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## Correlation of admission serum 25-hydroxyvitamin D levels and clinical outcomes in critically ill medical patients

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## SUMMARY

**Purpose:** The aim of this study was to determine the incidence of hypovitaminosis D and the correlation of admission serum 25-hydroxyvitamin D (25-OHD) levels and clinical outcomes in critically ill medical patients.**Methods:** A prospective, observational study was conducted. All critically ill medical patients admitted to the medical ICU were recruited. Blood sampling for serum 25-OHD was taken within 24 h after ICU admission. The levels of 25-OHD were dichotomized into deficiency and sufficiency groups. A serum 25-OHD level <20 ng/dL was defined as a vitamin D deficiency. All demographic data as well as biochemical tests were recorded. The primary outcome was incidence of hypovitaminosis D and 28-day mortality. The secondary outcomes were ICU and hospital mortality, ICU and hospital length of stay, mechanical ventilator days, and ICU-acquired infection.**Results:** From 116 cases, the incidence of hypovitaminosis D was 64.66%. The median serum 25-OHD was 15.1 (3.0, 67.2) ng/dL. There was no difference in 28-day mortality between the vitamin D statuses (20% vs. 17.1%,  $p = 0.70$ ). However, the ICU-acquired infection tended to be higher in the vitamin D deficiency group but this was not statistically significant (25.3% vs. 19.5%,  $p = 0.07$ ). Other secondary outcomes were comparable

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between the groups. Vitamin D levels were significantly correlated to the severity of illness of critically ill medical patients ( $r = -0.258$ ,  $p = 0.005$ .)

**Conclusions:** The incidence of hypovitaminosis D in critically ill medical patients in our region was high. In this current finding, vitamin D deficiency in critically ill medical patients may not related to 28-day mortality, ICU and hospital mortality, ICU and hospital length of stay, mechanical ventilator days or ICU-acquired infection, but vitamin D levels were significantly correlated to the severity of the illness. However, the larger study is required to confirm this finding.

**Trial registration:** The study protocol is retrospectively registered at the Thai Clinical Trial Registry (TCTR) with the identification number TCTR20180211004.

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## 1. Introduction

Vitamin D is a fat-soluble vitamin which is normally synthesized in the human skin and is mediated mainly by ultraviolet-B (UV-B) radiation from sunlight. Vitamin D compounds are subsequently activated in the liver to 25-hydroxycholecalciferol (calcidiol) and eventually converted to 1,25-hydroxycholecalciferol (calcitriol) in target organs for active functions [1]. Although vitamin D can be obtained from food products, such as milk, butter, fish, and mushrooms, the main source of vitamin D essentially comes from skin synthesis. There are several factors involved in vitamin D synthesis in humans that include latitude, season, atmospheric conditions, race, skin color, and even genetics [2].

Although vitamin D is typically recognized for the support of musculoskeletal functions and the regulation of serum calcium and phosphate levels, recent evidence demonstrated other pleiotropic actions of vitamin D, which included enhanced epithelial barrier integrity, regulation of inflammatory responses, and immunologic responses in both innate and adaptive immunity [3]. A total, serum 25-hydroxyvitamin D (25-OHD) level is currently accepted as the indicator of vitamin D status in humans [4]. From the current evidence, the deficiency of vitamin D has been correlated to poor clinical outcomes such as increased infectious complications, impairment of physical function, and mortality [5–9]. However, the results of this correlation, as well as the clinical outcomes in critically ill patients, were inconsistent and inconclusive.

Several studies demonstrated the correlation of ICU mortality and complications with hypovitaminosis D [2,10–12], but some studies could not confirm these findings [3,13]. Apart from that, the incidence of vitamin D deficiency in critical illnesses was reported to have a wide range spanning between 20 and 70%, which was also dependent on the location of the study site [13,14]. The level of hypovitaminosis D in Southeast Asian countries may be lower than other parts of the world because of plentifully sunshine within these geographical areas. A previous observational study in our area in Thailand showed that the incidence of vitamin D deficiency in hospitalized patients was only 20%. Furthermore, this was considered to be at a mild deficiency level [15]. Additionally, there was no correlation of vitamin D levels in the clinical outcomes of hospitalized patients.

Therefore, we conducted this prospective, observational study to determine the incidence and correlation of admission serum 25-OHD level to clinical outcomes including mortality, infection rate, and length of stay in critically ill medical patients.

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