International Journal of Biotechnology and Biomedical Sciences
p-ISSN 2454-4582, e-ISSN 2454-7808, Volume 4, Issue 2; July-December, 2018 pp. 83-88

http://www.krishisanskriti.org/Publication.html

Impact of Vitamin D on Adiposity and Insulin Resistance Syndrome

Dr Binata Nayak

Assistant Professor, Dept of Home Science. (Food & Nutrition Division)
University of Calcutta 20 B Judges Court Road, Kolkata-700027

Abstract—*There is a relationship between exposure to sunlight of our body and synthesis of vitamin D. Vitamin D level of our body can be maintained by consumption of vitamin D rich foods. The rich sources of vitamin D are mainly in animal sources like- cod liver oil, butter, fish, ghee etc. Vitamin D can play various functions in our body. Beside those, it can also helps in the secretion of insulin from pancreatic β cell of intestine. The deficiency of vitamin D can occur due to lack of vitamin D rich foods consumption or lack of exposure to sunlight. Due to low level of vitamin D in our body there is a chance of deposition of fat in adipose tissue and leads to obesity. In obesity, the fatty acid level can increase which leads to insulin resistance (IR).Moreover, it can be said that, low level of this vitamin can also cause of IR by increasing the chance of obesity. So, there is a relationship between vitamin D deficiency, obesity and IR or they may be vise versa. Therefore, IR can lead to diabetes mellitus by decreasing the glucose uptake capacity by cell. Diabetes mellitus is the cause of some chronic and acute complications. Therefore, it can be said that, vitamin D rich foods consumption and vitamin D supplementation may help to reduce the chance of increase free fatty acid level and obesity and thus decreasing the risk of IR.*

Keywords*: Vitamin D, Adiposity, sunlight, insulin resistance.*

INTRODUCTION

Obesity is a state in which there is a generalized accumulation of excess adipose tissue in the body leading to more than 20% of the desirable weight.

Obesity, defined by the World Health Organization as a body mass index (BMI) of 30 kg/m2 or more, is pandemic, affecting at least five million Australians and substantial numbers in most developed nations. If overweight (BMI 25–29.9) is included, then approximately 14 million Australians, and 70% of Americans aged over 60, are obese or overweight. Older people who have excess body fat accumulation face increased risk for coronary heart disease, hypertension, metabolic syndrome, osteoarthritis, diabetes mellitus, and other co-morbidities. It is imperative that modifiable risk factors for obesity be identified, particularly those which might be readily addressed. There is a consistent association in the published literature between increasing BMI and lower serum 25-hydroxyvitamin D (25D) concentrations. Early, smaller studies, reported an association. between obesity and low serum 25D concentrations, as well as high concentrations of parathyroid hormone (PTH) and 1,25-dihydroxyvitamin D (1,25D). However, further, larger studies found obesity to be associated with lower 25D concentrations, high PTH concentrations and low 1,25D concentrations. It has also been reported that body fat content is inversely related to serum 25D concentration, and that this associations is stronger than those between 25D and BMI and body weight. A bi-directional genetic study, which limits confounding, has suggested that higher BMI leads to lower 25D, with the effects of lower 25D on BMI likely to be small. The association between reduced 25D concentrations and obesity is therefore well-established, although the mechanisms for the lower 25D concentrations are not fully described, and there is uncertainty as to what the health consequences of these lower concentrations might be. This paper attempts to summaries the current state of knowledge regarding the causes of these reduced 25D concentrations, as well as the possible effects of vitamin D supplementation on obesity.

A large energy intake (hyperfagia) combined with sedentary behavior leads to a positive energy balance, causing overfilling of the adiposities. Fat storage normally takes place in the fat depots in de the body, mainly under the skin. When an abundance of calories is accumulated by chronic caloric overfeeding the fat depots will get overfilled and fat storage will also take place in the abdomen. This abdominal or visceral fat is stored between the organs in the abdomen.

CAUSES OF OBESITY:-

Obesity is a complex mutifactorial chronic disease developing by numerous factors like –

- **Genetic factor:-** Genetic inheritance probably influences 50-70% a chance of becoming fact. Within families the chance is 80% if both parents are obese and 50% if one parent is obese.
- **Age and Sex:-** It can occurred among any age and any sex. Many studies have shown that more females than males are found to be overweight among all age groups.
- **Eating habits:** -Some eating behavior may lead to obesity-

- Eat excess calorie and fat rich foods can cause obesity.
- Some may eat faster taking less time for chewing, therefore they tend to consume more food.
- Non inclusion of fruits and vegetables.
- Some eat more food when they are unhappy.
- People who eat more junk foods.
- People who eat more frequently in outside.

- **Physical activity: -** Lack of physical activity can lead to deposition of more fat.
- **Stress: -** Stress is another cause of obesity

Beside those above causes of increasing obesity, there is a most important cause for this condition is lack of Vit-D status in human body. Many researches also said that obesity is a cause of low Vit-D status that also leads to IR.

- **Possible Mechanisms for Lower 25D Concentrations in Obese Individuals:**
- **Lower Dietary Intake:**

Vitamin D intake has been reported as being lower in obese men, but not women, when compared to their non-obese counterparts. Low calcium and D intake have also been associated with obesity in both men and women, but this association does not necessarily imply a causal relationship.

- **Altered Behavior:**

It is possible that obese individuals expose less skin to the sun less often than non-obese individuals, resulting in reduced synthesis of vitamin D. BMI, % body fat and sunbathing have been shown to be related in a population-based sample, although another study found no relationship in a study of individuals aged over 65 years. This latter finding may be explained by the known decline in cutaneous vitamin D synthetic capacity associated with age. It has also been noted that obesity results in larger body surface area, and thus could be expected to increase cutaneous vitamin D synthesis.

- **Reduced Intestinal Absorption:**

Hypovitaminosis D is well-documented in those who have had bariatric or gastric bypass procedures, in which a malabsorptive state is deliberately induced, but there is no evidence that obesity itself results in reduced absorption of dietary vitamin D. Given that vitamin D is fat-soluble, and that calcium absorption has been shown to be increased in diets high in fats, it is unlikely that obesity affects vitamin D-calcium homeostasis through altered gut absorption.

- **Reduced Activation and/or Increased Catabolism :**

1,25D acts to limit production of its precursor, 25D. Because early studies suggested that 1,25D concentrations were elevated in obese individuals, it was thought that this may lower 25D levels. Given that further, larger studies have suggested that 1,25D concentrations tend to be lower in obese individuals; this feedback mechanism is unlikely to be relevant. Adipose tissue (AT) in obese women expresses the enzymes for both the formation of 25D and its active metabolite, 1,25D and for degradation of vitamin D. Subcutaneous AT has also been found to have lower expression of one of the enzymes responsible for 25-hydroxylation of vitamin D (CYP2J2), as well as a tendency toward a decreased expression of the 1-α hydroxylase. These data suggest that both 25-hydroxylation and 1-α hydroxylation are impaired in obesity. *In vitro* studies have demonstrated that 1,25D inhibits adipogenesis and induces adipocyte apoptosis. Under normal physiological conditions the serum 1,25D concentration is tightly regulated, yet there can be significant differences between 1,25Dconcentrations within different tissues owing to in situ production. These factors make interpretation of the clinical significance of *in vitro* studies very difficult.

CORRELATION BETWEEN V_D DEFICIENCY AND OBESITY:

The main source of V_D is ergosterol and cholecalciferol. There sources are converted to its active form that is 1, 25-dihydroxy Vit-D by several mechanisms which is already discussed in earlier. This active form is essential for its function in our body. 25-hydroxy Vit-D_3 is the main circulating V_D metabolites which are commonly used as the marker of V_D status in our body then many complications can occurred and among those complications obesity is one of them. A low V_D intake was also associated with decreased BMI.

Increased fat mass has been associated with increased bone size but reduced volumetric density with obesity. It has been well established in human leads to lower serum levels of 25-hydroxy Vit-D. Some study shows that as obese children are usually sedentary and therefore less likely to play outdoors, their exposure to sunlight may be limited and consumption of unhealthy high caloric food might be low in minerals Vitamin content obesity is also the primary risk factors for the development of impaired glucose tolerance (IGT). Type 2 Diabetes Mellitus (T2DM) and many other metabolic syndromes (MeS). Studies have shown that lifestyle factors contribute to this development. Bioavailability of V_D in obese Subject might be low because; of its deposition in a fat tissue and higher body fat mass might be associated with higher risk of V_D deficiency.

Individuals with impaired fasting glucose (IFG and I or). IGT are referred to as having prediabetes. Prediabetes is frequently associated with obesity and other components of MeS. Obesity in turn is commonly associated with hypovitaminosis – D due

to the capacity of adipose tissue to store 25-hydroxy Vit-D_3 making it biologically unavailable.

EXPLANATION OF REDUCED V_D LEVEL AND INCREASED ACCUMULATION OF EXCESS FAT IN ADIPOSE TISSUE, LEADS TO OBESITY :-

It has become increasingly clear that the V_D is related to obesity in adults as well as children too. Obesity has been found to be associated with lower levels of serum 25(OH) V_D. If low V_D is occurred there is increased the level of PTH hormone.

- PTH stimulates the renal hydroxylation of 25(OH) V_D to its active form 1, 25 dihydroxy V_D.
- 1, 25 dihydroxy V_D in turn elevates the Calcium influx into adiposities.
- In these cells intracellular Calcium enhances lipogenesis and inhibits lipolysis.
- Both these effects would promote lipid storage in fat tissue and leads to overweight and or obesity.

WHY THERE IS IR IN OBESE PERSONS?

As we have seen that, low V_D and obesity are correlated with each other, so, it can be said that or, the research explained that low V_D level in the obese patients had a decreased risk of IR. Recently it is reviewed that high serum 25(OH)D concentration may be associated with lower risk of IR by increasing pancreatic β cell function as β cell have Vit-D receptor for its activity i.e. insulin secretion. It can be conclude that low Vit-D can leads to high PTH level that has also been shown to suppress insulin release and to promote IR in adiposities.

So, if V_D level is comparatively low in serum then it cannot be binds directly to the β cell V_D receptor which is very crucial to secrete insulin.

Then we can say that if obese person have reduced V_D level they have to prone increased IR, decreased bioavailability of V_D due to excess storage in body fat, obesity may interact with low V_D and increase the chance of IR. The storage of V_D in fat tissues can result in lower V_D availability for influencing pancreatic β cell function or activating V_D receptor, thereby increasing the risk of adverse insulin secretion and leads to IR.

MECHANISM THROUGH WHICH HIGH CONCENTRATION OF FREE FATTY ACIDS CAUSE INSULIN RESISTANCE

Elevated concentration of free fatty acid in the blood diffuse into muscle cells where they are converted to fatty acyle Co-A, Diglyceride (DAG) and ceramides. These lipotoxic substances activates PKC pathway, triggering a serine or threonine kinase (Protein kinase B [PKB] or Akt) cascade that results in the phosphorylation of IRS-1 and IRS-2. This phosphorylation inhibits the tyrosine kinase phosphorylation that is required for transmission of insulin signal, thereby decreasing the activation of PI3K pathway, which decreases the rate of fusion of GLUT-4 containing vesicles with the plasma membrane and hence the amount of glucose cannot enter into the cell.

So, there is conclusive evidence that, obesity is associated with insulin resistance (IR), hyperinsulinemia, non insulin dependent diabetes mellitus, hyperlipidemia, hypertension etc. The mechanism might be due to the lipolytically sensitive abdominal depots providing excess free fatty acid to a muscle tissue that has decreased capacity for their oxidation. The excessive exposure of tissues to fatty acids impairs insulin function and increases blood insulin levels. All this ultimately results in reduced insulin sensitivity making a person insulin resistance. This intern results in hyperinsulinemia. Majority of India suffers from diabetes due to insulin resistance and not due to insufficient insulin secretion.

INSULIN RESISTANCE AND TYPE-2 DIABETES MELLITUS

Diabetes is a condition where blood glucose level is elevated than normal. There are many causes of T2 DM like-physical inactivity, poor nutrition, and one of obesity. T2DM is a cause of insulin resistance. T2 DM is a major met disorder that has become increasingly prevalent all over the world.- Diabetes has taken place as one of the most important diseases worldwide, reaching epidemic proportions. Global estimates predict that the proportion of adult population with diabetes will increase 69% for the year 2030. According to the WHO, there were 31.7 million people suffering from diabetes in 2000 in India. This number is estimated to increase to an alarming level of 79.4 million by 2030. Impaired V_D status has been mitosis D may be considered a major health problem with more than one billion people worldwide. . The study also found a significant inverse association of 25(OH)D with some of the individual components of the metabolic syndrome, including abdominal adiposity hypertriglyceridemia hyperglycemia etc and the study also said that defects in pancreatic β cell function and I or insulin sensitivity are often present to develop glucose intolerance or Type 2 Diabetes mellitus. It was suggested that V_D could play a role in the pathogenesis of T2DM by affecting either insulin sensitivity or β cell function or both.

Insulin resistance is characterized by the impairment of insulin action. Classically, the insulin-resistant state is defined by the impairment of glucose uptake in muscle and the increment of endogenous glucose production by the liver resulting in hyperglycemia, both in fasting and postprandial states. However, in a broader sense, the insulin resistant state is also characterized by the impairment of insulin action on lipid metabolism (*e.g.* increment of lipolysis in adiposities) or on protein metabolism (*e.g.* impairment of protein synthesis in muscle). Also, IR affects the function of other organs such as vessels (leading to vasoconstriction/hypertension); brain (resulting in increased caloric intake); pancreas (decreased in

beta-cell mass and in glucose sensing); bone (possibly decreasing bone mass and strength) among others effects.

MECHANISM LINKING V_D TO INSULIN ACTION AND SECRETION:-

Vit-D deficiency is a global health problem which has been shown to effect both insulin secretion and action. The relationship between V_D level and insulin sensitivity index measurement remained significant after adjustment for age, sex, ethnicity and BMI. Animal studies suggest a relationship between V_D and pancreatic β cell function

It is important to examine the role of V_D metabolites i.e. 1, 25(OH) V_D in pancreatic β cell function. Pancreatic β cell can also express V_D receptors.

The 1α-hydroxylase enzyme is not only present in renal tissue but also present in pancreatic β cells were 1, 25(OH) D_3 is formed the active form of V_D. An intracellular calcium concentration and calcium flux over the cellular membrane are important regulators of insulin secretion. It has been suggested that V_D may exert its effects on the β cell by its ability to regulate calcium. Decreased V_D level impaired intracellular signaling pathway after insulin binds to its cellular receptor. The V_D receptor acts as a transcription factor when bound to 1, 25 Vit D_3 polymorphosis in the V_D receptor gene may influence insulin action and secretion.

V_D STATUS, OBESITY AND T2DM:-

Normally, the β cells are able to increasing insulin production and secretion. Glucose sensors located on β cells sense, increases insulin secretion and reduces the chances of elevating blood glucose level and in turn reduce the chances of T2DM. We know that T2DM is a condition where blood glucose level is increased than normal due to β cell dysfunction and it is a very serious disease. This chronic disease can leads to some conditions viz nephropathy, neuropathy, CVD, retinopathy etc.

Earlier it has been discussed that 1, 25(OH) D3 is essential for insulin exocytosis by increasing the expression of Calbindin – D28K in β cells.

So, it can be said that V_{D3} is essential for insulin secretion and help to maintain glucose homeostasis..

IR is defined as the inability of target tissues such as adipose tissue, skeleton muscle to respond adequately to the body's insulin secretion. IR can occur for post receptor defect of insulin signaling.

In this review, it has been found that, IR can occur due to increase the free fatty acid level in blood in obesity. And obesity can happened due to low level of vitamin-D deficiency. In IR there is sufficient production of insulin but it does not work properly and thus blood glucose level is elevated as well as insulin level is also increased. So, hyperinsulinemia has been found. Due to IR, T2DM is happened.

Therefore it can be said that, in T2DM, hyperglycemia is a one of the common condition which increases as IR by increasing insulin signaling.

Dietary Management

- **DIET FOR IMPROVING VITAMIN-D STATUS:**

The mainstay management for vitamin D deficiency is vitamin D supplementation to prevent this problem. Several studies support that vitamin D supplementation may affect glucose homeostasis or improve insulin secretion. A significant increase in serum calcium levels and a reduction in serum free fatty acid levels have been found after taking vitamin D supplementations.

The main source of vitamin-D for people is exposure to sunlight. The foods that contain vitamin-D are-salmon, oily fish, cod liver oil, butter, soymilk, fortified juice etc.

As only vitamin-D supplement or vitamin-D rich diet is not sufficient to reduce weight so there must be needed some dietary guidelines for reduce weight and can improve diabetes.

- **OTHER DIETARY GUIDELINES:**

- Principle of dietary management
    1. Low calorie
    2. Normal protein
    3. Vitamins and minerals(except sodium)
    4. Restricted simple carbohydrates
    5. Restricted fat
    6. Liberal fluid
    7. High fiber diet
- **Energy**: According to the body needs the energy should be given. About 20 kcal per kg ideal body weight is prescribed for sedentary worker and 25kcal for moderate worker.
- **Protein**: About 0.8-1 gm of protein per kg body weight should be given
- **Fat:** Low fat diet must be included in diet. Foods rich in high fat like- nuts, oil seeds should be restricted. Skimmed milk should be taken as it contains less fat.
- **Carbohydrates**: High simple carbohydrates content foods like- simple sugar, sweets etc must be avoided as they may increase fat in body. Complex carbohydrates like- whole grains (oats, whole grain breads), beans, lentils etc are beneficial for both for diabetes and obesity. Fiber rich foods like- green leafy vegetables should be take.

- **Vitamins and minerals**: Due restriction of fat, fat soluble vitamins may be restricted. So fat soluble vitamin like- vitamin A, vitamin D should be given. And sodium rich foods should be restricted as it may cause increase blood pressure. Calcium rich foods especially dairy products should be taken as it may reduce body fat.
- **Fluid**: Liberal fluid should be taken as it helps to cut down food intake.
- **Fiber:** Inclusion of high fiber diet has many advantages for obese person like-
- Low in calorie density.
- Rich sources of vitamins and minerals.
- Give satiety
- Helps in bowel movement
- Reduce blood cholesterol

DISCUSSION

The rich source of vitamin D is first of all sunlight. If we can exposed to the sunlight then our body can synthesized a required amount of vitamin D. Beside this, butter, ghee, cod liver oil etc are rich source of vitamin D. Vitamin-D is a fat soluble vitamin and it has number of important roles in the body including formation of bones, joints etc. Vitamin-D exits in the two forms viz Vitamin D_3 (cholecalciferol) of the animal origin and Vitamin-D_2 (ergocalciferol) of the plant source. During exposure to sunlight ultra violet B (UVB) penetrate skin and absorbed by 7-dehydrocholesterol (previtamin) and then it goes to rearrangement and form Vitamin D_3 (cholecalciferol) in our body. V_D receptors have been found in the tissues of brain, pancreas, colon, breast etc [29]. V_D also has in vitro and in vivo effects on pancreatic β cell and insulin sensitivity and on immunoregulatory function etc. Researchers have pointed out that normal or raising level of V_D among the general population could prevent various chronic diseases like- DM, HTM, CVD etc.

Beside these functions, vitamin D has another function in our body that is to in the secretion of insulin from β cell of pancreas. Insulin secretion is dependent on changes in intracellular calcium concentration and 1, 25 dihydroxy Vitamin D has been shown to regulate β cell. Calcium flux V_D may be involved in β cell secretary activity and in modulating the tissue response to insulin.IR is a pathological condition in which cells fail to respond normally to the hormone insulin or the inability of the body to control blood glucose with normal levels of insulin. (23) IR is the inability of the body to control blood glucose with normal levels of insulin. IR can cause Physical inactivity, Obesity, Abnormal Insulin molecule, Zn deficiency, Vitamin-D deficiency. Several studies also describe an association between V_D status and insulin sensitivity. The relationship between V_D level and insulin sensitivity index measurement remained significant after adjustment for age sex, BMI. Animal and in vitro studies suggest and relationship between V_D and pancreatic β cell function. Rabbits, rats, mice with V_D deficiency display impaired insulin secretion that improves with V_D supplementation.

25-hydroxy Vit-D_3 is the main circulating V_D metabolites which are commonly used as the marker of V_D status in our body then many complications can occurred and among those complications obesity is one of them. A low V_D intake was also associated with increased BMI. So, decreased level of vitamin D causes increased secretion of PTH hormone which increased calcium influx that is the cause of fat deposition in adipose tissues and leads to obesity. Due to hypovitaminosis, increased calcium influx which leads to deposition of fat in adipose tissue and causes obesity. In this condition, excess fatty acid increases the PKC pathway and IR occurs. Due to IR there is sufficient amount of insulin but it does not work. Thus, the level of insulin is increased than normal that leads to hyperinsulinemia. Then we can say that if obese person have reduced V_D level they have to prone increased IR. The storage of V_D in fat tissues can result in lower V_D availability for influencing pancreatic β cell function or activating V_D receptor, thereby increasing the risk of adverse insulin secretion.

On the other hand, IR can lead to diabetes. In IR insulin cannot work properly due to may be the defective insulin secretion or when β cell cannot work properly and cause diabetes. So, it can be said that the obese persons can have IR due to deficiency of vitamin D and that's why they can prone to diabetes. The prevalence of Vitamin-D deficiency in women with type-2 DM is more common. Low level of Vitamin-D is also common among in all life stages. Recently it is regarded that decreased Vitamin-D status is a cause of development of increased insulin resistance that causes metabolic syndrome like diabetes. Several investigations have found that people with impaired glucose tolerance or diabetes mellitus have decreased concentration of serum 25(OH) D_3. IR is also found among prediabetic subjects due to lack of vitamin D level. Recent epidemiological findings suggest that low serum 25(OH) D_3 is associated with an increased risk of metabolic syndrome.

So, it can be said that sun exposure has additional health benefits to vitamin D production. Vitamin D rich foods like butter, ghee consumption help to reduce low level of this vitamin in our body. Except these, individual can take vitamin D doses in required amount, when necessary to prevent the deficiency of this vitamin. So, Vitamin-D supplementation can improve the insulin secretion and decreased the chance of elevation of fatty acid level and decrease the risk of obesity and thus reduce the chance of IR

CONCLUSION

Vitamin D is essential for insulin secretion and its work. Vitamin D deficiency can lead to insufficient insulin secretion.

Moreover, deficiency of vitamin D can lead to decreased calcium influx and causes fat deposition which leads to obesity. It can also conclude that in obesity, free fatty acid can inhibit the activation of PI3K which is essential for insulin work and increase the PKC pathway and causes IR. IR can causes diabetes by decreasing glucose uptake by cell. Finally it has been conclude that, as low vitamin-D causes obesity and then this situation leads to IR and T2DM, so it can be said that obesity may also cause vitamin-D deficiency that lead to IR. So, they may be viz versa. To overcome from this problem vitamin D supplementation must be taken. Vitamin D rich foods should be included in diet. If necessary vitamin D doses can be taken as capsule or tablets.

BIBLIOGRAPHY

[1] Shaum M. Brian K. Joint Effect of Obesity and Vitamin D Deficiency on Insulin Resistance and Type 2 Diabetes Mellitus. *Diabetes Care.*Vol (55). PP: 2048-54. 2012.

[2] Dutta D. Maisnam I. Sinha A. Ghosh S. Serum Vitamin D Predicts Insulin Resistance In Individual With Prediabetics. *Indian J Med Res*. Vol (138). PP: 853-60. 2013.

[3] Roth L. C. Hoognagle A. N. Kratz M. Vitamin D Deficiency in Obese Children and Its Relationship to Insulin Resistance and Adipokines. *J Obesity.* PP: 1-7. 2011.

[4] Ekdom K. Marcus C. Vitamin D Deficiency Is Associated With Prediabetes In Obese Person. *Vitamin D Deficiency and Obesity.* 2016.

[5] Alexy U. Reinehr T. Kersting M. Vitamin D Status and Parathyroid Hormon (PTH) In Obese Children before and After Weight Loss. European Journal of Endocrinology. Vol (157). PP: 225-32. 2007.

[6] www.article.mercola.com. 30/ 06/2016. 12.57p.m. the Link between Vitamin D and Insulin Resistance.

[7] Wood R J. Martini. Richard J. Vitamin D Status and the Metabolic Syndrome. *Nutrition Reviews.* Vol (64). Sub Vol (11). PP: 479-86. 2006

[8] Gulseth H L. Wium C. Vitamin D and Insulin Action and Secretion –An Overview of Current Understanding and Future Perspectives. *European Endocrinology.* PP: 13-8. 2010.

[9] Www.naturalnews.com. 22/06/2016. 3.49p.m. Low vitamin D linked to IR.

[10] Sung C C. Liao M T. Lu C. *Role of vitamin D in IR. J Biomedicine and Biotechnology.*PP:1-11. 2012.

[11] Lan R. Helen J. Michelle C. Vitamin D and IR. *Clinical Endocrinology.* Vol (84). PP: 159-71.2016.

[12] Koppe L. Pascaline M. IR in CKD: New *Lessons from Experimental Models. J Nephrol Dial Transplant.*Vol (29). PP: 1666-674. 2014

[13] Nikooyeh B. Tirang R. Kalayi A. Vitamin D Deficiency Is Associated With Metabolic Syndrome In Subject With T2DM. *J Nutrition and Food Science Research.*Vol-1. PP: 3-10. 2014.

[14] Acar Y. Erol B. Relation of Serum 25-Hydroxy Vitamin D Level with IR in T2DM Patients and Normal Subjects. J Insulin Resistance and Vitamin D. PP: 305-14. 2012.

[15] Moreira T S. Hamadeh M J. The Role of Vitamin D Deficiency in the Pathogenesis of T2DM. *The European e-J of Clinical Nutrition and Metabolism.* Vol (15). PP: 155-65. 2010.

[16] Ullah A. Khan A. Khan I. Diabetes Mellitus and Oxidative Stress- A Concise Review. *Sandi Pharmaceutical Journal*.2015.

[17] Chambial S. Gupta A. Oxidative Stress in T2DM Patient with Microalbuminuria. *International Journal of Health Sciences and Research.* Vol (3) (10). PP: 29-5.2013.

[18] Srilaxmi B. Diet in Obesity and Underweight. Dietetics. 6th edition. New Age International (P) Ltd. PP: 222-39.2011.

[19] Srilaxmi B. Diet in Diabetes Mellitus. Dietetics. 6th edition. New Age International (P) Ltd. PP: 325.2011.

[20] Gaag E V. Brekhoff L. Effect of Food and Vitamin-D Supplements on Serum 25 (OH) D3 Concentrations in Children during Winter Months. *Foods.* Vol (3). PP: 633. 2014.

[21] www.dietitions.co. 16.11.2016. 3.50 p.m. Food Sources of Vitamin-D.

[22] Srilaxmi B. Fat Soluble Vitamins- Vitamin D, E, K. Nutrition Science. 3rd edition.. New Age International (P) Ltd. PP: 234-43.2011.

[23] Satyanarayan U. Chakrapani U. Vitamins. Biochemistry. 4th edition. Reed Elsevier India (P) Ltd. And Books and Allied (P) Ltd. PP: 124. 2013.

[24] Gopalan C. Sastri B. V. R. Dietary Guideline- Proximate Principles: Common Foods. Nutritive Value of Indian Foods. PP: 47-88.

[25] Ozfirat Z. Chowdhury T A. Vitamin-D deficiency and T2DM. *Department of Dia and Metabolism. Barts and the London School of Medicine and Dentistry, London, UK*. 2009.

[26] Govers E. Slof E M. Guidelines for the Management of Insulin Resistance. *International Journal of Endocrinology and Metabolic Disorder*. Vol(1). PP: 1-7. 2015

[27] Pereira M A. Jacobs D R. Dairy Consumption, Obesity, and the Insulin Resistance Syndrome in Young Adults. *American Medical Association.* Vol (287) (16). PP: 2081-88. 2002.

[28] Castro B.A.V. Kolka M.C. Obesity, insulin resistance and co morbidities Mechanisms of association. *Arq Bras Endocrinol Meta.* Vol (58) (6). PP: 600-09. 2014.

[29] Voet D. Voet G. J. Pratt C.W. Biochemical signallig, receptor tyrosine kinase Fundamental of biochemistry. 4h edition. John Wiley and Sons, Inc. PP: 402-14. 2013

[30] V. Simon. Vitamin-D and Obesity. *Nutrients.* Vol (5) 2013.