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Vitamin D level in children and its relation to immunity and general health condition

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The beneficial role of vitamin D in the prevention and/or treatment of chronic diseases have been a point for research due to its complex action on the immune system. In spite of this all age groups in several countries worldwide have either vitamin D insufficiency or deficiency. This work aimed to study the relation between vitamin D status and CD4 and Thymosin ß4 (Tβ4) as marker of immune status in children as well as the general health condition among children attending the Nutrition Immunologic Clinic. Forty eight children attending the Nutritional Immunology Clinic at NRC were enrolled in this study. After taking a written informed consent clinical evaluation, anthropometric measurements, Body Mass Index were done for every participant. A blood sample was taken for serum vitamin D, CD4 and Thymosin beta-4 levels.28 males and 20 females were grouped according to their serum vitamin D level into Group1: Children with insufficient vitamin D level < 30µg/l.Group2: Children with optimal vitamin D level > 30µg/l. The two groups had homologous distribution of age, gender and BMI percentiles. Significantly lower levels of CD4 and Tβ4 were detected in group 1 .Tβ4 levels were insignificantly higher among group two. Recurrent upper respiratory tract infections last year, frequency of dental caries and fracture were comparable in the studied groups. A significantly positive correlation was detected between vitamin D and bothCD4and Thymosin ß. This study concluded that an optimal vitamin D level is crucial to the appropriate functioning of our immune system

Keywords: vitamin D deficiency, body mass index, recurrent infection,Thymosin ,CD4.

INTRODUCTION

Vitamin D deficiency is a pandemic health problem prevalent in both developed and developing countries, with a report from 30% up to 80% worldwide among children and adults (Oren et al. 2010). Vitamin D is essential for normal growth and development, its deficiency compromises long-term health problems and chronic disease in addition to the well-known musculoskeletal effects of vitamin D deficiency (Lenders et al. 2009).Although researches have stressed on the important role of vitamin D for the immune system, due to the polyvalent action of vitamin D for the human health (Catia and Antonio, 2012), still no enough researches were done on the influence of vitamin D on Thymosin ß4 (Tβ4) and the cluster of differentiation CD4 levels which are important for maintaining a healthy immune system (Sibaii H and El-Zayat, 2016).

Researchers have demonstrated that vitamin D is a potent modulator of the T-cell phenotype: it inhibits the T-helper1 (Th1) cells associated with cellular immune response while conversely enhancing T-helper2 (Th2) cells response (Boonstra et al.2001).

CD4 are glycoprotein that acts as a co-receptor that assists the T cell receptor (TCR) in

communicating with an antigen-presenting cell ,in addition to its important function in T-cell activation (Wang et al. 2013). In the same aspect Tβ4 have been reported in lymphocyte maturation and differentiation through assisting the development of B cells to plasma cells to produce antibodies. Tβ4 have also been recognized in controlling cell morphogenesis and motility as well as preventing fibrosis, it also plays a role in wound repair by acting as a modulator of wound healing and inflammation and regulating immunity (Rath et al.2007).

This study was conducted to study the relationship between of vitamin D level and the general health condition among children attending the Nutrition Immunologic Clinic of the Medical Research Centre of Excellence (MRCE) at National Research Centre, Giza, Egypt. It also aimed to study the relation between vitamin D status and CD4 and Thymosin ß4 (Tβ4) as marker of immune status in children.

MATERIALS AND METHODS

Present study was a cross sectional study approved by the Medical Ethical Committee of the National Research Center, enrolling 48 children attending the Nutrition Immunologic Clinic of the Medical Research Centre of Excellence (MRCE), National Research Centre. Children suffering from chronic illness or on daily vitamins, minerals and /or trace elements supplement were excluded from the study.

After taking a written informed consent from the legal guardian of each child enrolled in the study, a careful medical history taking and clinical examination were done for each participant. Demographic Data were collected**,** number of attacks of upper respiratory tract infection in the last year was documented and Anthropometric measurements were done using standardized equipment and following the recommendations of the International Biological program (Hiernaux and Tanner 1969). Body Mass Index (BMI) was calculated by the formula weight/height^2 (weight in kg divided by height in meters^2). Then BMI categories were defined as underweight, normal, overweight and obese according to the World Health Organization (WHO 2007) Child Growth Charts Standards for age and sex using AnthroPlus software for personal computers (WHO 2009).Vital signs including blood pressure, Radial pulse, respiratory rate and body temperature were recorded. Screening questionnaires were completed by the physician to detect any symptom of vitamin D deficiency. A blood sample was taken for detection of serum vitamin D level, CD4 and Thymosin beta-4.The candidates were grouped according to their serum vitamin D level into

Group1: Children with insufficient vitamin D level below 30µg/l

Group2: Children with optimal vitamin D level above or equal 30µg/l

(Canadian Paediatric Society 2007; Holick et al. 2011).

RESULTS

A total of forty eight children were enrolled in this study they were 28 males and 20 females. According to vitamin D level, the children were divided into two groups. Group 1 included 39 children found to have Vitamin D level of 6.12±5.92 thus having vitamin D insufficiency (less than 30 ug\ml). On the opposite side Group 2 included the remaining 9 participants whose vitamin D level was 43.5±10.4 thus having an optimal vitamin D (more than or equal to 30 ug\ml). The vitamin D level was significantly lower in group 1 compared to group 2 with a P-value of 0.00. Group 1 constituted of 21 males and 18 females representing 75% and 90% of the total participants respectively. The candidates in group1 and group2 had homologous distribution of age, gender and BMI percentiles. While significantly lower levels of CD4 were detected in group 1 compared to group 2 with a P-value of 0.000 Regarding Thymosin levels being lower among group 1 (vitamin D below 30ug\ml) than group 2(vitamin D more than or equal 30ug\ml) but this difference was statistically insignificant (Table 2). A non-significant P-value was noticed between both groups regarding recurrent upper respiratory tract infections last year, frequency of dental caries and fracture.

Table 1: Age, gender and BMI percentiles distribution in group1 and group 2

	Group 1 (n=39)	Group 2 (n=9)	P-value
Age mean ± SD	9.87 ±4.1	7.88±2.72	0.151
M:F ratio	21:18	7:2	0.248
BMI percentile mean ± SE	57.52±5.26	42.60±9.951	0.924

SD=standard deviation -SE=standard of error -Significant p≤0.05

Table 2: Levels of CD4 and Thymosin ß4 in group1 and 2

	Group 1 (n=39)	Group 2 (n=9)	P-value
CD4 mean ± SD	0.7967±0.51	2.1278± 1.8	0.000
Thymosin mean ± SD	154.62 ±128.8	307.44±214.2	0.240

Table 3: Frequency of recurrent upper respiratory tract infection last year, Dental caries and Fracture in group1 and group 2

	Group 1 n=39	Group 2 n=9	p-value
Recurrent upper respiratory tract	14 (35.89%)	3 (33.33%)	0.64
Dental caries	27(69.2%)	6(66.7%)	0.58
Fracture in the last year	5(12.8%)	1(11.1%)	0.688

A significantly positive correlation was detected between vitamin D and Thymosin ß4 levels (r=0.496 P-value=0.00), similarly a significantly positive correlation was also noted between vitamin D and CD4 levels (r=0.616 P-value=0.00) (figure1 and 2).

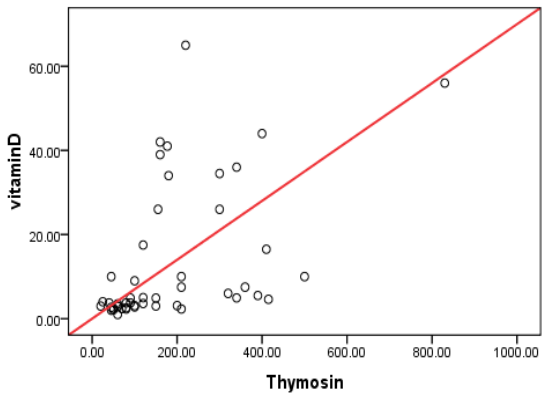

Figure: 1. Correlation between Vitamin D and Thymosin

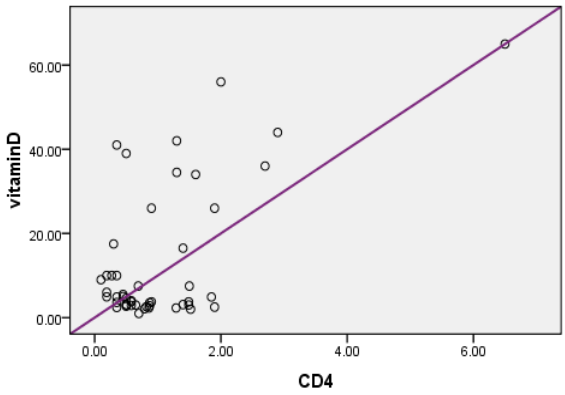

Figure: 2. Correlation between Vitamin D and CD4

DISCUSSION

Vitamin D is considered an essential micronutrient. It is well known for its important role, together with Calcium, in bone mineralization. Vitamin D, in its active form 1, 25-hydroxyvitamin D, has a complex action on the immune system, by modulating and inhibiting its activity in different ways. In the present study, we found that 81.2% of the children had vitamin D level less than 30ug\ml which is defined as insufficient and 66.6% of the 48 children enrolled in this study had vitamin D level lower than 10ug\ml. Accordingly an analysis of 217 obese adolescents in USA revealed that 55% of the patients were vitamin D deficient (defined as 25(OH) D levels <20 ng/ml) while 22% had levels below 10 ng/ml (Smotkin et al.2007). Another study of vitamin D levels in toddlers and infants found 12.1% of the children attending this pediatric clinic (44 out of 365) had levels below 20 ng/ml (Gordon et al.2008) ,while in adult population study done in Iran prevalence of vitamin D deficiency was up to 14.2% (Sima et al 2004)

In the present study, the children mean age was 9.87 ±4.1 years matching the age range in which the playtime spent outdoors is expected to be long. Moreover, living in a sunny place like Egypt should have promoted the cutaneous generation of vitamin D3. Contrary to our anticipation, vitamin D levels were low in a large sector of our study group (in 39 out of 48 participants i.e. more than 80%). This unpredicted low vitamin D level found in this age group can be explained by dark skin color, hot summer weather

that prevent these children from playing outdoors, cultural dress style, using sunscreen cream. Same explanations were reported in other regional studies as in Jeddah, KSA in a cross-sectional study where high prevalence of Vitamin D deficiency was observed in apparently healthy children (Mansour and Alhadidi,2012). In another study on 530 healthy children aged 6 to 7 years in central Iran, Ardestani et al. (2010) found that 26% of the subjects had a serum 25-OH, D level below 33 ng/ml. All these previous studies support what was mentioned that vitamin D levels may differ by latitude and skin pigmentation worldwide but there is growing evidence that living in sunlight areas may not provide adequate amounts of vitamin D so other studies should work on this point (Holick et al.1981).

There was no association between the vitamin D level and the gender of the participants. In addition, no correlation was found between the BMI percentile of the enrolled children and their vitamin D levels. Although this correlation hadn't been studied in children and adolescents studies in adults have had shown evidence of an association between body fat and deficiency of vitamin D (Lenders et al. 2009), (Huh and Gordon 2008) when Vitamin D deficiency had been reported as a risk factor diseases such as osteoporosis, cardiovascular diseases, autoimmune diseases besides some types of cancer (Scragg et al.1995; Bellia et al. 2013; Muldowney et al. 2011) .

As regards immunity and general health condition of the participants the frequency of recurrent upper respiratory tract infection and/or gastrointestinal infection attacks in the last year weren't significantly different in both groups. Although Yildiz et al. reported that patients with insufficient vitamin D levels had markedly higher annual incidence rates of disease with an incidence that decreases directly and proportionally with the increase in serum 25-(OH) vitamin D levels (Yildiz et al. 2012; Abdulhamit et al. 2014).

Positive significant correlation between vitamin D and CD4 was found in this study, CD4 that represent helper cells and contain significant amount of vitamin D receptors as mentioned by Ritterhouse et al. (2014) that vitamin D is important for the innate and the adaptive immune system.

Also a positive significant correlation between vitamin.D and Thymosinβ4 was found which may raise a speculation about a release of thymosin beta 4 secondary stimulation of Vitamin D receptors in the thymus, as it is well established the presence of vitamin D receptors in immune system cells and its various regulatory effects of these cells . This also goes with what Prowedini et al. (1989) had explained about vitamin D effects on adaptive immune cells because of the expression of the nuclear vitamin D receptor and vitamin D-activating enzymes in both T- and B-cells.

CONCLUSION

We conclude from our study that an optimal vitamin D level is crucial to the appropriate functioning of our immune system. We also recognized that living in a sunny region does not guarantee an adequate vitamin D level. We recommend a special reconsideration of all sunny countries where an unpredicted concealed vitamin D insufficiency could be disclosed by further studies.

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