Introduction and Aim of The Work

INTRODUCTION

There has been great interest in the role of vitamin D in multiple organ systems, vitamin D affects non osseous organ systems and other physiologic and molecular processes ,when vitamin D bind with its receptor initiates a series of events that can affect cellular proliferation and differentiation, inflammation, the immune system, and the endocrine system, including the renin-angiotensin system, insulin resistance ,and lipid metabolism .Vitamin D deficiency show an association with or the development of increased left ventricular mass index ,increased cardiac fibrosis, coronary artery calcification, increased renin-angiotensin activity; vascular endothelial dysfunction,vascular smooth muscle cell hypertrophy; and hypertension, insulin resistance , podocyte damage, glomerulosclerosis ,and cancer.(***Stephen Rostand, David Warnock,2008)***

In humans, the primary source of vitamin D is UV-B induced conversion of 7dehydrocholesterol vitamin D in the skin. Just 10–20% of our vitamin D comes from dietary sources, such as fish, eggs, or vitamin D fortified milk. vitamin D is hydroxylated in the liver into 25(OH)D - the main circulating vitamin D metabolite, which is largely bound to vitamin D binding protein in serum .25 (OH)D is transformed by renal or extrarenal 1αhydroxylase into1,25dihydroxyvitamin D,which circulates at much lower serum concentrations than 25(OH)D, but has a much higher affinity to the vitamin D receptor***(Dusso, et al.,2005).*** Serum levels of 1,25(oH) $_2$D are mainly determined by renal 1,25(oH)$_2$D production, which is closely related to calcium homeostasis, and is up regulated by parathyroid hormone, the concentration of which increases when calcium levels are low***.(Peterlik&Cross,2005)***

Studies have, however, shown that many other cell types, including those of the vascular wall, express 1αhydroxylase with subsequent intra cellular conversion of 25(oH)D to 1,25(oH)$_2$D, which exerts its effects at the level of the individual cell or tissue. ***(Bouillon et al.,2008)***

The natural form of vitamin D in all animals and the form synthesized in human skin on exposure to sunlight is cholecalciferol (vitamin D_3). Ergocalciferol (vitamin D_2) is a synthetic product derived by irradiation of plant sterols/ergosterol. Until very recently, the two forms of the vitamin were considered to be interchangeable and equivalent; however, since the availability of the measurement of serum 25(OH)D as an indicator of vitamin D functional status, it has become clear that vitamin D_2 is substantially less potent, than vitamin D_3. ***(Armas et al.,2004)***

It should be noted that, all of the evidence brought to the relationship of vitamin D status to health and disease has been developed mainly for cholecalciferol (vitamin D_3).***(Holick MF et al.,2008)***

It has been noted in randomized, controlled trials that vitamin D co-therapy substantially improved response to standard anti tubercular therapy in patients with advanced pulmonary tuberculosis ***(Nursyam et al.,2006).*** Also, phagocytic function of human macrophages is enhanced in individuals who received vitamin D supplementation.***(Martineau et al.,2007)***

Treatment with activated vitamin D [1,25(OH)D or related analogs] may lead to regression of LVH, suggesting a cardioprotective action***(Kim et al.,2006).*** Activated vitamin D has been shown to down regulate proliferation and hypertrophy in cultured cardiomyocytes ***(Nibbelink et al., 2007).*** Moreover, activated vitamin D when administered to dialysis

patients improved diastolic function and reduced LV thickness when compared with patients who did not receive activated vitamin D. ***(Bodyak,et al.,2007)***

Both type 1 and type 2 diabetes have been associated with low vitamin D status, both current and antecedent ***(Scragg et al., 2004***). Adults who had received 2000 IU/d vitamin D during the first year of life had 80% reduction in risk of incident type 1 diabetes, relative to individuals who had not received such supplement. ***(Hyppo¨nen,et al.,2001)***

It was known that $1,25(OH)_2D3$ was one of the most potent hormones for inhibiting both normal and cancer cell proliferation and inducing maturation . Although the exact mechanism by which $1,25(OH)_2D$ is able to regulate cellular proliferation and differentiation is not fully understood, a large number of genes control proliferation, differentiation, apoptosis, and angiogenesis and are either directly or indirectly influenced by $1,25(OH)_2D3$. ***(Bernardi et al.,2002& Spina et al.,2006)***

Epidermal cells have a VDR, and their proliferation is inhibited by $1,25(OH)_2D3$. This observation lead to the concept that $1,25(OH)_2D3$could be used to treat the hyperproliferative skin disorder psoriasis. Topical application of $1,25(OH)_2D3$ was found to be very effective for treating psoriasis with no untoward toxicity.1,25(OH)2D3 and several of its analogs are now one of the first-line treatments for psoriasis (11). *(Holick MF,2007)*

There is a large body of epidemiologic data showing an inverse association between incident cancer risk and antecedently measured serum