Serum Vitamin-D Levels in Non-Diabetic-Hypertensive and Type 2 Diabetic-Hypertensive Patients

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ABSTRACT

Background: The Renin Angiotensin System (RAS) is one of the main contributors to insulin resistance which leads to T2DM and its complications. The ACE2/Angiotensin-(1-7)/Mas axis has lately been anticipated to function as a negative regulator of the RAS, consequently, rendering a shielding task against progress of type 2 diabetes, as well as, lowering blood pressure. A disruption in this balance may be implicated in the pathogenesis of hypertension in T2DM patients. Depleted vitamin D levels are allied with both hypertension and diabetes, possibly through its negative control on the RAS.

Aim: To measure and compare serum Vitamin D levels in Type 2 Diabetic-Hypertensive and non-Diabetic-hypertensive patients. We aimed to highlight the potential use of Vitamin D as a preventive therapy for hypertension and diabetes mellitus.

Methods: A particular population of selected subjects was categorized into 2 groups, with 49 subjects in each group. Diabetic and hypertensive patients were selected from the SIMS diabetic Clinic and medical wards, Lahore. Anthropometric parameters, as well as, BSR were recorded in the clinics. Blood samples were collected and stored for evaluating the biochemical parameters in the Physiology Laboratory, UHS.

Results: The serum vitamin D levels were higher in group B than those of group A.

Conclusion: Although the current study reinforced the fact that both T2DM and hypertension are risk factors for CKD, we were unable to prove that Vitamin D levels are lower in patients with hypertension compounded with diabetes mellitus.

Keywords: Vitamin D level, non-diabetic, hypertensive

INTRODUCTION

The RAS plays a vital position in BP management and fluid homeostasis. It can be broadly divided into two, beneficially antagonistic arms; the classical, pressor arm, with the ultimate production of angiotensin II (Ang II) and a counterbalancing, depressor arm, including angiotensin 1-7. In a healthy individual, both arms work synergistically, balancing each other perfectly. Many diseased states arise due to imbalanced activity of RAS, further highlighting its importance.

Although sunshine is the best source of vitamin D, essential for calcium homeostasis, supplements may be required in populations who are unable to obtain adequate exposure to the sun. Due to the shift to sedentary indoor lifestyles, vitamin D shortage has become a worldwide problem (Aly et al., 2016).

Vitamin D levels are influenced by numerous physiological and environmental dynamics such as age, gender, body mass index, season, in addition to geological location (Wimalawansa, 2018). A study conducted in Pakistan revealed more than 98% study subjects to be vitamin D deficient (70% being severely deficient), with females generally having lower vitamin D levels than males (Roomi et al., 2015). The cultural and religious differences in dressing, use of sunscreen, degree of pollution, color and condition of the skin, also vary the amount of sunlight dermal exposure and consequently, the vitamin D blood levels (Wimalawans, 2018).

Depleted 25(OH) D levels have been linked to all-cause mortality combined with cardiovascular events, especially hypertension (Forman et al., 2008; Forman et al., 2007; Griffin et al., 2011) and systolic blood pressure (Jorde et al., 2010; Judd et al., 2008; Kunutsor et al., 2013). The truly noteworthy hypothesis associating vitamin D to blood pressure is its probable task as an inverse endocrine manager of the renin-angiotensin system. Animal studies showed that vitamin D acted as a down regulator of renin (Li, 2012; Li et al., 2002). In human cross-sectional studies, reduced vitamin D status was coupled with greater plasma renin activity (PRA), higher Angiotensin II concentrations, modified responses to Angiotensin II, in addition to greater RAS activity in vascular tissue (Dong et al., 2012; Resnick et al., 1986; Tomaschitz et al., 2010; Vaidya et al., 2011). As vitamin D impedes renin creation (Li et al., 2002) and local pancreatic islet renin-angiotensin system over-activity (Cheng et al., 2013), with time it reduces raised blood pressure (Muscogiuri et al., 2017). Vitamin D is allied with β-cell function, incident diabetes, peripheral insulin sensitivity, and mortality in diabetes, presumably through its supervision of the RAS. The intra-pancreatic and circulating RAS are conceded to negatively modify peripheral insulin...
sensitivity along with β–cell function. Thus, it may be
templated that the down-regulation of the RAS by
vitamin D might arbitrate its advantageous consequences
on glycemic control in addition to diabetes (Vaidya and
Williams, 2012).

MATERIALS AND METHODS

This Cross Sectional, Comparative study was conducted in
the Department of Physiology, University of Health
Sciences, Lahore, over a period of 1 year. The research
was approved by the Ethical Committee of the institution. A
total of 96 hypertensive subjects, between the ages of 30-
60 were selected from the medical OPD and diabetic
centers of SIMS. They were categorized into 2 groups;
Group A including 46 non-dieabetic and Group B
comprising 49 diabetic, hypertensive patients. After
obtaining written, informed consent from each participant,
general and systemic examinations were conducted to rule
out any underlying disease. Blood pressure was estimated
by using sphygmomanometer. Body mass index was
calculated with the help of formula; BMI=body weight (Kg)/
height (m²). Random blood sugar was determined on the
spot. Five milliliter blood was drawn from ante-cubital vein
under aseptic conditions. It was placed in serum tubes.
Tubes were then centrifuged for 10 minutes, at a speed of
3000 revolutions per minute (rpm) to obtain serum. With
the help of disposable blue tips, serum was drawn and
stored in aliquots at -40 °C. Serum 25 (OH) Vitamin D
together were verified by 25 OH Vitamin D Total ELISA kit
manufactured by DIA source Immuno Assays S.A.
Germany, with an automated EIA analyzer (Bio-Rad
Laboratories, Hercules, CA, USA).

RESULTS

We obtained a non-significant difference (p= 0.415)
between the Median (IQR) of Vitamin D levels in non-
diabetic, hypertensive subjects (14.39 mg/dl) and diabetic,
hypertensive subjects (15.78mg/dl) as seen in table 1. Substantial negative correlation of sVitamin D level in
group A was seen with height (Spearman rho = -0.370, p =
0.019) and uACE2 (rho =-0.336, p = 0.034) and in group B
was perceived with waist circumference (Spearman rho = -
0.354, p = 0.023), and BSR (Spearman rho = -342, p =
0.029).

![Fig. 1: Comparison of means of Vitamin D in Group A & group B.](image)

Table 1: Data Distribution & Comparison of All Parameters in Group A & Group B.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A</th>
<th>Group B</th>
<th>p-value</th>
<th>*distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.0 (45.0-60.0)</td>
<td>55.0 (48.0-60.0)</td>
<td>0.843</td>
<td>Non-normal</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.6±0.1</td>
<td>1.6±0.1</td>
<td>0.203</td>
<td>Normal</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.5 (62.0-74.0)</td>
<td>75 (68-88.5)</td>
<td>0.001</td>
<td>Non-normal</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>89.2±11.7</td>
<td>107.9±11.9</td>
<td>0.000</td>
<td>Normal</td>
</tr>
<tr>
<td>Hip (cm)</td>
<td>100.3±6.8</td>
<td>111.0±13.7</td>
<td>0.000</td>
<td>Normal</td>
</tr>
<tr>
<td>BMI</td>
<td>26.0 (24.9-28.1)</td>
<td>30.4 (26.2-34.8)</td>
<td>0.000</td>
<td>Non-normal</td>
</tr>
</tbody>
</table>

Biochemical Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A</th>
<th>Group B</th>
<th>p-value</th>
<th>*distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSR (mg/dl)</td>
<td>102.5 (98.0-133.5)</td>
<td>200.0 (144.0-267.5)</td>
<td>0.000</td>
<td>Non-normal</td>
</tr>
<tr>
<td>sCr (mg/dl)</td>
<td>1.0 (0.8-1.3)</td>
<td>1.1 (0.8-1.4)</td>
<td>0.306</td>
<td>Non-normal</td>
</tr>
<tr>
<td>sVit. D (ng/dl)</td>
<td>14.4 (10.2-20.9)</td>
<td>15.8 (11.1-23.6)</td>
<td>0.415</td>
<td>Non-normal</td>
</tr>
<tr>
<td>uGlucose (mg/dl)</td>
<td>0.7 (0.9-0.7)</td>
<td>0.6 (0.5-0.9)</td>
<td>0.440</td>
<td>Non-normal</td>
</tr>
<tr>
<td>uACE (ng/dl)</td>
<td>26.5 (19.5-34.3)</td>
<td>22.9 (16.0-28.2)</td>
<td>0.007</td>
<td>Non-normal</td>
</tr>
<tr>
<td>uACE2 (ng/dl)</td>
<td>4.0 (2.3-5.9)</td>
<td>4.3 (2.9-7.1)</td>
<td>0.440</td>
<td>Non-normal</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>64.5±92.77</td>
<td>55.4±71.56</td>
<td>0.788</td>
<td>Non-normal</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>82.0±38.8</td>
<td>88.5±50.00</td>
<td>0.310</td>
<td>Normal</td>
</tr>
</tbody>
</table>

*value generated according to Shapiro Wilk Test
** Mean±SD for normally distributed, Median(IQR) for non-normally distributed Data.
Diabetes and hypertension are two of the chronic ailments whose incident rate is rising every day. According to WHO (Organization, 2016), global prevalence of diabetes among adults over 18 years has risen from 4.7% in 1980 to 8.5% in 2014. In 2015, an estimated 1.6 million deaths were directly caused by diabetes. WHO (2016) expects diabetes will be the seventh leading cause of death in 2030.

One in three adults worldwide has raised blood pressure (van de Vijver et al., 2012) (responsible for over half the deaths due to stroke and heart attack) was reported in the world health statistics, 2012 (Organization, 2012), with evidence of dramatic increase in the conditions that trigger heart disease and other chronic illnesses (Martin, 2008), particularly in low and middle-income countries. Given the ever-rising incidence of diabetes and hypertension, along with their related morbidity and mortality, a lot of research is aimed at understanding the pathophysiology of both DM and hypertension. But we found the serum vitamin D levels to be greater in group B. This may be because Vitamin D levels are influenced by numerous other physiological and environmental factors such as age, gender, body mass index, season and geological location (Wimalawansa, 2018). Although we tried to match both groups demographically, seasonal variation could not be excluded and may have confounded our results. The cultural and religious differences in dressing, use of sunscreen, degree of pollution, color and condition of the skin, also vary the amount of sunlight dermal exposure and, consequently, the vitamin D blood levels (Wimalawansa, 2018). Most of these factors were difficult to be catered for in our setup and may have also played a role in the outcome of our research. Another factor which may be responsible for the unexpected result could be the treatment the subjects were receiving. Treatment with RAS inhibitors and allopurinol may cause an increase in 25, Hydroxyl D3 serum levels, whereas treatment with statins could decrease these levels (Yuste et al., 2015). Although we tried to obtain an adequate drug history, most of the patients, especially those of group A, were unaware of what drugs they were receiving and had no written documentation. Therefore, our results could have been confounded by their medication.

**CONCLUSION**

Vitamin D is an important player in the development of both hypertension and DM, but we failed to indicate that vitamin D levels are lower in subjects with both chronic illnesses as predicted. This may be due to the fact that vitamin D levels are influenced by a plethora of factors and we were unable to account for them.

**REFERENCES**

7. No effect of vitamin D.


