“Vitamin D status and COVID 19 in Lebanon among adults: A cross-sectional study in South Lebanon”

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THESIS SUMMARY

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The Project

Title: “Vitamin D status and COVID 19 in Lebanon among adults: A cross-sectional study in South Lebanon”

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Preface

This thesis is submitted as a part of the Master of Philosophy (MPhil) degree in International Community Health at the University of Oslo. According to the requirements of the MPhil Thesis, November 2022, from the Department of Community Medicine and Global Health; the current submission follows criteria two (one article submitted or near submission to an international peer-reviewed journal plus a summary) in the form of a thesis accepted.

The thesis summary begins with an abstract of the article near submission for publication. Introduction and methodological considerations are presented with detailed methods and materials. Results and discussion of the findings are not included in this summary in accordance with department regulations for MPhil thesis criteria two but additional results and discussion points are mentioned. A copy of the near-submission article is included, article and relevant appendices are included.

Abbreviations

BMI: Body Mass Index

CI: Confidence Interval

COVID 19: Coronavirus Disease 2019

CPBA: Competitive Protein-Binding Assays

HPLC: High Protein Liquid Chromatography

IOM: Institute of Medicine

IRB: Institutional Review Board

LC-MS/MS: Liquid Chromatography-Tandem Mass Spectrometry

NSD: Norwegian Social Science Data Services

OR: Odds Ratio

PCR: Polymerase Chain Reaction

PPE: Personal Protective Equipment

RDA: Recommended Daily Allowance

REK: Regional Committees for Medical and Health Research Ethics

SD: Standard Deviation

SPSS: Statistical Package of Social Sciences

TSD: The Services for Sensitive Data

WHO: World Health Organization

25(OH)D: 25 Hydroxyvitamin D

Abstract

Vitamin D status and COVID 19 in Lebanon among adults

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Abstract

Background: The current COVID 19 pandemic has affected almost every nation in the world and led to the development of respiratory tract symptoms. Vitamin D has been proposed to play an important role, especially in upper respiratory tract infections. Recently, numerous studies and reports associating low serum 25-hydroxyvitamin D (s-25(OH)D) levels and adverse outcomes in COVID 19 have also emerged. Therefore, we aimed to assess the association between Vitamin D status and COVID 19 among adults in Lebanon.

Method: This is a cross-sectional study where the participants were recruited from one of the largest university hospitals in south Lebanon. The participants (n 384) aged 18-75 years who came to the hospital to perform a COVID 19 test were asked for their participation. Background variables were collected with a structured questionnaire. Blood samples were collected and analyzed for s-25(OH)D concentration using Electrochemiluminescence immunoassay, and COVID 19 was tested.

Results: The mean s-25(OH)D was 46.8 (SD 28.1), with no significant difference between men and women. Almost 63% of women and men had Vitamin D insufficiency (s-25(OH)D <50 nmol/L). Furthermore, 28 % of the participants had positive PCR results. There was no significant association between s-25(OH)D levels and PCR results ((OR = 0.982, 95% CI: 0.961-1.004), p=0.10)). Adjustment for sociodemographic factors did not alter the results.

Conclusion: There was a high prevalence of Vitamin D insufficiency among adults participating in COVID 19 test hospital in Lebanon, and it was not associated with COVID 19. Further research is required to investigate the health consequences of poor s-25(OH)D status for this population.

Keywords: COVID 19, S-25(OH)D, Lebanon, Socio-demographic factors, Vitamin D supplements

Chapter 1: Introduction

1.1 Lebanon: Demography and population profile

Lebanon is a small country located in the Middle East with a total of almost 10,500 Km^2; it is neighbored by Syria to the north and Israel/ Palestine to the south and faces the Mediterranean sea (1). The Republic of Lebanon became a nation-state in late1943 after gaining independence from France and since then ruled by a political system that is founded on confessionalism, in which political power and positions are granted according to religious proportionality (2). This country has a total of 18 recognized religions, making it so diverse, but the three largest religious denominations (Christian Maronites, Shia Muslims, and Sunni Muslims) which occupy the highest government position (3). Lebanon is divided into eight governorates (Beirut, North, Akkar, South, Nabatiyeh, Beqaa, Baalbeck-Hermel, and Mount Lebanon). Every one of those governorates is further subdivided into small administrative areas called "Kada," and every small "Kada" is made up of several independent municipalities. The total number of Lebanese "Kadas" is 25, and the total number of municipalities is 1561 within the country (1). Given the geographic location of Lebanon and the ongoing political instability from within the country, and the surrounding conflicts and wars in the neighboring countries (Syrian war and Palestinian-Israeli conflict), the country's population consists of a total of 1.5 million Syrian refugees and almost 1 million Palestinian refugees out of the estimated 6 million people residing in the country (1,4). Thus, Lebanon is considered to have the world's largest refugee population per capita in the world and the densest refugee population (1).

Lebanon witnessed a massive explosion in august 2020, alongside a rapid increase in COVID 19 cases, which has been contrasted similarly to the Hiroshima bombing (5). The explosion resulted in a total of 200 death, more than 5000 injuries, and a total of 300,000 people who became homeless (6). Moreover, the explosion led to the destruction of the hospitals, which are located within 1.5 kilometers, and many others were put off work for several weeks (5,6). The net result was a severe demand for healthcare services at a time of crisis, the psychological strain on all the healthcare workers, and the transformation of the country into a crisis management unit for both COVID 19 and dealing with explosion casualties (5).

Moreover, the country that used to be labeled as "water secure" became a "water deficit" due to the lack of water protection policies on the national level, the tremendous number of refugees who came into the country, the economic crisis, and the poorly managed water network in the country (1).

1.1.1 Lebanon and COVID 19

Lebanon has dealt with a lot of socioeconomic challenges topped up by the Seaport explosion and financial uprising (5). Lebanon has been struck by the COVID 19 Pandemic with the recording of the first case in the country being recorded by a Lebanese woman returning from a visit to Iran on the 21st of February 2020 (4). According to the Lebanese ministry of public health, the country has now a total exceeding 1 million confirmed COVID 19 cases and 10,400 confirmed deaths, with a vaccination rate not exceeding 35% for two doses of vaccinated citizens and 24% for three doses of vaccinated ones (7). The Lebanese population is living in extreme poverty or needs social assistance (8).

It should also be mentioned that Lebanon has already been suffering from an economic crisis that hit the country starting on the 19th of October 2019, when people started protesting the financial situation and the currency inflation. The situation is continuing to escalate until now (9).

However, It is noted that the Lebanese Government has made a national vaccination plan, to vaccinate a huge proportion of the population with support from various entities such as the COVAX panel (a global alliance platform that is funded by the WHO), a loan from the World Bank and several negotiations with private companies (10). Even with providing the vaccines free of charge to the public and mass media promotion and awareness campaigns on the roles of vaccines and their benefits in terms of protection and breaking the chain of spreading of COVID 19, the vaccination rate was not exceeding 35% for two doses vaccinated citizens and 24% for three doses vaccinated citizens respectively (7).

In addition to the mentioned above, the Lebanese crisis has affected both residents and refugees with the latter being affected the most (11). Several agencies that are directly aiding Lebanon, such as the United Nations Higher Commission for Refugees, the United Nations Refugee Agency, the United Nations World Food Programme, and the United Nations Children's Fund, reported their worries about the refugee community residing in Lebanon would not be able to afford the minimal survival expenditure basket and that many Syrian refugees are in extreme poverty (11).

1.1.2 Lebanon and Vitamin D

The vitamin D status in the general Lebanese population is not fully known. Still, several studies have already suggested that Vitamin D deficiency is highly prevalent among adults in Lebanon (12) and in the Middle East in general due to several factors, mainly cultural practices, and low Vitamin D supplementation during breastfeeding (13). It is worth noting that Arabi et al. mentioned in their research article a study that was done in Lebanon among community-dwelling 316 participants aged between 30-50 years from both urban and rural areas that showed that 75% of the studied sample had a serum 25(OH)D level below 30 nmol/l and that one-third of this sample has severe serum 25(OH)D deficiency with levels below 12 nmol/l (12). Even though knowingly that the above-mentioned study was dated a decade ago, it does highlight the Vitamin D status of the Lebanese community and the need for nationwide community studies.

This study was formed in an attempt to fill gaps in the literature by investigating the association between COVID 19 and Vitamin D and their risk factors among adults in Lebanon. The findings presented in the article (Appendix 1) contribute as a sample of the Vitamin D status among the Lebanese community and attempt to test the association by considering the impact of Body Mass Index (BMI), age, education, and gender. And it is hoped that the findings of this study will be used to help support the Lebanese people in fighting the COVID 19 pandemic and improve awareness among the community regarding Vitamin D.

Chapter 2: Literature review

This section describes the literature review that has been used to develop this thesis. The search strategies will first be described, followed by a compilation of relevant background information regarding the following topics: COVID 19, Vitamin D, Age, Gender, Education, BMI, the definition of Vitamin D, its sources, how it is metabolized and mechanism of action and Recommended Daily Allowance (RDA), mechanisms of assessing vitamin D status and its relative cut-off points, Vitamin D status in Lebanon, the population at risk of Vitamin D deficiency, health consequences of Vitamin D deficiency and factors affecting vitamin D status.

First, a comprehensive search for systematic reviews on COVID 19 and Vitamin D in Lebanon was conducted to gain an overview of the thesis topic. As there were no such reviews done in Lebanon, reviews encompassing the whole of the Middle East in particular and the rest of the world, in general, were considered. PubMed, and Google scholar, with a filter for Systematic

reviews, were searched using the following Medical Subject Heading (MESH) terms: [COVID 19] + [Vitamin D] + [risk factors].

A total of 5 systematic reviews were found, three of them were removed due to being irrelevant to the topic, and only two were selected. The first systematic review was entitled " COVID 19 gender susceptibility and outcomes: A systematic review," done by Lakbar et al. in 2020; it suggested that COVID 19 might be associated with worse outcomes in males than that in females, thus suggesting a gender difference with regards to COVID 19 outcome.

The Second systematic review was entitled "Obesity in patients with COVID 19: a systematic review and meta-analysis," done by Huang et al. in 2020; it suggested that obesity increases the risk of hospitalization, Intensive care unit admission, and death among patients with COVID 19 and that excessive visceral adiposity is associated with severe COVID 19 thus suggesting that BMI does affect COVID 19 outcome.

2.1 Search Strategies:

Academically advanced research techniques were employed and included two databases: PubMed and Google Scholar. Terms and keywords directly relating to my research topic were used. A sample of these terms included:

Covid 19, Vitamin D, Age, Gender, BMI, vitamin D and Lebanon, vitamin D and Covid 19, Vitamin D deficiency and Risk factors, Covid 19 and Risk factors, Association between vitamin D and Covid 19 MESH words were used in PubMed

Synonyms of keywords were used in both, and time span limitations (last ten years) were used after. Only results published in "English" were included. "Snowballing technique" and "traction of the citations" were also used to build knowledge on the topic. The results were then filtered, duplicates were removed using "Zotero," and the citation was done using Vancouver style throughout the article and the summary manuscripts.

PubMed library and Google Scholar were researched extensively, and a comprehensive search for primary articles on the association of COVID 19 and Vitamin D was made, following limited relevant data found through the search of systematic reviews. A total of 86 Articles were identified; after carefully reading the articles and assessing them, a total of 33 articles were eliminated due to having irrelevant topics. Out of the remaining 53 articles, a total of 2 systematic reviews were identified as directly relating to the topic. Both systematic reviews were read carefully and were

essential as a beginning point of the early stages of developing the research proposal.

The most relevant articles found through this search pattern are listed and described below. One article was from Lebanon with regards to Vitamin D, while the others were from various other countries spread worldwide. With regard to COVID 19, three articles were found from Lebanon related to risk factors, and the rest were from worldwide resources. Regardless of the origin of the articles, they provided information on the methodology used in addressing COVID 19 and Vitamin D association and associated risk factors and acted as a knowledge base and initiation point for the study into the existing literature on topics relevant to this thesis. Moreover, several articles were identified from the references list within the identified articles, and reports from the World Health Organization and Ministry of public health in Lebanon were utilized to conclude estimates and relevant figures around the topic being researched.

Article	Methodology	Relevant Results	Comments
Corriero et Al. 2022 (11)	Peer-reviewed literature published between 2015-2021	Lebanon is facing food insecurity and water shortage, and high inflation rates that have been severely aggravated by COVID 19	The importance of studying the association between COVID 19 and Vitamin D to aid the people of Lebanon during COVID 19 pandemic
Arabi et Al. 2021 (12)	A random sample of Lebanese adults living in the greater Beirut area aged 45.3 with 15 years below or above that target was selected, and a total of 446 participants	Vitamin D deficiency in the Lebanese population is highly prevalent using both the 50 and 30 nmol/L cut-off points with a rate of 71.9% and 39.1%, respectively, and several risk factors were identified	This study was the only available study found in Lebanon that addresses the community's level of Vitamin D and sheds lights the importance of studying the Vitamin D status in Lebanon and that the general image is that the deficiency is high
Huang et Al.	A systematic review and meta-	The study concluded that Obesity increases the risk	This study highlights the association between obesity

(2020)	analysis were done utilizing a total of 45650 participants from 30 studies	of hospitalization, Intensive care unit admission, and death among COVID 19 patients	and the outcome of COVID 19 and raises the question of assessing the effect of obesity and contracting COVID 19

Table 1 primary articles that helped develop the idea of this research

2.2 COVID 19 and sociodemographic factors

"SARS-COV-2", Also known as COVID 19, is a worldwide pandemic that started on the 11th of March 2020 as declared by the Word Health Organization (WHO); it originally started in China in late 2019 and later on began to spread out to the rest of the world causing severe impacts on different countries on many aspects such as increased rates of poverty and economic crisis on top of the apparent health-related turmoil (14). Today, the WHO states that there are more than 521 million confirmed cases and greater than 6 million confirmed deaths due to this pandemic even though vaccines have been developed and mass vaccination started (15).

2.2.1 Gender and COVID 19

It is thought by some researchers that the female gender is associated with low levels of vitamin D (16,17). However, when it comes to COVID 19, it is thought that the female gender is associated with less risk of catching COVID 19, and the mortality rate is lower among females compared to the male gender after being infected with COVID 19 although they face a lot of challenges in the society, economy, and employment wise (18,19). Yet, it was noted due to the lack of available studies on this topic by Lakbar et al that this area needs to be addressed furthermore in the future (19).

2.2.2 Age and COVID 19

Several studies suggested that older adults are at higher risk of vitamin D deficiency due to many factors ranging from dietary habits, social habits, and problems in the metabolism of vitamin D (20,21). A recent study suggested that Aging is related to higher risks of catching COVID 19 and leads to higher mortality and that everyone above or equal to 70 years of age is at moderate risk of COVID 19 regardless of health status (22).

2.2.3 Education and COVID 19

Literacy and educational levels showed controversial results when tested with vitamin D status. However, it is different for education and COVID 19 as recent studies suggest that people with

higher educational levels are less likely to be infected with COVID 19 as they tend to follow the government's regulations and recommendations and have lower mortality rates (23–26).

2.2.4 Body Mass Index (BMI) and COVID 19

Several studies have linked BMI to COVID 19 and Vitamin D levels. It is believed that people who have high BMI are thought to have lower vitamin D levels compared to those with normal BMI as it is thought that vitamin D is diluted in fat cells, and thus, they need higher levels of Vitamin D to achieve the normal status (27,28). Moreover, obesity (high BMI) is linked to higher odds of having COVID 19 and developing severe symptoms and higher mortality (29–31).

2.3 Vitamin D status and related factors

This section will go through the definition of Vitamin D, its sources, how it is metabolized and mechanism of action and RDA, mechanisms of assessing vitamin D status, and its relative cut-off points.

2.3.1 Definition of Vitamin D and its sources

Vitamin D is a prohormone that is produced in the skin or from diet and is first converted to 25-hydroxyvitamin D (25-(OH)D) in the liver. At the kidney level, the 25-(OH) D gets further metabolized to 1α, 25-dihydroxy vitamin D3 (1,25D3) or calcitriol which is the biological most active form of Vitamin D. It has several roles in the human body, besides its prominent role in calcium homeostasis, it serves other functions ranging from regulation of cell proliferation to differentiation and apoptosis in several cell types and tissues (32). This article will focus on the proposed key role in preventing upper respiratory tract infections (33) due to the potential it might have on COVID 19. The two primary forms of Vitamin D, D2 (ergocalciferol) and D3 (cholecalciferol), are obtained in the skin after sun exposure mainly and some forms of Vitamin D enriched food and supplements (32).

2.3.2 Vitamin D metabolism and mechanisms of action

Vitamin D is biologically inactive; it requires two enzymatic processes to become active. The cutaneous 7-Dihydrocholesterol is initially converted into preVitD3 after getting ultraviolet light from the sun. The first metabolism occurs at the level of the liver, where the cholecalciferol is hydroxylated to become 25-hydroxy-VitD (25(OH)D) by the cytochrome P450 hydroxylase enzymes (CYP27A1 and CYP2R1). The newly formed 25(OH)D then undergoes the second metabolism at the level of the kidneys to become 1,25-dihydroxy vitamin D3. The newly formed

1,25-dihydroxy vitamin D3 binds to the vitamin D receptor and interacts later with the vitamin D response elements to regulate the gene transcription, parathyroid hormone, and many more (32).

2.3.3 Recommended Daily Intake

The exact amount of Vitamin D needed for musculoskeletal health is still debatable; the endocrine society has concluded that to guarantee bone health, a serum of at least 75 nmol/L is optimal for adults; thus, to achieve that level an RDA of 1500-2000IU/day is advised.

On the other side, the Institute of Medicine (IOM) has recommended a dietary allowance of 600 IU/day as optimal to keep 97% of the population with a serum 25(OH)D above the level of 50 nmol/L (34).

2.3.4 Methods for assessing serum-25(OH)D and cut-off

There exist several assays to measure serum 25(OH)D level, such as using Radioimmunoassay, Competitive Protein-Binding Assays (CPBA), High Liquid Protein Chromatography (HPLC), and finally, Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)(35). For this study, electrochemiluminescence is being utilized, which is a form of CPBA technique. Serum 25(OH)D is now considered the barometer of Vitamin D (36). However, it should be mentioned that S-25(OH)D can be either reported in nmol/L or ng/ml. The cut-off levels which are going to be utilized in this study are dependent on the institute of medicine cut-off levels as such: <12.5 nmol/ for severe insufficiency, 12.5-29.9 nmol/l for insufficiency, 30-49.9 for the deficiency, and above 50 nmol/L for the optimal range.

2.3.5 Vitamin D status in the Lebanese population

As it was mentioned earlier in section 1.1.3, and to the researcher's best knowledge, the whole population's Vitamin D level is not explicitly assessed, but it was noted by some researchers, including El-Rassi et al. that even though the Middle East region is located in a very abundant area of sunshine, it has one of the highest rates of rickets cases in the world due to several reasons such as sociodemographic factors, and behavioral factors that exhibited by the citizens of these countries (13). Thus, this article will take into consideration assessing those behavioral and sociodemographic factors.

2.3.6 Groups at risk of Vitamin D deficiency

Several categories are risk of being vitamin D deficient, to mention some, high BMI among females (27), aging associated with frailty (20), female gender (16), and those who do not engage in physical activity and tend to cover their body or wear a veil (37–39).

2.3.7 Health consequences of low Vitamin D status

Suboptimal levels of serum 25(OH)D is associated with several complications in the health of humans, it has been associated with an increased risk of osteoporosis and fractures and increased potential of falls, and some studies are suggesting that it might be related to cancer, cardiac diseases, diabetes, autoimmune diseases and depression (40).

2.3.8 Factors affecting Vitamin D status

As mentioned earlier, several factors affect Vitamin D status; however, this research focused on the common risk factors between Vitamin D and COVID 19 to adjust for possible confounders to better assess the potential association.

It has been suggested that high BMI is a strong predictor of Vitamin D deficiency among females regardless of age and season (27). It is also noted by some studies that aging is linked to higher rates of Vitamin D deficiency which in turn aggravates the aging process and worsens comorbidities (20,41).

Female gender has been associated with increased risks of Vitamin D deficiency and increased risks of cardiac diseases, especially coronary artery diseases (17). Education, on the other hand, has a mixed relationship with Vitamin D as some studies suggest that it doesn't affect the Vitamin D status, as seen in a study in Saudi Arabia (42), while other researchers found an established link between education and Vitamin D among adults aged above 30 years (43).

Chapter 3 Rationale for the study

The literature review conducted has identified knowledge gaps regarding the association between Vitamin D status and COVID 19 and knowing that COVID 19 leads to the development of respiratory tract symptoms, the importance of studying the role of Vitamin D on COVID 19 increases. The association between Vitamin D status and COVID 19, to our knowledge, has not been studied in Lebanon yet, and as we mentioned earlier that Lebanon is currently suffering from several burdens (economic, health, and political).

Moreover, we hope that the findings from this study will contribute by providing support to the Lebanese healthcare system to fight this pandemic amid the economic, political, and health crises.

3.1 Knowledge Gap

Upon reviewing the literature and extensively looking at the studies published regarding COVID 19, several studies have been identified addressing the possible relationship between Vitamin D and COVID 19 and taking into consideration either gender or age or education or BMI individually. However, this study aims to address the association between COVID 19 and Vitamin D and adjust for age, gender, education, and BMI. Moreover, this study adopted a cross-sectional design to study multiple variables at a given point in time.

3.2 Hypothesis

Null hypothesis H0: There is no association between s-25(OH)D status and COVID 19

Hypothesis H1: There exists an association between s-25(OH)D and COVID 19

3.3 Objectives

3.3.1 General Objective

The objective of this study is to assess the association between Vitamin D status and COVID 19 and to adjust for possible confounders among adults in Lebanon.

3.3.2 Specific objectives

1. To assess the vitamin D status (s-25(OH)D) levels among adults in Lebanon
2. To investigate the association between vitamin D status and COVID 19 outcomes among adults in Lebanon
3. To examine the role of sociodemographic factors (gender, age, education, BMI) on the association between Vitamin D deficiency and COVID 19 among adults in Lebanon

Research questions:

1. What is the vitamin D status among adults in Lebanon?
2. Is there an association between Vitamin D status and COVID 19 among adults in Lebanon?
3. Does the association between vitamin D and COVID 19 differ in terms of age, gender, BMI, and education?

Chapter 4: Methodology

4.1 Overview

This study was conducted from scratch as an MPhil thesis; the study took place in Lebanon, South Area, in a city called Sidon. The study was done in collaboration between the Department of Community Medicine and Global Health, Institute of Health and Society, University of Oslo, Oslo, Norway, and the Medical Division at Hammoud Hospital University Medical Center. Hammoud Hospital University Medical Center is one of the largest medical centers in the area that serves approximately 24,000 Patients every year, divided between inpatient and outpatient. The data collection for the study took place between 23rd November 2021 till the 5th of April 2022.

4.2 Study Design/Technique

The study design was a cross-sectional study design. The study design was based on the study's objectives; in other words, this study aims to test the association between Vitamin D status and COVID 19 and adjust for sociodemographic factors and social behaviors related to Vitamin D status. Thus, the design was chosen as cross-sectional, followed by a quantitative analysis of the associated factors and collected data.

4.3 Study planning

This section will describe all the phases this study has gone through, from the early stages of development to the end. The study mainly started with a meeting that was held with the main supervisor at the University of Oslo; the topic was agreed upon as this is a topic of common interest among both. A research proposal was formulated with the appropriate literature review and knowledge gaps were identified; a research question was developed, and a study design was in place. The ethical committee at the University of Oslo approved the research topic and proposal, and ethical recommendations were made. The Institutional Review Board (IRB) at the Hammoud Hospital University Medical Center was approached, the study was approved, funding was obtained, and the study was initiated.

This section will describe the whole process in detail:

4.3.1 Study area and Population

This study occurred in the city of Sidon, in the South governorate, that has chosen randomly. The facility where the data collection occurred Hammoud Hospital University Medical Center was

chosen for convenience; the hospital is a university medical center that has been functional in the area for more than 50 years. The hospital is a university medical center with an IRB authorized by the ministry of public health to grant ethical approvals for studies to be conducted in Lebanon.

As the hospital is situated in the center of the city of Sidon, it is surrounded by many Syrian refugee camps and the largest Palestinian refugee camp in Lebanon (Ain El Helwe camp). Thus, the center can recruit participants for the study actively. The hospital was approached with a research proposal being submitted to the medical department at the hospital, a Co-supervisor was appointed by the hospital, discussion occurred, and the plan was organized for the initiation of the study in late November 2022. A study moderator who works at Hammoud Hospital University Medical Center has been appointed to coordinate and facilitate the research, and a designated phlebotomist was appointed to withdraw blood samples for the serum 25(OH)D tests and nasal swabs for the COVID 19 PCR tests.

4.3.2 Sample Size Calculation

The sample was calculated using Cochran's formula for large populations. The formula has considered the following parameters: Precision level +/- 5%, confidence level 95%, and estimated proportion of 0.5.

The formula is as follows: $x = \frac{Z^2 pq}{e^2}$

Where:

-e is the desired level of precision (i.e., the margin of error)
-p is the (estimated) proportion of the population that has the attribute in question,
-q is 1 – p.
-Z is the value from the standard normal distribution reflecting the confidence level that will be used (Z = 1.96 for Confidence Interval 95%)

Thus, $\mathbf{((1.96)^2\ (0.5)\ (0.5))\ /\ (0.05)^2 = 385}$

Therefore, the sample size of 385 is enough to give us the confidence interval desired.

The actual sample size calculated was 385; however, after the removal of outliers, the total sample size analyzed was 384, and thus the total of 1 participant was eliminated.

4.4 Inclusion criteria

-Any person with Residency status in Lebanon, regardless of citizenship, is eligible for participation in the study.

- Both males and females aged between 21 years till 75 years
- Ability to understand English/ Arabic and provide consent and sign the informed consent
- Participants who can stand up to take measurements of height and weight

4.5 Exclusion Criteria

- Candidates who refuse to sign a consent and participate in the study
- Candidates who are consuming Vitamin D supplements for a period exceeding three months
- Candidates who arrive and have severe symptoms of COVID 19 and are unable to provide informed consent and unstable and require immediate hospital admission

4.6 Participants and sampling

All the candidates who arrived at Hammoud Hospital University Medical Center to undertake a COVID 19 PCR test were assessed for eligibility and were invited by the study moderator to participate in the study. A total of 490 (N=490) were eligible and were asked to participate during the study collection time from the 23rd of November 2021 to the 5th of April 2022.

A total of 385 candidates consented to participate in the study, and thus a participation rate of 78.6% was achieved.

One participant was excluded from the study analysis, as one having an age above 75 years old and thus ineligible to participate in the study but was recruited by mistake by the study moderator 105 persons did not want to participate in the research and have not given a reason for that.

4.7 Ethical Approvals

The study has been designed as a master's thesis (MPhil in International Community Health) at the University of Oslo. The study was assessed by the program's ethical committee and supervisors were appointed, and approval was granted and advised to seek ethical clearances from both Norway and Lebanon was given, Appendix 4. The study has been approved by the Reginal Committee for Medical and Health Research Ethics (REK) (ref: 13793253 on 05/05/2021) Appendix 2, Ethical clearance was also obtained from the Norwegian Research center for Research Data (NSD) (ref: 513677 on 1/07/2021) Appendix 3. Finally, the project was approved

by the IRB committee at Hammoud Hospital University Medical Center (ref: IRB26082021 on 22/04/2021).

All participants were given relevant and necessary information (written and verbal information) about the study, and written consent was obtained from all participants. And the data was collected digitally using Nettskjema (University of Oslo digital questionnaire platform) and was linked to TSD (Service for Sensitive Data), where it was anonymously stored and imported into SPSS and stored securely (https://www.uio.no/english/services/it/research/sensitive-data/index.html). Moreover, for people who cannot read, the study moderator will read them the study introductory sheet and the informed consent, and they can sign it or use a fingerprint signature. Also, to note that the informed consent forms were administered in both English and Arabic languages, and participants were informed about their right to withdraw from the study without any explanation at any time.

Both serum 25(OH)D and COVID 19 results were given to participants in writing, and SMS form per hospital method of routine communication of results with their clients and the participants with suboptimal serum 25(OH)D levels were called and encouraged to seek guidance from a general practitioner.

4.8 Independent Variables

Variables	Measures
Sociodemographic factors	Age, Gender, Educational level, Weight, Height
Lifestyle-related factors	History of Vitamin D supplementation in the last 14 days, sun exposure habits and body covering, including veil usage, and finally, the previous history of COVID 19 infection
Tests	s-25(OH)D level measurement, PCR test for COVID 19

Table 2: Independent Variables

4.9 Funding

As the study was conducted in Hammoud Hospital University Medical Center, and the study utilized a study moderator, phlebotomist, and Co-supervisor and had costs for Personal Protective Equipment (PPE) for protecting staff from COVID 19 and follow-up calls to patients with suboptimal serum 25(OH)D levels and some other associated research expenses.

A budget planning has been done with the hospital according to their pricing, and for transparency, the funding has been approved by the University of Oslo at the Department of International Community Health, and the funds were sent directly to a bank account allocated by Hammoud Hospital University Medical Center for this study.

Below is a summary of the expenses associated with the conduct of this study:

Item needed	Estimated Cost
Vitamin D test	7700(20$/ Participant)
Study Moderator fees/ month	240$(120$/month)
Lab Technician Fee /month	160$ (80$/month)
Mobile Data/follow-up calls per project	50$
Printing Out Fees	20$
Others	50$
Total	8220$

Table 3 Outlined Summary of proposed expenses

The explanation for these funds is as follows:

-The Vitamin D Test Fee: Based on the offer Received from Hammoud Hospital University Medical Center, the associated fee for each vitamin D test is 20$ per participant, this is a discounted rate obtained for the purpose of Research.

- The Study Moderator Fee: The data collection process, from approaching the participants to administering the short-guided questionnaire, needs to be done with the assistance of personnel from the Hammoud Hospital University Medical Center staff, so the hospital provided us with the cost of 120$/ per month as an incentive for the personnel assisting in the facilitation of the study.

-The Lab Technician fee: This cost is related to the employee who will be designated to conduct the phlebotomy procedure of blood withdrawal from the participants and for the delivery of results of Vitamin D tests and data entry of the PCR and Vitamin D test results.

-The Mobile Data/Calls Fee: This fee is required to provide follow-up calls, communicate with the study moderator and lab technician who will be assigned to the study, and facilitate the conduction of the project.

-Printout Fee: This fee is required to print out the Log sheets that will keep the results of the participants and for the printout of other related materials to the study, such as informed consent in both Arabic and English language.

-Other Fees: This fee will be kept as a reserve for sudden incurred expenses such as transportation from and to the hospital and follow-up with the hospital administration and staff or error in Vitamin D testing/ COVID 19 tests.

Later, the fees were approved by the University of Oslo, Department of International Community Health, and were paid accordingly to the hospital-issued invoice, Appendix 7.

Chapter 5: Data collection

All the data were collected after obtaining all the necessary ethical approvals from Norway and Lebanon. All participants provided informed written consent for active participation in the study with either signature or fingerprint signature and were helped by the study moderator to understand all the aspects of participation. Participants signed informed consent as part of completing an electronic questionnaire that was filled with assistance from the study moderator utilizing Nettskjema, and the data was stored immediately at TSD (The Services for Sensitive Data at the University of Oslo) Appendix 5 and 6.

Another essential ethical aspect was anonymity; we protected the privacy of the participants by making the data nonperson identifiable for all the study conductors. The study moderator alone kept records of participants' names and contact details to be able to call them after obtaining serum 25(OH)D levels and providing them with education and referral to a General Practitioner (GP) in case the test came back below sufficient levels. The ethical consideration was thus following Regional Committees for Medical and Health Research Ethics and Norwegian Social Science Data Services.

All the participants were informed about their rights to withdraw consent at any time and that they could do so without providing any reason. Moreover, participants were told that after getting the results of the Vitamin D tests and COVID 19 they would be informed about the results per the hospital's policy and that those with suboptimal levels of vitamin D tests would be called by the study moderator to provide advice and will be encouraged to consult a general practitioner.

5.1 Sociodemographic and Lifestyle factors associated with the study population

The following sociodemographic and lifestyle factors have been collected:

-Age has been collected as a numerical (continuous) variable; all the ages have been collected based on the calculation of data of birth and calculated a single age in years and rounded up to the nearest whole year number.

-Gender has been collected as either male or female, and males were coded as 1 and females 2, respectively.

-Education was collected based on years of education at first into five groups: value 1 (having 0-9 years of elementary education), value 2 (having 9-12 years of high school education), value 3 (having 3-4 years of bachelor's degree),value 4 (having 1-2 master's degree or 3-5 years of Ph.D. degree) and value 5 (being illiterate). However, later after reviewing the data and during analysis, education was recoded into three groups only where value 1 (has elementary education), value 2 (has high school education), and value 3 (has a university education).

- History of Vitamin D supplementation in the last 14 days has been collected as either value 1 (Yes) or value 2 (No). The original plan was to collect data regarding the name of the supplement and the dosage and frequency of taking that supplement. Due to faulty transmission, the data has not been accurately provided and thus was omitted from the analysis. Therefore, we were only able to collect a Yes/No answer.

- The habit of sun exposure was measured as a categorical variable. It was collected into four different categories: value 1 (less than 15 minutes per day of sun exposure), value 2 (15-30 minutes of sun exposure per day), value 3 (30-60 minutes of sun exposure per day), and value 4 (more than 1 hour of sun exposure per day).

-The habit of body covering was assessed as a categorical variable. It was collected into three subcategories with value 1 (yes tends to always cover whole-body when outdoors), value 2 (sometimes tends to cover the whole body when outdoors), and value 3 (does not tend to cover the whole body when outdoors).

-The habit of avoiding direct sunlight was assessed as a categorical variable. It was collected into three subcategories with value 1 (Yes tends to avoid direct sunlight when outdoors), value 2 (sometimes tends to avoid direct sunlight when outdoors), and value 3 (No does not tend to avoid direct sunlight when outdoors).

-The habit of using sun cream before going out was assessed as a categorical variable. It was collected into three subcategories with value 1 (Yes tends to use sun cream when outdoors), value

2 (sometimes uses sun cream when outdoors), and value 3 (No, does not use sun cream when outdoors).

-The religious practice of hijab usage was assessed among the female study participants as a categorical variable, and it was collected into two subcategories, with the value 1 (yes wears a hijab), value 2 (no does not wear a hijab)

-The dietary lifestyle of consuming seafood/Fatty fish rich in vitamin D has been assessed in a categorical variable. It was initially collected as how many times per week it was consumed by the participants during the last 14 days with value 1 (eaten fatty fish once in the last 14 days), value 2 (eaten fatty fish twice in the previous 14 days), value 3 (eaten fatty fish three times in the last 14 days) and so on till value 7. However, given the responses of the study participants are so low, the fatty fish dietary lifestyle was recoded into a new category with value 1 (eaten fatty fish twice or less in the last 14 days) and value 2 (eaten fatty fish more than twice in the last 14 days).

-The history of previous COVID 19 infection was assessed in a categorical variable. The responses were collected into four different categories, value 1 (had a history of COVID 19 that is confirmed by a doctor and a Covid 19 test), value 2 (had a history of COVID 19 that is confirmed due to symptoms but no test has been done), value 3 (No history of COVID 19 that is confirmed by a doctor and a negative COVID 19 test), value 4 (No history of COVID 19 due to assumed lack of symptoms). As Lebanon is suffering from a severe economic crisis, where people are struggling to provide essentials of life, the population may not always be able to afford any form of COVID 19 tests.

5.2 Anthropometric Data

Height and weight measurements were measured using a hospital-provided scale that was calibrated every day prior to any data collection using (SECA 220- FS308). Height and weight were calculated as numerical (continuous) variables and were both measured in centimeters (cm) and kilograms (kg) and were noted by the study moderator and transmitted on the questionnaire.

Body Mass Index (BMI) was calculated after obtaining height and weight measurements using the formula. The formula is **BMI = kg/m^2**, where kg is a person's weight in kilograms and m^2 is their height in meters squared. The calculated BMI value was later recoded into groups prior to analysis, where the groups were as follows: value 1 (<18.6), value 2 (18.66-24.99), value 3 (25-29.99), and value 4 (>30). Where value 1 represents the underweight participants, value 2

represents the normal weight participants, value 3 the overweight participants, and finally, value 4 represents the obese participants.

5.3 Sampling for serum 25(OH)D and COVID 19

The venous blood test was taken from participants, and serum levels of Vitamin D (s-25(OH)D) were measured for all study participants. The results were reported in ng/ml units but were later converted into nmol/L (which is the mainly used unit) by multiplying all the results by 2.5.

A common universal normal range for s-25(OH)D has not been agreed upon; however, the cut-offs proposed by the Institute of Medicine were chosen as a level of < 12.5 nmol/ L for severe deficiency, $\geq$12.5-29.9 nmol/L for deficiency, 30-50 nmol/L for insufficiency and $\geq$50 nmol/L for adequate levels (34).

As mentioned earlier, the Vitamin D serum 25(OH)D level was measured by taking a blood sample and utilizing the machines "Roche Cobas e411 Analyzer" and "Abbot Architect Plus Ci4100". Both devices exist in the hospital laboratories, tests were done on a daily basis, and calibration was done per the hospital's policies and per the manufacturing company's guidelines.

The tests were done using the method of analysis of electrochemiluminescence immunoassay.

5.4 PCR testing for COVID 19

The status of COVID 19 infection was measured using a combined nasal/throat swabbing technique by PCR testing. The results were reported initially as positive/Detected and Negative/not detected and later were recoded as Value 0 (Negative for COVID 19) and value 1 (Positive for COVID 19). Complete Personal protective equipment was utilized by all personnel responsible for collecting the swab sample, and infection control measures were followed per hospital and national guidelines and policies.

The hospital ran the tests on a daily basis, and they utilized the machines of "Biofire Diagnostics," "Biofire film Array," "Cepheid Gene Expert" and "BMS Mic PCR"

5.5 Data Processing

Data were collected using an electronic survey accessed via a hospital-provided tablet with a secured Wi-Fi encrypted internet connection provided by the hospital. The vitamin D (s-25(OH)D) results and COVID 19 PCR tests were collected by the study moderator on a log sheet that was deidentified and filled and submitted to the researcher when the results were obtained alongside each study participant ID number.

The key connecting the participants to their ID was stored in the hospital where the study took place by the study moderator in the department of medical research and the project will end by December 1st, 2022, and the keys will be destroyed by Hammoud Hospital University Medical Center medical division per their hospital research policies. The analysis was undertaken at the TSD platform with access only provided to the principal investigator and master student.

5.6 Data handling and entry

Questionnaires were checked after the electronic survey and re-checked during data entry by the study moderator and me for any inconsistencies by going through 60 random submissions on TSD and reviewing the answers to make sure there was no missing data or wrongly entered. Data was secured and handled in accordance with the national regulations in Norway. The only missing data was found in the name of Vitamin D supplements taken by participants who reported taking Vitamin D supplements during the last 14 hours and their respective dosages. This element was not assessed or analyzed and was dropped down from the analysis plan.

Chapter 6: Data Analysis

6.1 Data Processing

All the data that has been collected as described earlier by the utilization of the TSD platform was extracted in the format of SPSS v24.0 licensed by the university of Oslo; data analysis was conducted within the TSD portal accessed only by the main investigator and the student.

6.2 Data Analysis

Before analysis was started, data were checked for normal distribution and checked for any possible outliers and missing data. The sample was equally distributed, and normality was confirmed using visual tests, including histograms and Q-Q Plots. Only one participant was eliminated from the data as his age was outside the inclusion criteria, and his age was beyond the maximum given age set. No participants were found with missing or incomplete data and thus, all the remaining participants were included in the data analysis.

Data were analyzed separately by dividing them based on gender and comparison. For the statistical tests carried on, P-values and/or 95% confidence intervals are presented, with significance being set at $P < 0.05$. All assumptions were checked.

Descriptive statistics were performed: frequencies and percentages for categorical variables and mean and standard deviation for continuous variables. Comparison between men and women

concerning different sociodemographic variables and factors related to s-25(OH)D and COVID 19 were studied with Chi-Square statistics and independent sample t-test. Statistical significance was set to $p < 0.05$. Logistic regression was performed with COVID 19 status as the dependent variable, and 25(OH) D level, sociodemographic variables, and factors related to s-25(OH) D (sun exposure, body coverage, and fatty fish intake, vitamin D supplementation) were set as independent variables. After assessing the association between serum 25(OH)D and COVID 19, adjustment was made to assess for the possible effect of age, gender, BMI, and education on the association, and there was no association noted.

6.3 Vitamin D-related Data

After collecting all the data and running the relative analysis, data collected were divided into risk factors affecting serum 25(OH)D directly and risk factors affecting the association between serum 25(OH)D and COVID 19 as they affect both serum 25(OH)D and COVID 19 equally.

All their risk factors affecting both serum 25(OH)D and COVID 19 were analyzed, and adjustments for their presence were made; no association was found. For the purpose of this study, only gender, age, education, and BMI was represented in the tables.

The remaining data that were collected in the questionnaire and were labeled as serum 25(OH)D specific are as follows: history of taking Vitamin D supplements in the last 14 days, the dosage and name of the supplement, the time spent outside (sun exposure), body coverage habits while outdoors, the wearing of the hijab/veil among female participants and the consumption of fatty fish food (rich in Vitamin D). These data were analyzed and were found not related to the association between COVID 19 and serum 25(OH)D, but they will impact 25(OH)D directly; they will be included in a separate study with a focus on Vitamin D status among adults in Lebanon and the associated risk factors and communication with REK has been already started, and extension of the research project has been requested. This data will help give an insight into the Vitamin D status in Lebanon as our literature review showed knowledge gaps about this topic due to a lack of studies and data in that field in Lebanon.

Chapter 7: Methodological Considerations

The study was designed as a cross-sectional study design; it is ideal for describing a variable's magnitude and exploring the association between Vitamin D and COVID 19 and the socio-demographic and lifestyle factors. However, this design estimates the association between exposure and outcome at the same time but doesn't allow us to assess the causality between

vitamin D levels and COVID 19 infection as would randomized control trials do. Another aspect would be that the chosen methodology doesn't allow us to assess the severity of COVID 19 and follow up later with mortality. In our context, a cross-sectional study was the most feasible in terms of time and budget.

7.1 Strengths and limitations of the study

The strength of the study is in the high response rate achieved of 78.6%. Another point of strength in the study would be the fact that the study included taking s-25(OH)D levels alongside taking the Covid 19 PCR test in the same time frame thus, it assisted in the minimization of recall bias. Furthermore, the same tools were used throughout the carrying of anthropometric measurements, which were calibrated. The same laboratory was used for the analysis of s-25(OHD) and COVID 19 PCR tests.

The study had some limitations including the lack of collecting any data regarding the clinical health and other comorbidities of the studied population, the study included the people who were arriving at the center to perform a COVID 19 test (who could afford it); thus, the participants are of a particular financially capable sector who has access to medical care and therefore the generalizability to the Lebanese population might be limited and is carried forward with caution.

Moreover, current COVID 19 immunization records were not addressed during data collection, which could have altered the association between COVID 19 and s-25(OH)D, and the season when the data was collected might have played an essential factor in the s-25(OH)D levels of the participants. However, to be noted that during the time data the study was planned, Vaccination for COVID 19 was recently started and was very limited in Lebanon.

In addition, around 105 potential participants refused participation in the study; this could have contributed to a selection bias in our study participants.

Information bias

Information bias is the deviation of data from the true value caused by inaccurate measurements of variables; it appears when there are systematic errors affecting the accuracy and reproducibility of the measurement of a risk factor or specific condition, it can be divided into misclassification, observer and recall bias (44). In this study, information bias was minimized by using standardized tools and analysis, and the questionnaire was interviewer-administered and completed only by the study moderator. However, the possibility of information bias cannot be excluded as study

participants during data collection had to self-report their previous history of having COVID 19 without asking for proof or proper medical documentation; this element can be slightly inaccurate and may contribute to some information bias.

Recall bias

Recall bias occurs when the study participants are systematically less likely to recall or relate information relation to exposure depending on their outcome status or recall information regarding their outcome depending on their exposure (45). The study participants, during data collection, had to report recalled information regarding their dietary habits, social habits, and sun exposure and thus, a recall bias might have occurred. However, given that most studied participants had a higher educational level and above, we consider the answers provided are relatively credible.

Confounders

In research, confounding variables are common and can alter the study's validity. Because it interacts with both the exposure and the outcome, the confounder will disrupt the association between both the exposure and the outcome (46). This study tried to minimize potential confounder bias by collecting data on variables thought to be confounders, as informed by the literature review and the analysis of DAGs. However, there is a possibility that confounders were missed such as COVID 19 immunization history, thus distorting the association between Vitamin D and COVID 19.

External Validity

The degree to which findings concluded from a study can be extrapolated to a broader population than the study group is known as external validity (47). As the study measured the social behaviors of participants and their dietary habits concerning Vitamin D, it helped to understand the overall Vitamin D status of the community, and most of the participants turned out to be at suboptimal levels. Education has been provided, and community awareness will be spread to their neighboring communities, thus leading to a better Vitamin D status among the adults in Lebanon.

The project will provide good baseline data on associations between Vitamin D status and COVID 19, and it will contribute to initiating appropriate and effective preventive and treatment measures.

Overall, apart from the discomforts of blood taking and nasal swabs, both participants and society will benefit from the project.

7.2 Timetable

Activity	Period
Research Protocol writing and Research planning	January 2021- April 2021
Ethical Clearance obtaining	May 2021-July 2021
Data collection and data cleaning	November 2021- April 2022
Data analysis and data interpretation	May 2022-August 2022
Thesis writing	September 2022-October 2022
Thesis submission	October 2022- November 2022
Article submission	TBC

Table 3 Timetable of events during the research process

7.3 Dissemination of results

This research work was conducted as a part of an M.Phil. Program in International Community Health (ICH), consequently, the thesis is submitted to the Department of Community Medicine and Global Health at the University of Oslo. The thesis thus will be available online on the DUO system at the university's Library. An article was written based on the data, co-authored with the Supervisor, Co-supervisors and is planned to be published soon afterward.

Feedback to participants was provided, and feedback of results to relevant stack holders was also provided, including the Department of Community Medicine and Global Health at the University of Oslo, Oslo, Norway, and Hammoud Hospital University Medical center, where the study took place.

7.4 The Researcher

The Researcher had a main role in protocol writing, research design and plan, data collection and analysis, data interpretation, thesis writing, and finally, article writing and editing till publication.

7.5. Supervision and Collaboration

The supervision for this study was provided by Dr. Ahmed Madar, Department of Community Medicine and Global Health at the institute of health and society, University of Oslo. Dr. Ahmed provided direct supervision at all stages of the process utilizing his extensive knowledge, skills, and experiences in the field of research, and he has contributed tremendously to the production of this study.

Dr. Haakon Meyer, Norwegian Institute of Public Health (NIPH) in Oslo, Norway has a wealth of knowledge in research and Vitamin D; he has contributed to the data interpretation and analysis and the writing of the article and thesis.

Dr. Samia Filali Zaatari, Hammoud Hospital Medical Center, Lebanon, as a co-supervisor who was the main contributor to the data collection and facilitator of the study in Lebanon through obtaining ethical clearance from Lebanon and the Institutional Review Board at the hospital.

7.6 DAG

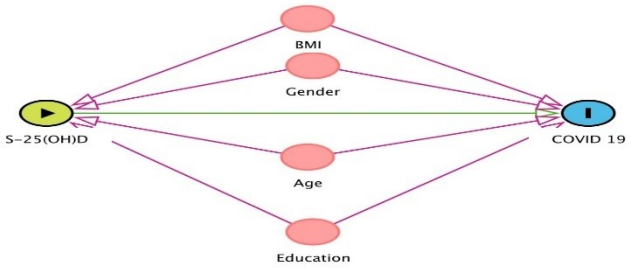

Figure 1: DAG Representing the studied association between COVID 19, and s-25(OH)D adjusted for age, gender, BMI. and education

7.7 Challenges

The study has faced several challenges during development. The study was initially advised to start earlier than November, but due to the financial crisis going on in the country, the hospital has informed us that they will be waiting for the finances to be transferred prior to buying the serum 25(OH)D testing kits. A delay in financial transfer occurred due to issues with the Lebanese banking system, and later the funds were received.

After successfully receiving the funds, the hospital notified us that due to financial crisis, the leading supplier for the serum 25(OH)D testing kits in south Lebanon does not have the needed quantity of 385 tests at the store and that he has ordered the requested amount to be imported. Later, the kits were supplied, and the study was started.

During the period of data collection, the participants were identified and invited to participate, but there was a total of 105 participants who refused to participate in the study. Originally data collection was supposed to be conducted in a 2-month period, but due to the financial crisis, locals were reluctant to go and seek treatment at the hospital because of the cost associated with the COVID 19 tests. Recruitment was carried on from the period of 23rd of November 2021 till the 5th of April 2022.

7.8 Conclusion and recommendations

The study aimed to assess the association between Vitamin D status and COVID 19 among adults in Lebanon. The results of this study indicate a high prevalence of Vitamin D insufficiency among adults who were participating in COVID 19 testing hospital in Lebanon. However, the vitamin D status of the participants was not associated with COVID 19 results. Further research is required to investigate the health consequences of poor s-25(OH)D status for this population and address the possible risk factors that are leading to a poor S-25(OH)D status in Lebanon.

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9.Article:

Vitamin D status and COVID 19 in Lebanon among adults: A cross-sectional study in South Lebanon

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Abstract

Background: The current COVID 19 pandemic has almost affected every nation in the world and leads to the development of respiratory tract symptoms. Vitamin D has been proposed to play an important role especially in upper respiratory tract infections. Recently, numerous studies and reports associating low serum 25-hydroxyvitamin D (s-25(OH)D) levels and adverse outcomes in COVID 19 have also emerged. We aimed to assess the association between Vitamin D status and covid 19 among adults in Lebanon.

Method: This is a cross-sectional study where the participants were recruited from one of the largest university hospitals in south Lebanon. The participants (n 384) aged 18-75 years who came to the hospital to perform a COVID 19 test were asked for their participation. Background variables were collected with a structured questionnaire. Blood samples were collected and analyzed for s-25(OH)D concentration using Electrochemiluminescence immunoassay and COVID 19 was tested.

Results: The mean s-25(OH)D was 46.8 (SD 28.1) with no significant difference between men and women. Almost 63% of women and men had vitamin D insufficiency (s-25(OH)D <50 nmol/L). Furthermore, 28 % of the participants had positive PCR results. There was no significant association between s-25(OH)D levels and PCR results ((OR = 0.982, 95% CI: 0.961-1.004), p=0.10)). Adjustment for sociodemographic factors did not alter the results.

Conclusion: There was a high prevalence of vitamin D insufficiency among adults participating in covid 19 test hospital in Lebanon and it was not associated with Covid 19. Further research is required to investigate the health consequences of poor s-25(OH)D status for this population.

Keywords: COVID 19, 25(OH)D, Lebanon, Socio-demographic factors, Vitamin D supplements

1. Introduction

COVID 19, a worldwide pandemic was declared by the World Health Organization (WHO) on March 2020 (1). The WHO statistics showed more than 521 million confirmed cases and more than 6 million confirmed death (2). Researchers started looking into risk factors, treatment options, vaccines, and prognostic markers (3). One of those possible preventive measures could be Vitamin D (4–8). Vitamin D has been proposed to play a key role especially in the prevention of upper respiratory tract infections(9).

Lebanon is a country facing socioeconomic challenges and financial instability (10) with an estimated population of 6.7 million (11), of which 4 million Lebanese and migrant refugees needing social assistance (12). According to the Ministry Of Public Health (MOPH), the country has a total exceeding 1 million confirmed COVID 19 cases and 10400 confirmed deaths with a vaccination rate not exceeding 35% for 2 doses vaccinated citizens and 24% for three doses vaccinated citizens (13).Vitamin D status for the entire population is not known, although it is suggested to be a protective factor for COVID 19 (9). Several studies indicated that 25(OH)D deficiency is highly prevalent among adults in Lebanon (14) and in the Middle East in general (15).

Several studies had shown that there is a link between COVID 19 and sociodemographic factors such as gender, age, education and Body Mass Index (BMI). The female gender is associated with less risk of catching COVID 19, and lower mortality rate (16,17). Aging is related to higher risks of contracting COVID 19 and leads to higher mortality (18). The elderly people are at higher risk of 25(OH)D deficiency due to many factors ranging from dietary habits, social habits, and decrease in the metabolism of 25(OH)D (19,20). People with higher educational level are less likely to be infected with COVID 19 as they have higher chances of adhering to recommendations and have

access to more spacious houses and thus able to perform social distancing (21–24). However, educational level did not have a significant effect on 25(OH)D status of the study population in Saudi Arabia (25). Researchers suggested that high BMI is linked to higher odds of having COVID 19 and developing severe symptoms and higher mortality (26–28). In addition, higher BMI has been associated with lower vitamin D status (29,30).

Several studies highlighted behaviors related to vitamin D status. For instance, women who wear veil tend to have lower 25(OH)D level due to a reduced sun exposure over the body surfaces (31–33). Moreover, other studies suggested that vitamin D fortified foods or supplements are essential for maintaining a sufficient 25(OH)D level (34,35) to achieve the 600IU/Day RDA for adults as specified by the Institute of Medicine to be in the adequate safe level of sufficient 25(OH)D status(36). However, the link between sun exposure and Covid 19 is not studied yet to our best knowledge.

Knowing that Covid 19 leads to the development of respiratory tract symptoms, the importance of study the role of Vitamin D on Covid 19 increases. Furthermore, Lebanon is currently suffering from several burdens (economical, health, and political). This study will provide the results of the association between Covid 19 and Vitamin D status in the Lebanese population. Thus, we sought to study this association and to identify its possible associations with sociodemographic indicators and behaviors among adults residing in Lebanon.

2. Materials and Methods

Study Design and Participants

The participants were recruited between November 23rd 2021 and April 30th 2022 from Hammoud Hospital University Medical Center (HHUMC) located in the city of Sidon that serves more than 24,000 residents and refugees per year from the region. This current study targeted all persons that sought the hospital for PCR testing and met the eligibility criteria. The Cochran formula was used for sample calculation which allows to identify the desired sample size given a desired level of precision, confidence level, and estimated proportion of the attribute present in the population. The participants were based on the following inclusion criteria are residents of Lebanon, aged between 21 and 75 years old, able to understand Arabic or English to sign the informed consent. Those who could not read and write were helped by the study-moderator to provide a fingerprint or signature.

In addition, the participants need to be able to stand or ambulate to measure accurate weight and height. Exclusion criteria: Participants with severe conditions of COVID 19, participants unable to sign the informed consent or participate in the study, participants who were on Vitamin D supplements for a period exceeding 3 months and those who refuse to participate in the study.

Survey instrument and anthropometric measurements

An interview administered questionnaire was used by a study moderator using a hospital Provided Tablet device with direct link to the University of Oslo's platform for storing and processing of sensitive research data(TSD).

The questionnaire addressed the following aspects: age, gender, educational level, history of vitamin D supplementation in the last 14 days, sun exposure habits and body covering including hijab usage and finally the previous history of COVID 19 infection.

Height and weight were both measured using a scale that the study moderator ascertained was calibrated every day prior to taking measurements and height measuring board (using SECA 220-FS308). Overweight and obesity was defined as BMI ≥25 and ≥30 kg/m^2 respectively.

COVID 19 testing and blood testing

The COVID 19 testing was conducted at Hammoud Hospital University Medical Center using a combined throat and nose swabbing technique and analyzed by " Biofire Diagnostics Biofire film Array", "Cepheid Gene Expert" and "BMS Mic PCR" . Blood sampling was withdrawn from the study participants to test for s-25(OH)D using "Roche Cobas e411 Analyzer" and "Abbot Architect Plus Ci4100" using Electrochemiluminescence immunoassay method. Calibration and cross-calibration for both methods happened every 3 months per the manufacturing company guidelines and internal hospital policies.

A common universal normal range for s-25(OH)D has not been agreed upon, however, we chose to use, the cut-offs proposed by the Institute of medicine as level of < 12.5 nmol/ L for severe deficiency, ≥12.5-29.9 nmol/L for deficiency , 30-50 nmol/L for insufficiency and ≥50 nmol/L for adequate levels (36).

Follow-up

The participants who tested Positive for COVID 19, were contacted by the hospital and informed about the Lebanese MOPH quarantine guidelines. Moreover, every participant was explained of her/his vitamin D levels in written after the blood analysis are completed. For those with severe vitamin D deficiency (<12.5 nmol/L) some advice on how to improve their vitamin D statuses were given and at the same time they were connected to health services that they use to get help (treatment).

Ethics

The study was approved by Regional Community for Medical and Health Research Ethics (REK) in Norway (study code: 270246), Norwegian Research Center for Research Data (NSD) (study code: 513677) and finally, Hammoud Hospital University Medical Center Institutional Review Board (IRB) (study code: 26082021). Informed consent was signed and collected from all the participants.

For checking the quality of the data collection, a random sample of 10% of the data was selected and examined manually which revealed a problem in the transcription of data related to the name of vitamin D supplement and dosage used by study participants, however, the remaining data was accurate . Data entry and analysis was done using SPSS Version 28.0.01.

Descriptive statistics were performed: frequencies and percentages for categorical variables, mean and standard deviation for continuous variables. Comparison between men and women concerning different sociodemographic variables, factors related to s-25(OH)D and COVID 19 were studied with Chi-Square statistics and independent sample t-test. Statistical significance was set to $p < 0.05$. Logistic regression was performed with COVID 19 status as the dependent variable and 25(OH) D level, sociodemographic variables, and factors related to s-25(OH) D (e.g. sun exposure, body coverage and food intake) as independent variables.

3. Results

A total of 385 participants completed the data collection out of them 1 was excluded from the study: being aged more than 75 years thus leading to a final sample of 384 participants. Characteristics of the study population are shown in Table 1. A total of 103 either did not fulfil the inclusion criteria or refused the participation of the study.

Sociodemographic characteristics of the sample

Mean age was 38.8 years old (SD 12.4), and there were 175 men (45.6%) and 209 women (54.4%) Regarding the education of the participants, most of them (62.8%) had a university degree and higher, whereas 22.9% have a secondary degree and 14.3% have an elementary school or less. Generally, men had higher levels of education than women, but this difference was not significant. The overall mean BMI of the participants was 27.1 (SD 5) kg/m^2 and men had significantly higher BMI than women (p=0.001)

Table 1: Sociodemographic characteristics of the study population (N=384)

	Women	Men	All	p-value
Gender	54.4 (209)	45.6 (175)	100.0 (384)	
Mean age, years (SD)	39.1 (12.5)	38.5 (12.3)	38.8 (12.4)	0.63 (NS)
Education years, % (n)*				
elementary school or less	16.3 (34)	12.0 (21)	14.3 (55)	0.17 (NS)
secondary school	19.6 (41)	26.9 (47)	22.9 (88)	
Tertiary Education	64.1 (134)	61.1 (107)	62.8 (241)	
Weight (Kg), mean (SD)	69.214.7)	86.8, (16.2)	77.2 (17.7)	<0.001
Height (cm), mean (SD)	161.9 (6.2)	176.3 (7.3)	168.4(9.8)	<0.001
BMI (Kg/m^2)	26.3 (5.1)	27.9 (4.8)	27.1(5.0)	<0.001

Vitamin D status and COVID 19

Table 2 presents the levels of s-25(OH) D. The mean level of s-25(OH) D was 46.8 (SD 28.1) nmol/L. The mean level tended to be slightly higher among women 49.2 (SD 33.6) than men 44.0 (SD19.3), although the difference was not statistically significant (p=0.07). Around 1/3 of the participants had vitamin D deficiency while 37 % had sufficiency .

Previous infection with Covid 19 was reported by 44% of the participants (32% confirmed and 12% due to Covid 19 symptom). When comparing women to men, there was no statistically significant difference in the reporting of previous Covid 19 infection (p=0.65).

All the participants took PCR testing at Hammoud hospital University Medical Center, and 28% had positive results. There was no gender difference in the proportion with positive PRC test (p=0.53).

Table 2: S-s-25(OH)D levels, self-reported Covid 19 and PCR results (N=384)

Variables	Women	Men	All	p-value
S-25(OH)D) levels (nmol/L), mean (SD)	49.2 (33.6)	44.0 (19.3)	46.8 (28.1)	P=0.07
S-25(OH)D) cut-off (nmol/L)% (n)				
<12.5	6.2 (13)	0.06 (1)	3.7 (14)	<0.001
12.5-29.9	28.2 (59)	24.0 (42)	26.3 (101)	
30-49.9	22.5 (47)	45.1 (79)	32.8 (126)	
≥ 50 nmol/L	43.1 (90)	30.3 (53)	37.2 (143)	
Have you, or have you, been infected with the Covid 19?				
Yes (confirmed by doctor with PCR test)	30.1 (63)	34.3 (60)	32.0 (123)	P=0.65
Yes (due to symptoms)	13.9 (29)	10.3 (18)	12.2 (47)	(NS)
No (confirmed by doctor with PCR test)	36.4 (76)	34.8 (61)	35.7 (137)	
No (due to lack of symptoms)	19.6 (41)	20.6 (36)	20.1 (77)	
PCR results				
Negative	73.2 (153)	70.3 (123)	71.9 (276)	P=0.53
Positive	26.8 (56)	29.7 (52)	28.1 (108)	(NS)

Association between s-25(OH) D levels and Covid 19 outcome

There was no statistically significant association between vitamin D status and being diagnosed with COVID 19 (OR = 0.982, 95% CI= 0.961-1.004 per nmol/l increase in 25(OH)D). After adjustment for gender, age, education and BMI no association has been found as well (table 3).

Table 3: Odds ratio, with 95% confidence interval (CI), for positive Covid 19 test according to s-25(OH) D (nmol/l) and potentially associated factors in adults living in Lebanon (n 384) aged 18–75 years, November 2021-April 2022.

Explanatory variables Category	N	OR(95% CI)	95% CI	P Value	Adjusted OR*	95% CI*	P Value
s-25(OH)D Level	384	0.982	0.961-1.004	0.103	0.981	0.959-1.003	0.090
Gender	384	0.866	0.554-1.352	0.526	0.888	0.563-1.401	0.610
Age	384	1.003	0.985-1.003	0.741	1.011	0.990-1.032	0.305
Education	384	1.150	0.842-1.572	0.379	1.222	0.866-1.725	0.254
BMI	384	1.056	0.811-1.376	0.685	0.997	0.753-1.319	0.982

*Adjusted for age, gender, education, and BMI

4.Discussion

Generally, due to limited data on the role of vitamin D status on Covid 19 infection in Lebanon, this present study was conducted to provide results about Covid 19 and Vitamin D status and their association as well as their possible relationships with sociodemographic indicators among adults residing in Lebanon. In this study we found that participants who were seeking PCR testing in a large university hospital in the South of Lebanon, 28.1% were tested positive and two thirds (63%) had a deficient or insufficient s-25(OH) D levels. The study showed no significant association between s-25(OH) D status and Covid 19 . In addition, our findings confirm that both women and men had low vitamin D status in Lebanon(14,15). There are mixed results on the role of vitamin D on Covid 19 outcome. However, our results are in line with the finding from recent results from both cross-sectional and randomized trial.(37–41)

To better understand the relationship between COVID 19 and vitamin D, sociodemographic factors such gender, age, education, and Body Mass Index were considered. To begin with is it thought that gender could play a role in the link between vitamin D status and COVID 19 onset(17,42). In our study, no association was found between Covid 19 and gender. These findings are not consistent with a study conducted by AlQuaiz et al that found that males had a higher prevalence of s-25(OH)D deficiency compared to females (43). Although there was no gender difference between COVID 19 cases, however, a study highlighted that the mechanism behind the gender difference among COVID 19 cases remains unknown, especially because male cases are more

severely affected than female cases(44). Generally, women of all ages are at a lower risk of contracting the virus, and men are more susceptible to more serious infections related to coronavirus that can lead to death(16). As did another study show that younger adults had a higher prevalence of 25(OH)D deficiency (43). It is worth noting that aging itself is a prominent risk factor for severe disease and death from COVID 19 (45).However, our study did not find any association between age and COVID 19.

Differences in educational levels influenced people's willingness to get vaccinated raising the possibility of an association between COVID 19 and 25(OH)D status (22). Moreover, a study conducted by Yoshikawa & Asaba reported that a lower level of education influences the severity of COVID 19(46). The results of our study upon adjusting for education had no effect on the presumed association of 25(OH)D and COVID 19. However, a study conducted by Othman Et al in Lebanon showed that having a university level of education, following the spread of the COVID 19 pandemic in Lebanon were significantly associated with a higher hygienic prevention practices score.(47). Also to note educational level did not have a significant effect on improving the 25(OH)D status (25,48).

According to literature, body mass index is associated with reduce circulating 25(OH)D level. This suggests to take into consideration 25(OH)D status in overweight and obese women (29). It is important to note that 25(OH)D deficiency has also been found to occur more frequently in patients with obesity that leads to an increased risk for hospitalization, ICU admission and death among patients with COVID 19(28). However, in our study adjusting for BMI did not have any effect on the presumed association being investigated.

It is worth noting that Vitamin D has been documented in many studies as a protective factor for acquiring a severe covid 19 with all its complications(6,49). A study conducted in Philippines on 212 reported COVID 19 patients, found that the severity of the infection is a highly associated with the 25(OH)D levels, according to this study, the patients with 25(OH)D levels in the categories, 20–30 and <20 ng/ml, were 12 times and 19 times more likely to die from COVID 19, respectively, as compared with COVID 19 patients with sufficient levels of 25(OH)D(50). Moreover, a recent systematic review and meta-analysis has concluded that 25(OH)D has potential in preventing respiratory infections, especially in those who have high levels of deficiency(51). In

our study we did not find association between vitamin D status and Covid 19 taking into consideration adjusting for gender, age, education and Body Mass Index (BMI).(28,44,45)

5. Strengths and limitations

To our knowledge, this is the first study conducted in South Lebanon exploring the relationship between vitamin D status and Covid 19 in Lebanon. The recruitment and data collection were done by same researcher and both women and men are equally represented in the study.

However, there are several limitations. First, the participants were recruited from a hospital where they came to take a PCR-test which is expensive, and a selection bias may be present as only for those who can afford the PCR test were included in the study. Another selection bias could have occurred because several eligible persons declined the participation in the study (participation rate 78.8%). On the other hand, comparison of the education levels of included participants to national education figures (62.8% among study participants vs 60.79% national average) suggests that the participants in this present study might possibly be representative of men and women with same age in Lebanon(52). Another possible limitation is that we do not have information about the immunization status of the participants and those who rejected to participate. Furthermore, although, the analysis was done in one batch and the Abbott Architect i1000 SR assay for 25(OH)D has been validated according to international guidelines, 25(OH)D was collected in different seasons which may affect the levels. Due to assay variability, it might be difficult to differentiate the categories of mild or moderate deficiency in our study participants. In sum, our results should be interpreted with caution with respect to generalizability of the findings.

6. Conclusion

There was a high prevalence of vitamin D insufficiency among adults participating in covid 19 testing at a hospital in Southern Lebanon, but s-25(OH)D was not associated with Covid 19. Further research is required to investigate the health consequences of poor s-25(OH)D status for this population. The health consequence of the low s-25(OH)D concentrations on different age groups in Lebanon should be further investigated. Furthermore, randomized controlled clinical trials should be conducted to assess the effect of vitamin D on covid 19 and the impact on the severity of covid 19.

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Author contribution

A. A. M, H. F.I.A. and S.F planned the study. S.F and F.L.A carried out the data collection, F.L.A performed data analysis and prepared the manuscript. H. E. M, S.F and A. A. M. critically reviewed the draft, contributed to the interpretation of the findings and all authors approved the final version of the manuscript. This study was funded by the Department of International Community Health at the university of Oslo, Norway.

8. Conflict of interest

The Authors declare no conflict of interest

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10. Appendices:

10.1 Appendix 1: Questionnaire

Questionnaire

- ID number_____
- Age in years _____
- Height in cm's _____
- Weight in Kg's _____
- BMI (calculated)_____
- Gender _____

- Educational Level:

  0-9 years of elementary school education

  9-12 years of high school education

  3-4 years bachelor's degree

  1-2 years master's degree or 3 -5 years PhD degree

  No school education at all (Illiterate)

- have you been taking Vitamin D supplements in the last 14 days?

  Yes

  No

- If yes, Name of the supplement (tablet or capsule form) and dosage

- Number of times per week taken

  7 6 5 4 3 2 1 <1

- Sun Exposure: How long are you out in the sun when it is sunny?

☐ under 15 minutes per day
☐ 15-30 minutes per day
☐ 30-60 minutes per day
☐ more 1 hour per day

❖ when you are out in the sun , you tend to:

		Yes	sometimes	No
Cover the whole body	☐	☐	☐	
Avoid direct sun exposure	☐	☐	☐	
Use sun cream	☐	☐	☐	
Use hijab	☐	☐	☐	

❖ Have you eaten fish spreads (salmon, mackerel, trout, herring) or Fish and other sea food in last 14 days ?

Number of times

Every (Day) 6 5 4 3 2 1

❖ Have you, or have you, been infected with the Covid-19?

- Yes (confirmed by doctor with test)

-Yes (I have assumed it due to symptoms)

-No (confirmed by doctor with test that I did not have the virus)

-No (I have assumed this due to lack of symptoms)

10.2.1 Appendix 2 Part 1 REK Decision Letter 1 :

REK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst D	Finn Skre Fjordholm	+47 22 84 58 21	25.06.2021	270246

Deres dato: 28.04.2021 /

Ahmed Madar

Prosjektsøknad: Vitamin D og Covid-19 i Lebanon
Søknadsnummer: 270246
Forskningsansvarlig institusjon: Universitetet i Oslo

Prosjektsøknad godkjennes med vilkår.

Søkers beskrivelse

The current COVID-19 pandemic has almost affected every nation in the world. However, the impact of the pandemic and its consequences hit differently in different countries depending on the health status of individuals and the coping mechanism of the countries. Lebanon is witnessing an unprecedented crisis with the rapid spread of COVID-19, financial meltdown, economic collapse. Vitamin deficiency is also widespread in the Lebanese population.
In recent years vitamin D has been proposed to play an important role especially in upper respiratory tract infections (Mitchell, 2020, p. 19). Thus, knowing that Covid-19 leads to the development of respiratory tract symptoms, the importance of studying the association between Covid 19 and Vitamin D status increases. The proposed project is a cross-sectional study and the main objective is to assess the association between vitamin D status and covid-19. The findings might also have implications for the prevention and treatment of the infection of Covid-19 in Lebanon and even globally. The findings might also have implications for the use of health care and the prioritization of resources in the country

Vi viser til søknad om forhandsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komite for medisinsk og helsefaglig forskningsetikk (REK sør-øst D) i møtet den 2.6.2021. Vurderingen er gjort med hjemmel i helseforskningsloven § 10.

REKs vurdering

Formålet med dette prosjektet er å undersøke sammenhengen mellom vitamin D og covid-19, og videre undersøke den samvirkende betydningen av alder kjønn, alder og BMI.

Prosjektet gjennomføres som en masterprosjekt i International Community Health ved UiO.

Komiteen vurderer at prosjektet faller innenfor REKs mandat etter helseforskningsloven, som forutsetter at formålet med prosjektet er å skaffe til veie "ny kunnskap om helse og sykdom", jamfør lovens § 2 og § 4 bokstav a.

Data skal samles inn i Libanon. Prosjektet gjennomføres basert på samtykke, og det skal rekrutteres 385 kvinner og menn mellom 21 og 75 år. Rekrutteringen vil gjennomføres av en uavhengig person og foregå blant personer som oppsøker Hammoud universitetssykehus for å foreta en koronatest.

Det skal samles inn biologisk material i form av en kapillærblodprøve for å måle nivået av vitamin D i blodet. Videre heter det i søknaden at det skal samles inn ekspektorat, men komiteen forstår det slik at det ikke skal samles inn slikt materiale, men benyttes resultater fra koronatestene som deltagerne uansett skal avlegge. Dette bør imidlertid fremkomme tydeligere i informasjonsskrivet. Det samme gjelder det faktum at de biologiske prøvene skal destrueres etter at de er analysert, og senest innen to måneder.

Deltagelse innebærer for øvrig utfylling av et egenutviklet spørreskjema der det spørres om alder, kjønn, vekt, høyde, utdanning, kosthold og soleksponering.

Komiteens vurdering

Komiteen mener dette fremstår som et nyttig prosjekt. Deltagelse er forbundet med få ulemper.

Imidlertid mener komiteen at det fremstår som noe uklart hvilken tilbakemelding om resultatene som skal gis deltagerne. I søknadsskjemaet heter det både at deltagerne vil bli oppfordret til å kontakte sin lege dersom prøvene viser lave nivåer av vitamin D (punkt 6.1), og at de skal få tilbakemelding dersom de ber om det (punkt 6.7). Komiteen mener det bør være klart for deltagerne at de vil få tilbakemelding dersom resultatene på prøvene som skal tas viser lave nivåer av vitamin D, og stiller som vilkår for godkjenning at det utarbeides en rutine for beredskap for dette. Informasjonsskrivet må også tilpasses den nye beredskapsplanen, slik at deltagerne på forhånd er informert om innholdet i den.

Komiteen merker seg også at informasjonsskrivet er presentert på engelsk, men at det skal legges frem for potensielle deltagere på engelsk eller arabisk. I søknadens punkt 4.1 heter det at deltagere som ikke kan lese vil få informasjonsskrivet opplest. Komiteen mener dette ikke er en ideell løsning, men dersom man valgte å ikke ta med analfabeter ville dette på den andre siden ekskludere denne gruppen fra deltagelse. Dette ville kunne skape skjevheter i utvalget og hindre denne gruppen fra å delta i forskning. Komiteen vurderer derfor at det er valgt en tilfredsstillende løsning, men mener at deltagernes samtykke likevel må dokumenteres. Dette kan gjøres på flere måter, og det er opp til forskningsansvarlig institusjon å sørge for at det etableres en rutine for dette som sikrer at det avlagte samtykket er dokumenterbart i ettertid.

Komiteen har vurdert søknaden og har ingen øvrige innvendinger til at studien gjennomføres som beskrevet i søknad og protokoll.

På denne bakgrunn setter komiteen følgende vilkår for godkjenning.

- Det utarbeides en beredskapsplan for tilbakemeldinger om resultatene på blodprøvene som skal samles inn
- Informasjonsskrivet må justeres i henhold til beredskapsplanen
- Det etableres en rutine som sikrer at deltagernes samtykke dokumenteres på en forsvarlig måte

Beredskapsplanen og det reviderte informasjonsskrivet kan sendes inn på skjemaet «Endring og/eller henvendelse» i REK-portalen. Innsendte dokumenter må presenteres med sporbare endringer ("track changes"), slik at det er mulig å se hva som er tatt ut og/eller lagt til.

Vedtak

REK har gjort en helhetlig forskningsetisk vurdering av alle prosjektets sider. Prosjektet godkjennes med hjemmel i helseforskningsloven § 10, under forutsetning av at ovennevnte vilkår er oppfylt.

Vi gjør samtidig oppmerksom på at etter ny personopplysningslov må det også foreligge et behandlingsgrunnlag etter personvernforordningen. Det må forankres i egen institusjon.

I tillegg til vilkår som fremgår av dette vedtaket, er godkjenningen gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad og protokoll, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 01.12.2022. Av dokumentasjonshensyn skal opplysningene likevel bevares inntil 01.12.2027. Forskningsfilen skal oppbevares atskilt i en nøkkel- og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for «Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse og omsorgssektoren».

Komiteens avgjørelse var enstemmig.

Sluttmelding
Prosjektleder skal sende sluttmelding til REK på eget skjema via REK-portalen senest senest 6 måneder etter sluttdato 01.12.2022, jf. helseforskningsloven § 12. Dersom prosjektet ikke starter opp eller gjennomføres meldes dette også via skjemaet for sluttmelding.

Søknad om endring
Dersom man ønsker å foreta vesentlige endringer i formål, metode, tidsløp eller organisering må prosjektleder sende søknad om endring via portalen på eget skjema til REK, jf. helseforskningsloven § 11.

Klageadgang
Du kan klage på REKs vedtak, jf. forvaltningsloven § 28 flg. Klagen sendes på eget skjema via REK portalen. Klagefristen er tre uker fra du mottar av dette brevet. Dersom

REK opprettholder vedtaket, sender REK klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag (NEM) for endelig vurdering, jf. forskningsetikkloven § 10 og helseforskningsloven § 10.

Med vennlig hilsen

Finn Wisløff
Professor em. dr. med.
Leder

Finn Skre Fjordholm
Rådgiver
REK sør-øst D

Kopi til:

Universitetet i Oslo

10.2.2 Appendix 2 Part 2 REK Decision Letter 2:

Ahmed Madar

270246 Vitamin D og Covid-19 i Lebanon

Forskningsansvarlig: Universitetet i Oslo

Søker: Ahmed Madar

REKs svar på generell henvendelse

Hei,

Viser til oppdatert informasjonsskriv og beredskapsplan sendt til REK i dag den 23.08.2021,

Oppdateringene er gjort i henhold til komiteens merknader og godkjennes.

Mvh

Finn Skre Fjordholm
REK

Vennlig hilsen
Regionale komiteer for medisinsk og helsefaglig forskningsetikk

Denne e-posten er sendt automatisk fra REK og kan ikke besvares

REK sør-øst D
Besøksadresse: Gullhaugveien 1-3, 0484 Oslo
Telefon:22 84 55 11 | **E-post:**rek-sorost@medisin.uio.no
Web:https://rekportalen.no

10.3 Appendix 3: NSD Decision Letter :

Notification form / Vitamin D and Covid-19 in Lebanon / Assessment

Assessment

Reference number	Type	Date
513677	Standard	29/07/2021

Project title
Vitamin D and Covid-19 in Lebanon

Data controller (institution responsible for the project)
University of Oslo / Faculty of Medicine / Department of Health and Society

Project leader
Ahmed Madar

Student
Firass Al Lababidi

Project period
01.07.2021 - 01.12.2022

Categories of personal data
General
Special

Legal basis
Consent (art. 6 no. 1 a)
Explicit consent (art. 9 no. 2 a)

The processing of personal data can begin, as long as it is carried out as described in the Notification Form. The legal basis is valid until 01.12.2027.

Notification Form

Comment
BACKGROUND
The project has been assessed and approved by the Regional Committees for Medical and Health Research Ethics (REK) in accordance with the Health Research Act (and others) § 10 (REK's ref: 270246).

It is NSD's assessment that the processing will also be in accordance with privacy legislation, as long as it is carried out in line with what is documented in the notification form dated 29.07.2021 with attachments, as well as in the message dialogue between the notifier and NSD. The treatment can start.

TYPE OF INFORMATION AND DURATION
The project will process special categories of personal data on health information and general categories of personal data until 01.12.2022, with further storage for 5 years for documentation purposes.

LEGAL BASIS
The project will obtain consent from those registered to the processing of personal data. Our assessment is that the project requires a consent in accordance with the requirements in art. 4 no. 11 and art. 7, in that it is a voluntary, specific, informed and unequivocal confirmation, which can be documented, and which the data

subject can withdraw.

The legal basis for the processing will thus be the data subject's express consent, cf. the personal data protection regulation art. 6 no. 1 letter a, cf. art. 9 no. 2 letter a, cf. Personal Data Act § 10, cf. § 9 (2).

PRIVACY PRINCIPLES

NSD considers that the planned processing of personal data will follow the principles in the Personal Data Protection Regulation regarding:

legality, fairness and transparency (art. 5.1 a), in that the data subjects receive satisfactory information about and consent to the processing

purpose limitation (art. 5.1 b), in that personal data is collected for specific, expressly stated and justified purposes, and is not further processed for new incompatible purposes

data minimization (art. 5.1 c), in that only information that is adequate, relevant and necessary for the purpose of the project is processed

storage limitation (art. 5.1 e), in that the personal data is not stored longer than necessary to fulfill the purpose

THE RIGHTS OF THE REGISTERED

NSD assesses that the information about the processing that the registered will receive meets the law's requirements for form and content, cf. art. 12.1 and art. 13.

As long as the data subjects can be identified in the data material, they will have the following rights: access (art. 15), correction (art. 16), deletion (art. 17), restriction (art. 18) and data portability (art. 20).

Basically, everyone who is registered in the research project has the right to have information registered about them deleted. However, according to Section 16 third paragraph of the Health Research Act, the right to demand deletion of one's health information will not apply if the material or information is anonymised, if the material after processing is included in another biological product, or if the information has already been included in performed analyses. The rule refers to the fact that deletion in such situations will be very difficult and/or destructive for the research, and thus prevent the purpose of the research from being achieved.

According to the Personal Protection Regulation art 17 no. 3 d, one can be exempted from the right to deletion if the processing is necessary for purposes related to scientific or historical research or for statistical purposes in accordance with article 89 no. 1 to the extent that deletion is likely to make it impossible or in to a serious degree will prevent the goals of said treatment from being achieved.

NSD therefore considers that an exception can be made to the right to delete health information according to the Health Research Act § 16 third paragraph and the Personal Protection Regulation art 17 no. 3 d, when the material has been processed so that it is included in another biological product, or if the information has already been included in performed analyses.

We clarify that health information is included in the analyzes carried out if it is compiled or linked with other information or test answers. We point out that other information must be deleted and no further information can be obtained from the participant.

We remind you that if a data subject contacts you about his rights, the institution responsible for data processing has an obligation to respond within one month.

FOLLOW YOUR INSTITUTION'S GUIDELINES

NSD assumes that the processing meets the requirements of the Personal Protection Regulation regarding correctness (art. 5.1 d), integrity and confidentiality (art. 5.1 f) and security (art. 32)

Services for Sensitive Data (TSD) is the data processor in the project. NSD assumes that the processing meets the requirements for the use of a data processor, cf. art. 28 and 29.

NSD assumes that the processing meets the requirements for the processing of personal data outside the EU (personal data protection regulation chapter 5).

To ensure that the requirements are met, you must follow internal guidelines and possibly consult with the institution responsible for processing.

REPORT SIGNIFICANT CHANGES
If there are significant changes in the processing of personal data, it may be necessary to report this to NSD by updating the reporting form. Before you report a change, we encourage you to read about the types of changes that need to be reported: https://www.nsd.no/personvernfjenester/fylle-ut-meldeskjema-for-personopplysninger/melde-endringer-i - registration form

You must wait for a response from NSD before the change is implemented.

FOLLOW-UP OF THE PROJECT
NSD will follow up during the process (every two years) and at planned termination to clarify whether the processing of the personal data has been completed/is ongoing in line with the processing that has been documented.

Contact person at NSD: Elizabeth Blomstervik

Good luck with the project!

10.4 Appendix 4 ICH Program Decision Letter:

UiO : Faculty of Medicine
University of Oslo

Firass Al Lababidi

Date: 5th May, 2021

Statement from the Program Ethical Committee

The Program Ethical Committee have processed your application, number 13793253 about your project *"Association between Vitamin D status and Covid 19 in Lebanon"*

The committee believe your project fall under the Norwegian Health Research Law (helseforskningsloven and forskningsetikkloven) and should be submitted to Regional Committees for Medical and Health Research Ethic (REC) for exception or approval. In addition, you also have to apply to the Norwegian Centre for Research Data (NSD) for approval.

If your project will be conducted outside of Norway, you should also secure required local approval.

Supervisors for **Firass Al Lababidi**'s master project is:

- **Ahmed Madar**, Institute of Health and Society at UIO
- **Samia Filali Zataari**, Hammoud Hospital Medical Center, Lebanon

Sincerely yours

Elia John Mmbaga
Associate Professor, MD, PhD
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www.med.uio.no/helsam
Org. no.: 971 035 854

10.5 Appendix 5 Informed Consent English Version

PARTICIPANT INFORMATION SHEET

INVITATION TO PARTICIPATE IN A RESEARCH PROJECT

Association between Vitamin D status and Covid 19 in Lebanon

You are invited to participate in a research project entitled "Association between Vitamin D status and Covid-19 in Lebanon". The purpose of this study is to gain a better understanding of relationship between vitamin D and Covid-19 and have a better insight on how to be more protected amid this covid-19 pandemic. You have been invited because you have a residency status in Lebanon, and you are coming to Hammoud Hospital University Medical Center (HHUMC) to take a PCR test for Covid-19. Your responses are invaluable as part of this research.

WHAT IS THE PROJECT ABOUT?

Participation in this research project is entirely voluntary. Please note that you are required to sign a consent letter and to complete a questionnaire in Arabic or English. If you can't read or write the project moderator will read and explain the content of this information and if you agree we will ask you to sign or put impression of your right thump to confirm that you have understood the study and will give consent. You can withdraw your consent at any time without giving any reason. All your personal information will then be deleted. It will not have any negative consequences for you if you do not want to participate or late choose to withdraw.

You will be asked to complete a short-guided questionnaire digitally with the assistance of a moderator at the hospital. The questionnaire should take approximately 10 minutes to complete.

We will ask you some background information such as age, gender, educational level, diet, and sun exposure habits. Your height and weight will be measured as well.

The blood samples will be taken in the usual way in the arm by an experienced healthcare worker at hospital.

However, you should be aware that like any other invasive procedure, there exists a risk of mild pain.

All data is confidential and is treated in accordance with the privacy regulations. Please ensure you do not disclose a third party's personal information anywhere on the questionnaire.

The project will collect and record personal information about you. The name and phone number will be recorded on a log sheet kept with the study moderator and a Personal Identification number (cod number) will be given to you. This number will be entered in the questionnaire that is linked to TSD, through NettsKjema on a digital tablet. The log sheet will be discarded after successful data entry and vitamin D result will be given to you if you request it. Other than the questionnaire, we will have access to your vitamin D and PCR test results, which means we will use your corona results from the corona tests that you are going to take anyway.

FORESEEABLE BENEFITS AND PREDICTABLE RISKS AND BURDENS OF TAKING PART

The Direct benefit of the study to the participant will be a free vitamin D blood level Test, that you will be informed you vitamin D levels and if you have low levels of vitamin D, you will be encouraged to contact to your general physician.

if association between vitamin D status and covid-19 is found, this will help with the prevention and treatment of covid-19 patients. The findings might also have implications for the use of health care and the prioritization of resources in the country. Furthermore, this will provide a good basis to initiate appropriate and effective preventive measures for the population. This will also provide opportunities to compare the result with other similar studies.

You will be asked to provide us with a blood sample for testing your vitamin D blood level through a needle

VOLUNTARY PARTICIPATION AND THE POSSIBILITY TO WITHDRAW CONSENT

prick that is like any other blood test you do on routinely basis. However, you should be aware that like any other invasive procedure, there exists a risk of mild pain.

Participation in the project is voluntary. If you wish to take part, you will need to sign the declaration of consent on the last page. You can, at any given time and without reason withdraw your consent. If you decide to withdraw participation in the project, you can demand that your tests and personal data concerning health be deleted, unless however, the data concerning health and tests have already been analyzed or used in scientific publications. If you at a later point, wish to withdraw consent or have questions regarding the project, you can contact to study investigators at the following contact details:

Researcher / Student: Firass AL Lababidi, MPhil. International Community Health, Department of Health and Society, UiO. Email: firassa@uio.no or call at +961 70239845

Study moderator: Samia Filali Zaatari, Quality and Risk management manger – Hammoud Hospital Medical

WHAT WILL HAPPEN TO YOUR PERSONAL DATA CONCERNING HEALTH?

University Center. Email: Samia_filali@hotmail.fr or call at +96103854250

Any personal data concerning health that has been recorded about you will only be used as described in the purpose of the project. You have the right to access information that has been recorded about you and the right to stipulate that any error(s) in the information that is recorded is/are corrected. You also have the right to know which security measures have been/will be taken when your personal data concerning health is processed.

All information will be processed and used without your name or personal identification number, or any other information that is directly identifiable to you. A code links you and your personal data via an identifier list. Only the Study moderator will have access to it. All the biological samples will be destroyed after they have been analyzed, and no later than within two months.

COMPENSATION

You/ legal representative will not receive any payment or other compensation for participating in this study. Any significant new findings that result from this study will be conveyed to you. If you have questions or concerns You can ask questions about this research study currently or at any time during the study, by contacting the proposed researchers working on the study or by contacting Dr. Samia Filali Zaatari on this email

:Samia_filali@hotmail.fr or by calling 07723888 If you have questions about your rights as a research participant or feel that you have been mistreated, please call the HHUMC Institutional Review Board at 07 723888

FINANCE

This project will receive funding through the International Community Health program at the University of Oslo in Norway. The Funding will cover the cost of vitamin D tests that are being performed in this study, in addition to minor expenses that could arise during the study conduction.

APPROVAL

The Regional Committee for Medical and Health Research Ethics has reviewed and approved the Research Project Reference number: *270246 from REC (25.06.2021)* and the IRB at Hammoud Hospital Medical University Center has approved this study and NSD Ethical Clearance Number : 513677

In accordance with the General Data Protection Regulation the controller University of Oslo and the project manager Firass AL Lababidi is independently responsible to ensure that the processing of your personal data concerning health has a legal basis.

The processing of personal data is in accordance with Hammoud Hospital University Medical Center data protection policies

CONTACT INFORMATION

If you have any questions regarding the research project, you can get in touch with Researcher / Student: Firass AL Lababidi, MPhil. International Community Health Department of Health and Society, UiO. Email: firassa@uio.no or call at +961 70239845

I CONSENT TO PARTICIPATING IN THE RESEARCH PROJECT AND THAT MY PERSONAL DATA CONCERING HEALTH AND BIOLOGICAL MATERIAL CAN BE USED AS DESCRIBED ABOVE

Participants Signature : _____

Participants Address : _____

Participants phone Number: _____

Participants Given ID number for the study: _____

I confirm that I have given information about the research project "Association between vitamin D and Covid 19 In Lebanon"

_____

Place and date

Signature

_____

Role in the research project

10.6 Appendix 6 Informed consent Arabic Version

دعوة للمشاركة في مشروع بحثي

ورقة معلومات للمشارك

العلاقة بين حالة فيتامين د و Covid 19 في لبنان

أنت مدعو للمشاركة في مشروع بحثي بعنوان "العلاقة بين حالة فيتامين د و Covid-19 في لبنان". الغرض من هذه الدراسة هو اكتساب فهم أفضل للعلاقة بين فيتامين (د) و Covid-19 والحصول على رؤية أفضل حول كيفية الحماية بشكل أكبر وسط جائحة كوفيد -19. لقد تمت دعوتك لأن لديك إقامة في لبنان ، وأنت قادم إلى المركز الطبي الجامعي بمستشفى حمود (HHUMC) لإجراء اختبار PCR لـ Covid-19. ردودك لا تقدر بثمن كجزء من هذا البحث.

ما هدف المشروع

المشاركة في هذا المشروع البحثي تطوعية بالكامل. يرجى ملاحظة أنه يتعين عليك التوقيع على الموافقة وإكمال استبيان باللغة العربية أو الإنجليزية. إذا لم تتمكن من القراءة أو الكتابة ، فسيقوم مشرف المشروع بقراءة وشرح محتوى هذه المعلومات ، وإذا وافقت ، فسنطلب منك التوقيع أو وضع بصمة عن إبهامك لتأكيد أنك قد فهمت الدراسة وسوف تمنح موافقتك. يمكنك سحب موافقتك في أي وقت دون إبداء أي سبب. سيتم بعد ذلك حذف جميع معلوماتك الشخصية. لن يكون لذلك أي عواقب سلبية بالنسبة لك إذا كنت لا ترغب في المشاركة أو إذا اخترت الانسحاب في وقت متأخر.

سيُطلب منك إكمال استبيان قصير رقمي بمساعدة وسيط في المستشفى. يجب أن يستغرق ملء الاستبيان حوالي 10 دقائق فقط. سنطلب منك بعض

المعلومات الأساسية مثل العمر والجنس والمستوى التعليمي والنظام الغذائي وعادات التعرض لأشعة الشمس. سيتم قياس طولك ووزنك أيضا. سيتم أخذ عينات الدم بالطريقة المعتادة في الذراع بواسطة عامل المختبر المتمرس في المستشفى. ومع ذلك ، يجب أن تدرك أنه مثل أي إجراء جراحي آخر ، هناك خطر حدوث ألم خفيف. جميع البيانات سرية ويتم التعامل معها وفقًا للوائح الخصوصية. يرجى التأكد من أنك لا تفعل ذلك للكشف عن المعلومات الشخصية لطرف ثالث في أي مكان في الاستبيان.

سيقوم المشروع بجمع وتسجيل المعلومات الشخصية عنك. سيتم تسجيل الاسم ورقم الهاتف على ورقة تسجيل يحتفظ بها مشرف الدراسة وسيتم إعطاؤك رقم تعريف شخصي (ID). سيتم إدخال هذا الرقم في الاستبيان المرتبط بـ TSD ، من خلال NettsKjema على جهاز لوحي رقمي. سيتم تجاهل ورقة السجل بعد إدخال البيانات بنجاح وسيتم تقديم نتيجة فيتامين (د) لك إذا طلبت ذلك. بل الاضافةللاستبيان ، سنتمكن من الوصول إلى نتائج اختبار فيتامين (د) و PCR ، مما يعني أننا سنستخدم النتائج التي ستجريها على أي حال.

الفوائدوالمخاطر المتوقعة

ستكون الفائدة المباشرة للدراسة للمشارك هي اختبار مستوى الدم بفيتامين (د) مجانًا ، وسيتم إبلاغك بمستويات فيتامين (د) وإذا كان لديك مستويات منخفضة من فيتامين (د) ، فسيتم تشجيعك على الاتصال بطبيبك العام.

إذا تم العثور على ارتباط بين حالة فيتامين (د) و covid-19 ، فسيساعد ذلك في الوقاية والعلاج لمرضى كوفيد -19. قد يكون للنتائج أيضا آثار على استخدام الرعاية الصحية وتحديد أولويات الموارد في البلد. علاوة على ذلك ، سيوفر هذا أساسًا جيدًا لبدء تدابير وقائية مناسبة وفعالة للسكان. سيوفر هذا أيضا فرصًا لمقارنة النتائج مع دراسات أخرى مماثلة. سيُطلب منك تزويدنا بعينة دم لاختبار مستوى فيتامين (د) في

الدم من خلال وخز إبرة يشبه أي فحص دم آخر تقوم به بشكل روتيني. ومع ذلك ، يجب أن تدرك أنه مثل أي إجراء جراحي آخر ، هناك خطر حدوث ألم خفيف.

المشاركة الطوعية وإمكانية الموافقة على الانسحاب:

لمشاركة في المشروع تطوعية. إذا كنت ترغب في المشاركة ، فسوف تحتاج إلى التوقيع على إعلان الموافقة في الصفحة الأخيرة. يمكنك في أي وقت وبدون سبب سحب موافقتك. إذا قررت سحب المشاركة في المشروع ، فيمكنك المطالبة بحذف اختباراتك وبياناتك الشخصية المتعلقة بالصحة ، ما لم يتم بالفعل تحليل البيانات المتعلقة بالصحة والاختبارات أواستخدامها في المنشورات العلمية. إذا كنت ترغب في وقت لاحق في سحب الموافقة أو لديك أسئلة بخصوص المشروع ، يمكنك الاتصال بدراسة المحققين على تفاصيل الاتصال التالية:

الباحث / الطالب: فراس اللبابيدي ماجستيرفي صحة المجتمع الدولي للمجتمع في جامعة اوسلو في النرويج البريد الإلكتروني: firassa@uio.no أو الاتصال على 70239845

مدير الدراسة: سامية الفيلالي الزعتري ، مدير الجودة وإدارة المخاطر - مستشفى حمود المركز الجامعي الطبي. البريد الإلكتروني: Samia_filali@hotmail.fr أو الاتصال على 03854250

ماذا سيحدث لبياناتك الشخصية المتعلقة بالصحة؟

سيتم استخدام أي بيانات شخصية تتعلق بالصحة تم تسجيلها عنك فقط كما هو موضح في الغرض من المشروع. لديك الحق في الوصول إلى المعلومات التي تم تسجيلها عنك والحق في اشتراط تصحيح / تصحيح أي خطأ في المعلومات التي تم تسجيلها. لديك أيضا الحق في معرفة التدابير الأمنية التي تم اتخاذها او سيتم اتخاذها عند معالجة بياناتك الشخصية المتعلقة بالصحة. ستتم معالجة جميع المعلومات واستخدامها بدون اسمك أو رقم تعريفك الشخصي ، أو أي معلومات أخرى يمكن التعرف عليها بشكل مباشر. يربط رمز بينك وبين بياناتك الشخصية عبر قائمة

معرفات. سيتمكن مشرف الدراسة فقط من الوصول إليه. سيتم تدمير جميع العينات البيولوجية بعد تحليلها ، وفي موعد لا يتجاوز شهرين.

التعويض

لن تتلقى أنت اوالممثل القانوني أي مدفوعات أو تعويضات أخرى مقابل المشاركة في هذه الدراسة. سيتم إبلاغك بأي نتائج جديدة مهمة ناتجة عن هذه الدراسة. إذا كانت لديك أسئلة أو مخاوف ، يمكنك طرح أسئلة حول هذه الدراسة البحثية حاليًا أو في أي وقت أثناء الدراسة ، من خلال الاتصال بالباحثين المقترحين الذين يعملون على الدراسة أو عن طريق الاتصال بالدكتورة سامية الفيلالي زعتري على هذا البريد الإلكتروني: Samia_filali@hotmail.fr أو عن طريق الاتصال على 07723888 إذا كانت لديك أسئلة حول حقوقك كمشارك في البحث أو تشعر بأنك تعرضت لسوء المعاملة ، يرجى الاتصال بمجلس المراجعة المؤسسية HHUMC على 07723888

الموافقات الاخلاقية

راجعت اللجنة الإقليمية لأخلاقيات البحوث الطبية والصحية ووافقت على الرقم المرجعي لمشروع البحث: 270246 من REC (25.06.2021) ووافق IRB في مستشفى حمود المركز الجامعي الطبي على هذه الدراسة في لبنان ورقم التخليص الأخلاقي NSD : 513677 وفقًا للائحة العامة لحماية البيانات ، فإن المتحكم بجامعة أوسلو ومدير المشروع فراس اللبابيدي مسؤولان بشكل مستقل عن ضمان أن معالجة بياناتك الشخصية المتعلقة بالصحة لها أساس قانوني.

تتم معالجة البيانات الشخصية وفقًا لسياسات حماية البيانات في المركز الطبي الجامعي بمستشفى حمود إذا كان لديك أي أسئلة بخصوص المشروع البحثي ، يمكنك التواصل مع الباحث / الطالب: فراس اللبابيدي ،على البريد الإلكتروني: firassa@uio.no أو الاتصال على 70239845

أوافق على المشاركة في مشروع البحث وأن بياناتي الشخصية المتعلقة بالصحة والمواد البيولوجية يمكن استخدامها على النحو الموصوف أعلاه

توقيعه او بصمته: _____

عنوان السكن: _____

رقم الهاتف : _____

الرقم الشخصي المعطى(ID): _____

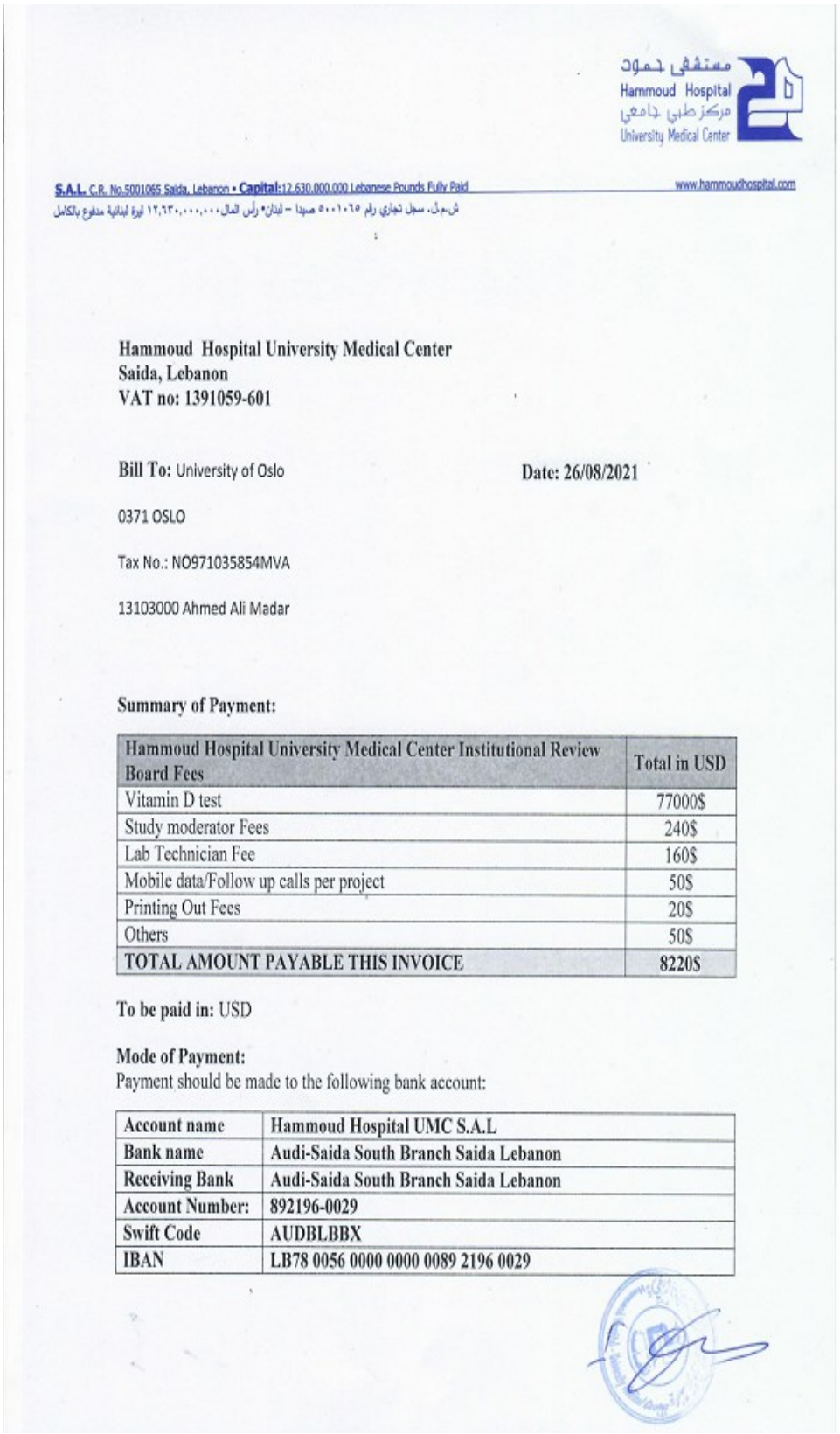
انا الشاهد أؤكد أنني قدمت كل المعلومات حول المشروع البحثي "العلاقة بين فيتامين د وكوفيد 19 في لبنان"

الاسم: ----------

المكان والتاريخ التوقيع: ----------

دوره في مشروع البحث:----------

10.7 Appendix 7 Invoice from Hospital



مستشفى حمود
Hammoud Hospital
مركز طبي جامعي
University Medical Center

S.A.L. C.R. No.5001065 Saida, Lebanon • Capital:12.630.000.000 Lebanese Pounds Fully Paid www.hammoudhospital.com
ش.م.ل. سجل تجاري رقم ٥٠٠١٠٦٥ صيدا – لبنان• رأس المال ١٢,٦٣٠,٠٠٠,٠٠٠ ليرة لبنانية مدفوع بالكامل

Hammoud Hospital University Medical Center
Saida, Lebanon
VAT no: 1391059-601

Bill To: University of Oslo **Date: 26/08/2021**

0371 OSLO

Tax No.: NO971035854MVA

13103000 Ahmed Ali Madar

Summary of Payment:

Hammoud Hospital University Medical Center Institutional Review Board Fees	Total in USD
Vitamin D test	77000$
Study moderator Fees	240$
Lab Technician Fee	160$
Mobile data/Follow up calls per project	50$
Printing Out Fees	20$
Others	50$
TOTAL AMOUNT PAYABLE THIS INVOICE	**8220$**

To be paid in: USD

Mode of Payment:
Payment should be made to the following bank account:

Account name	**Hammoud Hospital UMC S.A.L**
Bank name	**Audi-Saida South Branch Saida Lebanon**
Receiving Bank	**Audi-Saida South Branch Saida Lebanon**
Account Number:	**892196-0029**
Swift Code	**AUDBLBBX**
IBAN	**LB78 0056 0000 0000 0089 2196 0029**

10.8 Appendix 8 IRB Approval letter from HHUMC

مستشفى حمود
Hammoud Hospital
مركز طبي جامعي
University Medical Center

Institutional Review Board (IRB)

Dr. Ghassan Hammoud Street, P.O.Box 652, Saida, Lebanon • Tel. 961 (7) 723111 - 961 (7) 723888 • Fax 961 (7) 725833 • Email info@hammoudhospital.com www.hammoudhospital.com
شارع الدكتور غسان حمود، ص.ب. ٦٥٢، صيدا، لبنان • تلفون ٧٢٣١١١ (٧) ٩٦١ - ٧٢٣٨٨٨ (٧) ٩٦١ • فاكس ٧٢٥٨٣٣ (٧) ٩٦١ • بريد الكتروني info@hammoudhospital.com

Notice of IRB Approval

Ref :IRB26082021

To : Mr. Firas Lababidi

Approval Issued : April 22, 2021
Expiration Date : April 21, 2022
Review Type : Expedite

Date : April 22, 2021
Protocol Number : IRB Master Thesis research Approval

The Hammoud Hospital Institutional Review Board (IRB), which operates per ICH GCP guidelines, has reviewed the – initial submission for the Master Thesis researcfh "Association between Vitamin D status and Covid 19 in Lebanon: A cross-sectional study among adults aged between 21-75 years in south, Lebanon " in a meeting held on
April 22, 2021.

The approval is limited to the activities described in the Approved Research Protocol and all submitted documents are listed on page 2 of this letter.

The Committee reviewed the documents outlined below and ***approved*** Mr. Lababidi's– initial submission to this research in HHUMC. The following members of the IRB were present at the meeting: Ibrahim Omeis, MD, FANNS (President), Dr. Mohamed Mamlouk (Member) Mr. Hussein Mroueh(Lawyer), Atef El ALi, MD (Member), Mr. Arouba Kalash (Community Member), and Mrs. Ghada Aoun(- Social Worker-General Secretary).

APPROVAL CONDITIONS FOR HHUMC CLINICAL TRIALS

HHUMC Research Policies: All Individuals engaged in the research project must adhere to the approved protocol and all applicable HHUMC IRB Research Policies. PARTICIPANTS must not be involved in any research related activity prior to IRB approval date or after the expiration date.

Protocol Expiration: The IRB approval expiry date is listed above. It is your responsibility to apply for continuing review and receive continuing approval for the duration of the research project.

Modifications and Amendments: All protocol modifications must be approved by the IRB prior to implementation.

Notification of Project Completion: A notification of research project completion and closure and a summary of findings must be sent to the IRB office upon completion. Study files must be retained for a period of 3 years from the date of notification of project completion.

If you have any questions or concerning this infomation, please contact the IRB office by email at medical@hammoudhospital.org.

Ibrahim Omeis, MD, FANNS
Chair, of the Institutional Review Board
Hammoud Hospital University Medical Center
Saida, Lebanon
Tel: +961-7-721021 Ext. 1222-3
Fax: +961-7-725833
Email: iomeis@hammoudhospital.org

Documents Submitted:

- Research proposal
- Informed consent form ENGLISH version
- Informed consent form ARBIC version
- Participiatnt log sheet