Study of Vitamin D Deficiency in Inpatients Admitted with Chronic Diseases at Ain Shams University Hospital

Thesis

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List of Abbreviations

1,25(OH)2D .....1, 25-dihydroxyvitamin D

ALB.....Albumin

ALK.P .....Alkaline phosphatase

ALT.....Alanine aminotransferase

AST.....Aspartate aminotransferase

BUN .....Blood urea nitrogen

Ca.....Calcium

CCA .....Cholangiocarcinoma

CHF .....Congestive heart failure

CLD .....Chronic liver disease

COPD.....Chronic obstructive pulmonary disease

Cr .....Creatinine

CVD .....Cardio vascular disease

CVS .....Cerebrovascular stroke

CYP.....Cytochrome P

CYP24A1 .....Cytochrome P450, family 24, subfamily A, polypeptide1

CYP27B1 .....Cytochrome P450, family 27, subfamily B, polypeptide1

CYP2R1 .....Cytochrome P450, family 2, subfamily R, polypeptide1

DBP .....Vitamin D binding protein

DHCR7.....7-dehydrocholesterol reductase

DM.....Diabetes Mellitus

DNA .....Deoxyribonucleic acid

FEV .....Forced expiratory volume

FGF23 .....Fibroblast growth factor 23

List of Abbreviations (Cont.)

FVC .....Forced vital capacity

Gc-globulin.....Group-specific component

GWAS .....Genome-wide association study

HCC.....Hepatocellular carcinoma

HF .....Heart failure

HGB.....Hemoglobin

HS .....Highly significant

IBD .....Inflammatory bowel disease

IL.....Interlukin

IU.....International unit

KDa .....kilodalton

Mg .....Magnesium

MMP .....Matrix metalloproteinase

MS .....Multiple sclerosis

NAFLD .....Non-alcoholic fatty liver disease

NASH.....Non-alcoholic steato-hepatitis

NT-proANP .....N-terminal pro-ANP

NF- κB.....Nuclear factor kappa B

OPG.....Osteoprotegerin

PBC .....Primary biliary cirrhosis

PO4 .....Serum Phosphorous

PTH .....Parathyroid hormone

r.....Pearson correlation coefficient

RANKL.....Receptor activator of nuclear factor kappa-B ligand

List of Abbreviations (Cont.)

RAS .....Renin-Angiotensin system

RCT .....Randomized controlled trial

RXR.....Retinoic acid X receptor

SAPS.....Simplified Acute Physiologic Scores

SD.....Standard deviation

T.Bil .....Total bilirubin

TLR .....Toll-like receptor

T.prot.....Total proteins

T1DM .....Type 1 diabetes mellitus

TNF .....Tumour necrosis factor

VDI.....Vitamin D intoxication

VDR.....Vitamin D receptor

VDRE.....Vitamin D response element

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Abstract

Introduction: Vitamin D deficiency among hospitalized patients may be more widespread than realized. Vague musculoskeletal complaints in these chronically ill patients may be attributed to multiple underlying disease processes rather than a deficiency in vitamin D. However, the failure to diagnose an underlying deficiency places the patient at risk for continued pain, weakness, secondary hyperparathyroidism, osteomalacia, and fractures. **Aim of the Work:** Investigate the prevalence of vitamin D deficiency in hospitalized patients and its impact on the length of stay and outcome of hospitalization. **Subjects and Methods:** Eighty patients admitted to our department of medicine at Ain Shams University hospital, were sampled for their vitamin D level on admission. Sampling was part of the routine hospital workup. **Results:** Our results revealed that 37 patients (46%) were vitamin D insufficient, 32 patients (40%) were deficient and only 11 patients (14%) were sufficient. Vitamin D level had a highly significant inverse correlation with length of hospital stay ($r= -0.648$) ($p= <0.001$). In vitamin D deficient and insufficient groups there was a highly significant inverse correlation with outcome of hospital admission ($r=-4.952$) ($p= <0.001$), ($t=-4.314$) ($p=<0.001$) respectively. **Conclusion:** In conclusion we found that, vitamin D deficiency and insufficiency are significantly associated with a longer hospital stay and a poor outcome of hospital admission. vitamin D sufficiency may be a significant confounder in patients admitted to hospital with acute deterioration of their chronic illnesses. Significantly better outcome regarding morbidity and mortality in vitamin D sufficient patients urges the medical staff to pay attention to that poorly recognized albeit important problem.

Keywords: Vitamin D, Chronic Diseases, mortality, morbidity.

INTRODUCTION

Vitamin D is a fat-soluble vitamin that is naturally present in very few food variants, and available as a dietary supplement. It is mainly produced endogenously when ultraviolet rays from sunlight strike the skin and trigger vitamin D synthesis; vitamin D obtained from sun exposure, food, and supplements is biologically inert and must undergo two hydroxylations in the body for activation. The first occurs in the liver and converts vitamin D to 25-hydroxyvitamin D (25(OH)D), also known as calcidiol, the second occurs primarily in the kidney and forms the physiologically active 1,25-dihydroxyvitamin D [1,25$(OH)_2$D], also known as calcitriol ***(Food and Nutrition Board, 2010).***

Vitamin D promotes calcium absorption in the gut and maintains adequate serum calcium and phosphate concentrations to enable normal mineralization of bone and to prevent hypocalcemic tetany, it is also needed for bone growth and bone remodeling by osteoblasts and osteoclasts ***(Holick et al., 2007).***

Vitamin D deficiency is a common problem among Egyptian females across all age groups, for whom contributing factors include inadequate sun exposure possibly related to cultural/social factors, and insufficient

dietary calcium, wearing a sunscreen with a sun protection factor of 30 reduces vitamin D synthesis in the skin by more than 95% ***(Botros et al., 2015).***

Vitamin D has other roles in the body, including modulation of cell growth, neuromuscular function and reduction of inflammation. Also benefits on cardiovascular health, metabolism and prevention of cancer and autoimmune diseases have been described ***(Cranney et al., 2007).***

Many genes encoding proteins that regulate cell proliferation, differentiation, and apoptosis are modulated in part by vitamin D. Many cells have vitamin D receptors, and some convert 25(OH) D to 1, $25(OH)_2D$ ***(Jones et al., 2008).***

Vitamin D receptors are found in nearly all types of immune cells. Its action on innate immunity is stimulatory, while its action on adaptive immunity is mainly considered to be modulatory ***(Kempker et al., 2012).***

Muscle weakness due to vitamin D deficiency is predominantly of the proximal muscle groups and is manifested by a feeling of heaviness in the legs, tiring easily, and difficulty in mounting stairs and rising from a chair; the deficiency is reversible with supplementation. Muscle atrophy-particularly of type II fibers-has been described histopathologically ***(Bischoff-Ferrari et al., 2006).***

Vitamin D deficiency is rarely considered or treated in critically ill patients, however, recently reported three cases of life-threatening hypocalcemia secondary to vitamin D deficiency, highlighting potential acute complications ***(Holick et al., 2009).***

Deficiency of 25(OH)D prior to hospital admission is a significant predictor of short and long term all cause patient mortality and blood culture positivity in a critically ill patient population ***(Braun et al., 2011).***

Patients with 25 (OH) D deficiencies in medical intensive care unit have increased hospital mortality, longer mechanical ventilation, and longer MICU stay ***(Padhi et al., 2014).***

Vitamin D deficiency is defined as a 25(OH)D below 20 ng/ml, while Vitamin D insufficiency has been defined as a 25(OH)D of 21–29 ng/ml ***(Holick et al., 2007).***

Serum concentration of 25(OH) D is the best indicator of vitamin D status. It reflects vitamin D produced cutaneously and that obtained from food and supplements and has a fairly long circulating half-life of 15 days ***(Jones et al., 2008).***