivity, current healthcare costs) value spread over 10-year period is in the range of \$ 12.252 billion. Vitamin A deficiency among children under 5 years of age is generally characterized as $<0.35\mu\text{mol/L}$ severe deficient, $<0.35\text{-}0.70\mu\text{mol/L}$ mild deficiency and vitamin A level $>0.70\mu\text{mol/L}$ is considered as non-deficient or normal. Overall knowledge regarding the importance of vitamin A in Pakistan was 24%,

according to NNS 2011. In Pakistan 54% of the children less than five years of age are vitamin A deficient, 33.1 % were moderately deficient and 20.9% were severally deficient. Whereas, vitamin A deficiency, as measured by serum retinol levels, was quoted among 6% of mothers and 12.5% of pre-school children to be deficient. 58% mothers lacked in knowledge regarding foods contain vitamin A, whereas 78.1% of mothers were not aware about the consequences of vitamin A deficiency and only 7.2% mentioned night blindness to caused by vitamin A deficiency (Tanumihardjo *et al.*, 2016).

VAD Disorders

VAD is nowadays recognized as a national problem of 'public health significance' in over sixty countries. People with other comorbidities as cirrhosis and malabsorption are more prone to develop VAD. Because of higher energy demands, requirements for vitamins increased during adolescence as thiamine, riboflavin and niacin are necessary for the release of energy from carbohydrates. Folic acid and vitamin B-12 is needed for growth and sexual maturation. Vitamin D is needed for rapid growth of skeletal muscles. Vitamins A, C, and E are needed in increased amount for new cell growths. Adolescents vitamin needs are also associated with the degree of maturity rather than chronological age because of demands of growth (NNS, 2011). Vitamin A deficiency (VAD) is a nutritional deficiency of high magnitude that can be caused by insufficient intake of vitamin A food sources or by vitamin absorption, transport, or metabolism problems (Gaffey *et al.*, 2014).

Anemia

VAD is documented to cause anemia, termed as 'vitamin A deficiency anemia'. Vitamin A seems to impact anemia through modification of hematopoiesis, by improvement of immunity to infectious diseases and, hence, the anemia of infection, and through the modulation of iron metabolism. Epidemiological studies had shown that vitamin A deficiency in developing countries is linked with prevalence of anemia in populations (Semba & Bloem, 2002). Adolescence is a period of rapid growth, during that period requirements of micronutrients as iron and vitamin A level lead to increase in lean body mass and total body volume during the growth spurt, and following the menarche. Adolescents are at increased risk of developing anemia, with or without iron deficiency where other risk factors of anemia are found as malaria, tapeworm infestations or in adequate food supply. Vitamin A requirements also rise significantly during puberty reflecting the role of this nutrient in sexual maturation. Vitamin A is linked to play a pivotal role in immune system functioning and overall growth and development whereas its deficiency worsen the normal functioning (Leenstra *et al.*, 2009).

Autism

Autism spectrum disorders (ASDs) comprised of set of neurological disorders called developmental disorders manifests as difficulties in social communication and onset of repetitive behaviors and interests. Neurodevelopment is affected by vitamin A deficiency in gestation period by onset of autistic-like behaviors due to alterations in RAR β signal suppression of CD38 expression in the hypothalamus of the offspring, that can be improved by vitamin A supplementation during the early-life period (Lai *et al.*, 2018). Vitamin A deficiency is linked to unusual dietary habits, patients with psychotic conditions such as autism, food obsession and anorexia nervosa linked with hypovitaminosis A with the manifestation of disorders as retinopathy, xerophthalmia, and a characteristic rash phrynodema (Duignan, Kenna, Watson, Fitzsimon, & Brosnahan, 2015).

OPHTHALMIC CHARACTERISTICS

Xerophthalmia

The mildest forms of xerophthalmia as nightblindness and Bitot's spots are more prevalent in pregnant women and children in the general population is associated with vitamin A deficiency. An estimated 5–10 million children develop some form of xerophthalmia is major cause of blindness in about 5–10 million children and is associated by measles especially in Africa (Duignan *et al.*, 2015).

Nightblindness (XN)

Ophthalmic manifestation of VAD is associated with scarce restoration of rhodopsin. Young children and young women especially during their third trimester of pregnancy are mostly affected by VAD and have difficulty seeing under low lighting. This inability to dark-adapt prevents them from finding their way around at dawn or dusk. Children characteristically sit in a secure corner, unable to find their food or toys. Other conditions cause nightblindness, but these are rare in comparison and often genetically determined (retinitis pigmentosa, congenital stationary nightblindness). The diagnosis is readily made on objective criteria (testing vision in a darkened room; formal dark-adaptometry), but this is rarely necessary. Mothers readily recognize the problem, and populations in which deficiency is endemic usually have a specific word for the condition (commonly translated as 'chicken blindness', since chickens lack rods and cannot see at night). Nightblindness is rapidly reversed by systemic vitamin A (Congdon *et al.*, 2003).

Conjunctival xerosis (X1A) and Bitot's spots (X1B)

Vitamin A deficiency interferes with differentiation of mucus-secreting epithelium lining many bodily organs; the conjunctiva of the eye is simply the most exposed and prominent. Dry, nonwetable patches of keratinized epithelium appear on the conjunctival surface, most prominently adjacent to the temporal side of the cornea. With more severe

deficiency, the extent and severity of metaplasia causes a second xerotic patch to appear on the opposite (nasal) side. If sufficiently severe and prolonged, deficiency will result in prominent keratinization involving all of the exposed conjunctiva. Long before that, a mixture of desquamated keratin and saprophytic bacilli accumulates. Vitamin A Deficiency 2 late over the temporal (and later, nasal) patch of xerosis as foamy or cheesy, whitish material. This is called a Bitot's spot (X1B). With chronicity and other factors, localized, usually temporal Bitot's spots can persist long after the vitamin A deficiency is corrected. The rest of the conjunctiva will become clinically (and histologically) normal within 1 month (WHO, 2009).

Corneal xerosis (X2)

When the corneal epithelium keratinizes, the cornea loses its normal sheen and clarity. The individual is usually severely deficient and is in urgent need of vitamin A. Within 1 week of correction of vitamin A deficiency, the keratinized epithelium will peel off and the cornea will regain its normal appearance (Congdon *et al.*, 2003).

Corneal ulceration/keratomalacia (X3)

The preceding changes are all reversible. Once the cornea ulcerates or 'melts', the clinical outcome ranges from a localized scar (if treatment intervenes while the ulcer is small and still localized) to complete loss of the eye (melting of the entire cornea). While an ulcerated cornea can become secondarily infected, microorganisms are not responsible for the initial ulceration. Diagnosis can be problematic and is often delayed. Affected children admitted to hospitals for accompanying systemic illnesses (diarrhoea, protein-energy malnutrition, measles) commonly keep their irritated, painful eyes closed. Medical personnel rarely investigate the issue. In adults, particularly alcoholics in developed countries, the initial ulcers are mistaken for localized infections; only when they fail to respond to antibiotics are vitamin A deficiency and xerophthalmia considered. Ocular manifestations reflect different degrees of deficiency, but do not necessarily occur in a predictable sequence. In measles in particular, or other intercurrent illnesses resulting in acute and dramatic deterioration of vitamin A status, the cornea can melt in the absence of a history of nightblindness or evidence of conjunctival xerosis.

Xerophthalmic fundus (XF)

Prolonged VAD in Older children and adults manifests as plethora of small, white retinal 'dots' hardly symptomatic, involve alterations in retinal area which is further rectified with bimonthly Vitamin A supplementation as adjunct therapy (Lederberg *et al.*, 2003).

Systemic morbidity and mortality

Vitamin A rank impact the contagion hazard and implies a potent effect on its adversity.

Improvement in vitamin A status among children from 6 months to 6 years of age minimizes mortality by 22–55% as indicated by RCTs in deficient population of Asia and Africa (WHO, 2009). VAS is associated with decreased disease outcome and death rate from measles and diarrhea (Lederberg *et al.*, 2003; Black *et al.*, 2008). Low levels of vitamin A is linked with corneal damage. Indeed, 80% of African children in schools for the blind trace their blindness to an episode of measles. For its part, improving the vitamin A status of children reduces subsequent measles-related mortality by roughly 50% (WHO, 2009; Haider and Bhutta, 2017). Treating severe, hospitalized cases of measles with vitamin A reduces the severity of complications, particularly laryngotracheobronchitis, and cuts case-fatality in half (Lederberg *et al.*, 2003; Ioannidis, 2005). The pathogenesis of increased maternal mortality observed among vitamin A-deficient women is unknown. It may involve increased severity of infections (pre- and postpartum), exacerbation of iron deficiency anaemia, and/or the alterations in other physiological parameters sensitive to or affected by pregnancy (Haider and Bhutta, 2017).

Strategies

VAD can be averted by vitamin A supplementation, nutrition education and inclusion of vitamin A rich foods (Arlappa *et al.*, 2008). Vitamin A status can be improved by attributing variation in diet, supplementation and food fortification (Akhtar *et al.*, 2013).

Treatment

It has been seen that 2 types of situations that triggers the greater chances of visionless and expiry: first is blindness of eyes and health ailment (measles). Fast reaction and action of treatment is necessary for the recovery from it. Night blindness is actually disorder of austere fat soluble vitamin A deficiency and health ailment (measles) is more prone to spread in the world especially in developing countries just because of patients suffered from the health ailments has reduced or lowered vitamin A rate in their body. This health ailments is the need of quick management and handling to decreases the danger of further health issues that is associated with this deficiency. In very few and trace realities shows that greater degree of fat soluble vitamin a is given by oral cavity (commonly in the form of H₂O and layers of retinol esters as retinyl palmitate in fats) (Sommer, 2008). We cannot introduced the vitamin A injection within the muscles and through intravenous; in the most countries of world fat soluble vitamin A is introduced through muscles so this type of vitamin A introduction are not digested up to their full content and greatly unyielding. The only effect of Vitamin A absorption with in muscles is great dissimilation in which vitamin A is given in liquid contact and vitamin A. although the patients are suffered from the blindness of eyes and health ailments (measles) vitamin a should be given for two days on continuous basis. Commonly

two lac international units of vitamin A is given directly through oral cavity and then it also repeat in second day. So, 3 amount should be given after one month to take time for the hepatic organ to deposit the vitamin A. females who are in the age range of child giving as well as in the situation of visionless commonly give the minute and lesser amount of vitamin A (most probably the amount is ten thousand for one month). High amount of vitamin A is given to females (who are in first third months of pregnancy) are mostly toxic for fetus and enhance the danger of faults of birth of fetus. Although the actual danger of vision loss is measured opposite to the possible toxic effects of vitamin A. the females that have been suffered from the dryness of conjunctiva and dryness of cornea region as well as wound produced with in the eyes is given in greater and big amount of vitamin A (two lac international units) in the management schedule. Treatment of patients with compassionate in which appropriate diet and management of health ailments is major aim of fulfillment of fat soluble vitamin A deficiency. Soft and fragile portion of cornea needs the adequate management and regular checkup of eyes. In the kids which are patients of softening of eyes (full deadness of cornea) should protect the sight of these kids in the management of further health risk caused by fat soluble vitamin A deficiency and better treatment action plans will help to enhance probabilities of existence. Percentage of threatened stage of softness of eyes that are not undergo any management action is reached ninety percent; although the fat soluble vitamin A is given to kids for the management of softness of eyes mostly in countries of world , one fourth part and excess is generally expired at the peak time of this ailment (De-Regil,) *et al.*, 2016).

Prevention

Enhancing and upgrading the level of fat soluble vitamin A in the susceptibility group of people decreasing the effect of fat soluble vitamin A reduction on the health of these susceptible persons. Approximately 3 common methods are in consideration when we treat the susceptible persons; the selection will be rest up on the approaches conduct with in the culture, obtainable assets and further greatly common causative factors.

Vitamin A supplementation

Big amount of fortification and adjunction of vitamin A with the passage of time and after the appropriate time interval is the great and broad action plan as it consist of minute amount of yield in the passage of alteration in attitudes like to modify the attitude toward the food and the limitations exist in the passage of better enrichment. Kids require the large amount of aft soluble vitamin A approximately twenty five thousand international units to the two lac international units with in the life stage of 2 to 4 interval per 1 year. Although the separate and one portion of further episodic facilities of health as in the case of

vaccination. When we take amount at that level and rate according to guidelines this management action is purely protect for kids. For the small children who show the signs of adverse impacts of high blood pressure at the brain side will give the vitamin A amount at the rate of twenty five thousand international units and excess between the duration of two to four months. Vitamin A in the fats and oil form or in injection form should be given through oral cavity. Females in the age range of giving birth to the infants should the small amount of vitamin A so they cannot be toxic to them and their fetus. females may consume fifteen hundred to ten thousands international units of vitamin a on regular basis or they consume twenty five thousand international unit of vitamin A I in a week.

Fortification

Vitamin A is given in variety of ways either they should be incorporated to wheat, sugar or in soya sauce just like iodine is incorporated in table salt and in animal milk mostly cow's milk have appropriate introduction of vitamin A in to prevent from the adverse health effects. Unluckily, the persons that have low income cannot consume these foods of vitamin A fortified because they cannot buy it as it requires the protective ways of introduction of vitamin in Foodstuffs of normal consumption and complete standards methods is required. Although the enrichment of table sugar should give the appropriate amount of vitamin A to the people live in USA but the enrichment of staple food with vitamin A is ongoing in field of further study and it must be sow again and again in the Asia and Africa region. Fortunately persons should consume food item rich in vitamin A so they cannot produce deficiency in ourselves. Unluckily, people with low income should not be consumed vitamin A enriched food like meat and other products because they cannot afford it because of high price and at the areas at which infection rate is continuously raised and restrained for longer period of times amount and requirement of vitamin A is usually provided in large amount to prevent from further complication. It must be corrected through usage of new initiative (new ways) in field of nutrition like introduction of vegetables and food items in their gardens so that these people can also take advantage from this strategy or action plan and enhanced the level pf vitamin in susceptible persons.

Improved Diet

Fortunately persons should consume food item rich in vitamin A so they cannot produce deficiency in ourselves. Unluckily, people with low income should not be consumed vitamin A enriched food like meat and other products because they cannot afford it because of high price and at the areas at which infection rate is continuously raised and restrained for longer period of times amount and requirement of vitamin A is usually provided in large amount to prevent from further complication. It must be corrected through usage of new initiative (new ways) in field of nutrition like

introduction of vegetables and food items in their gardens so that these people can also take advantage from this strategy or action plan and enhanced the level pf vitamin in susceptible persons (De-Regil *et al.*, 2016).

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