Libyan International Medical University

Faculty of Pharmacy

Vitamin D Insufficiency Among Obese Adults In The Eastern Region Of Libya

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A thesis submitted to Libyan International Medical in partial fulfillment of the requirements for the Bachelor of Pharmacy degree.

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Declaration

This is to certify that research work embodied in this thesis entitled

"Vitamin D insufficiency among obese adults in the eastern region of Libya"

has been carried out by us under supervision of Prof. Mustafa Elfakhri, Dr. Salma Bukhatwa and Dr. Narges Kablan.

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Abstract

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. Globally, overweight and obesity are the fifth leading contributors to fatalities. According to the World Health Organization (WHO), body mass index (BMI) ≥ 25 is overweight, and BMI ≥ 30 is obesity. Vitamin D (calciferol), which comprises a group of fat soluble seco-sterols that are found in very few foods naturally, is photosynthesized from cholesterol in the skin of vertebrates by the action of solar ultraviolet B (UVB) radiation. The two major physiologically relevant ones are vitamin D_2 and vitamin D_3. There is a growing evidence that obesity and vitamin D deficiency are related, although the cause-effect relationship remains unclear.
Objective of this work was to find out whether obesity alters vitamin D level in obese adults in the Eastern region of Libya.

Data was collected during September 2015 with the aid of a structured questionnaire. One hundred and twenty patients visiting nutrition clinics both in Benghazi and Tobruk were interviewed. Clinical investigations data collected included vitamin D, calcium, lipid profile, fasting blood glucose, HbA1c, complete blood count (CBC), creatinine, Na^+, K^+, urea and TSH levels measurement. Data was analyzed using excel and presented as the mean ± SEM (n).

The mean age (years) of study sample was 30.93 ± 1.05 (118). Out of whole study sample 55.83% (n=67) had a family history of obesity and in about 80% of them this family history was from either mother side alone or father side alone or even from both mother and father. Adult obese subjects represented 63.33%, adult overweight subjects represented 25.83%, adult healthy subjects represented 3.33% and children represented 7.50% of whole study sample. Average level of vitamin D in overweight adults was 9.92 ± 1.37 (29), obese adults was 9.38 ± 0.70 (74), in healthy weight adults was 11.11 ± 1.72 (4) and in children was 9.98 ± 1.63 (9).

Vitamin D deficiency is highly prevalent not only in overweight and obese Libyan adults but also this may be extended to children and healthy adults as well.

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List of abbreviations

BMI	Body mass index
CBC	Complete blood count
CVS	Cardiovascular diseases
DM	Diabetes mellitus
FAO	Food and Agriculture Organization
HbA1c	Glycohemoglobin
HDL	High-density lipoprotein
HDL	High density lipoprotein
IHD	Ischemic Heart Disease
K^+	Potassium
Kcal	Kilo Calorie
LD	Libyan dinar
LDL	Low-density lipoprotein
LDL	Low density lipoprotein
Na^+	Sodium
PCOD	Polycystic ovary disease
RBC	Red blood cell
SEM	Standard error of the mean
TSH	Thyroid stimulating hormone

UVB	Ultraviolet B
VDRs	Vitamin D receptors
VLDL	Very-low-density lipoprotein
WBC	White blood cell
WHO	World Health Organization

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Chapter I
Introduction

General introduction

Globally, overweight and obesity are the fifth leading contributors to fatalities. [1] Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. [2] Generally, Overweight is having more body fat than is optimally healthy. Being overweight is common especially where food supplies are plentiful and lifestyles are sedentary, while obesity is a medical condition in which excess body fat has accumulated to the extent that it may have a negative effect on health, leading to reduced life expectancy and/or increased health problems. [3]

Body mass index

Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults. It is defined as a person's weight in kilograms divided by the square of his height in meters (kg/m^2). [2]

$$BMI = \frac{(\text{weight in kilograms})}{\text{height in meters}^2}$$

Equation 1: Metric method of body mass index (BMI) calculation

BMI provides the most useful population-level measure of overweight and obesity, as it is the same for both sexes and for all ages of adults. However, it should be considered a rough guide because it may not correspond to the same degree of fatness in different individuals. [2]

BMI according to the WHO

- a BMI greater than or equal to 25 is overweight.
- a BMI greater than or equal to 30 is obesity. [2]

In 2014, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 600 million were obese. Overweight and obesity are linked to more deaths worldwide than underweight. Most of the world's population live in countries where overweight and obesity kill more people than underweight (this includes all high-income and most middle-income countries). [2]

Etiology of the obesity

There are several factors that may lead to obesity such as the life style, diet and even the genetic factors that may also play a role in obesity.

Genetics

The percentage of obesity that can be attributed to genetics varies, depending on the population examined. [4] Postulated that certain ethnic groups, in an equivalent environment, may be more prone to obesity than others. [5] This is because of what is called 'thrifty gene hypothesis', where the genetic makeup of certain ethnic groups gives them the ability to benefit from rare periods of food abundance by storing energy as fat, an ability valued during times of varying food availability but disadvantageous in the modern life, which offers stable food supplies.[6] Surprisingly, obesity is much more prevalent in Libyan adults, which raises the possibility of environmental factors as the main cause of the increased prevalence of adult obesity in Libya.[7-9]

Diet

Energy intake and composition of diet play a major role in the pathogenesis of obesity. Total calorie consumption has been found to be related to obesity. From the late 1960s to the early 2000s, the average calories available per person per day have increased in Libya. [10]

Infant feeding in Libya

Breast-feeding is shown to be associated with a lower risk of overweight. Exclusive breast feeding during the first 3 or more months of infancy reduces the risk of overweight in childhood.[11,13] In Libya, the rate of artificial feeding is between 5.7% and 40.3%, [14,15] and 47.88% of mothers breast-feed their infants for less than 1 month, whereas 28.18% breast-feed their children for 1-3 months. [14] This may partially explain the high rate of obesity in children aged 5 or younger in Libya. [16]

Libyan diet

Epidemiological data suggest that a diet high in fat is associated with obesity. There is a dearth of recent and nationally representative data on food consumption in Libya. [9]

In 1996, Al-Arbah reported that cereals, oil, and sweeteners provided the largest shares of energy, 41, 12, and 11%, respectively. [17] Food and Agriculture Organization (FAO) analysis of

yearly production, import, and consumption shows that the staple Libyan diet is wheat (bread, couscous, and pasta). [9] Rice is another major staple in Libya. [18] The Libyan diet is low in vegetables and fruits. [19] According to the FAO, the quantities of food consumption between 1967 and 2001 have increased 1.5 times, from about 2,061 kcal daily to 3,327 kcal daily, which is well above population energy requirements of 2,144 kcal/capita/day. This means a Libyan adult consumes daily an extra 1,183 kcal. [18]

In 2001, according to the FAO, the proportions of main energy sources in the Libyan diet were 62% of carbohydrates, 27% of fat, and 11% of proteins. [18] Yet, we think that the contribution of fat to proportion of energy in Libyan diet is higher. [20,21] Furthermore, over the last decade, Libyan diet has become more influenced by Western food culture, and Libyans are now consuming more diets high in sugar and saturated fat in the form of fast food. [9]

In 1978, Jain et al. reported that the average Libyan diet contains about 3,040 kcal, 35% of which is constituted by fats. [20] Another study in 1995 by Najah found that the share of energy from lipids was 29%. [22] In 1999, Swedan estimated that the energy intake by Libyan adults was 2,149 kcal/day for men aged 15-50 years and 2,039 kcal/day for women of the same age range. [21]

Life style

Sedentary lifestyle lowers energy expenditure and promotes weight gain. Worldwide, there has been a marked shift toward less physically demanding work. In 2009, it has been reported that about 44% of Libyan adults do not get sufficient exercise (51.7% of women and 36% of men).[19] Supposed to this is mainly because of increasing dependence on mechanical transportation and greater availability of effort-saving equipment domestically. [19] Also, the increase in television viewing time, use of computers, and video games could be other possible contributors to the rise in the prevalence of obesity in Libyan children and adults. [19]

Health consequences

Obesity and overweight result in major morbidity and premature death as they are predisposing factors for diabetes mellitus, hypertension, dyslipidemia,[23] osteoarthritis,[24] certain malignancies,[25] and others. The risk of chronic disease in populations increases progressively from a BMI of 21 kg/m^2. [26] A high BMI is associated with increased rate of death from all the aforementioned causes and also from cardiovascular disease. [26] People with BMI 30 kg/m^2 at age 40 lived 6 years less than those with lesser BMI, and those with BMI between 25 and 29.9 kg/m^2 at age 40 lived about 3 years less than healthy subjects. [27] Obese subjects also had up to 2.4 times the number of sick leaves as did normal-weight subjects, and the annual drug costs were significantly higher in obese people. [28] In Libya, some studies showed that obesity is more prevalent among people with type 2 diabetes, [29] hypertensives [30] and females with polycystic ovary disease (PCOD), [31] than among the general population, which indirectly indicates that these diseases are more prevalent among obese than non-obese Libya (Fig. 1). [9]

Figure 1: Obesity and related diseases

Adopted from http://www.pvahosp.com/purina-om-dog-cat.pml

Vitamin D

Vitamin D (calciferol) comprises a group of fat soluble seco-sterols (Fig. 2). Vitamin D is found naturally only in a few foods, such as fish-liver oils, fatty fish, mushrooms, egg yolks, and liver (Fig. 3). Vitamin D is photosynthesized in the skin of vertebrates by the action of solar ultraviolet (UV) B radiation on 7-dehydrocholesterol. [32] Vitamin D comes in many forms, but the two major physiologically relevant ones are vitamin D_2 (ergocalciferol); Plant sterol and vitamin D_3 (cholecalciferol); Animal sterol. [32]

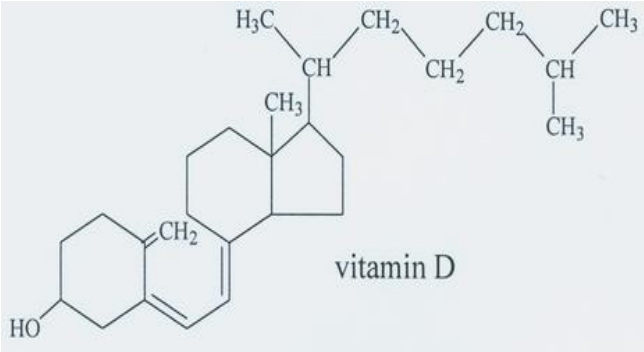


Figure 2: Chemical structure of vitamin D
Adopted from https:\\ http://pixshark.com/vitamin-d-structure.htm

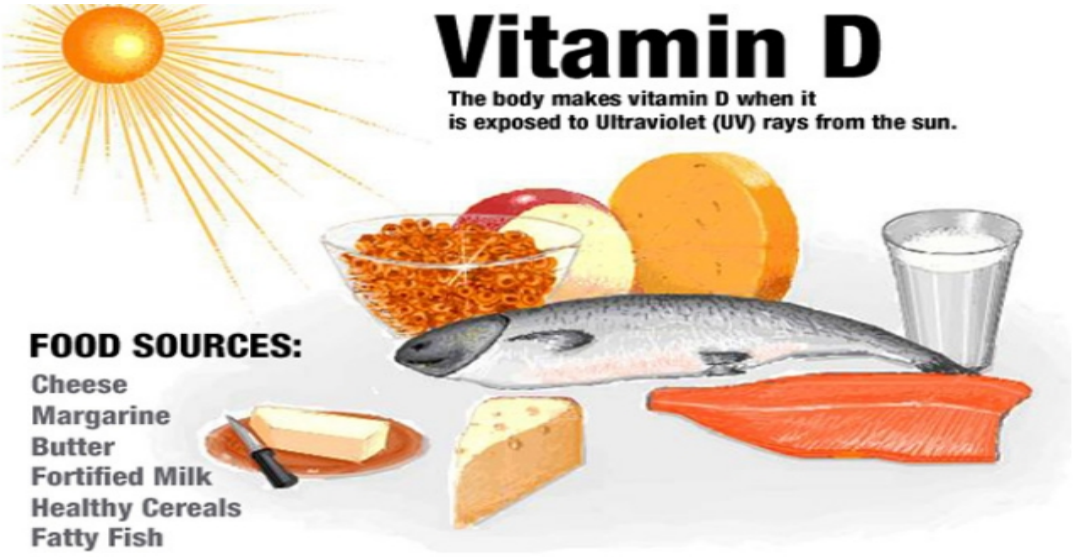


Figure 3: Food source of vitamin D
Adopted from https:\\ http://www.dermaharmony.com/skinnutrition/vitamind3.aspx

Serum calcidiol

The serum calcidiol [25(OH)D; Fig. 4B] concentration is the best indicator for determining adequacy of vitamin D intake of an individual since it represents a summation of the total cutaneous production of vitamin D and the oral ingestion of either vitamin D_2 or vitamin D_3.[33,34]

Serum calcitriol

Similarly, the serum calcitriol [$1,25(OH)_2$ D; Fig. 4B] level is not a good indicator of vitamin D. This hormone's serum concentrations are tightly regulated by a variety of factors, including circulating levels of serum calcium, phosphorus, parathyroid hormone, and other hormones. [34]

Chemistry & Classification

Vitamin D belongs to the quartet of fat soluble vitamins (A, D, E, and K). This accounts for its distribution primarily in adipose tissue and its very slow turnover rate. Structurally, it is a seco-steroid with a ring structure similar to cholesterol except for a broken C–C bond in the B ring (Fig. 4 a & b).

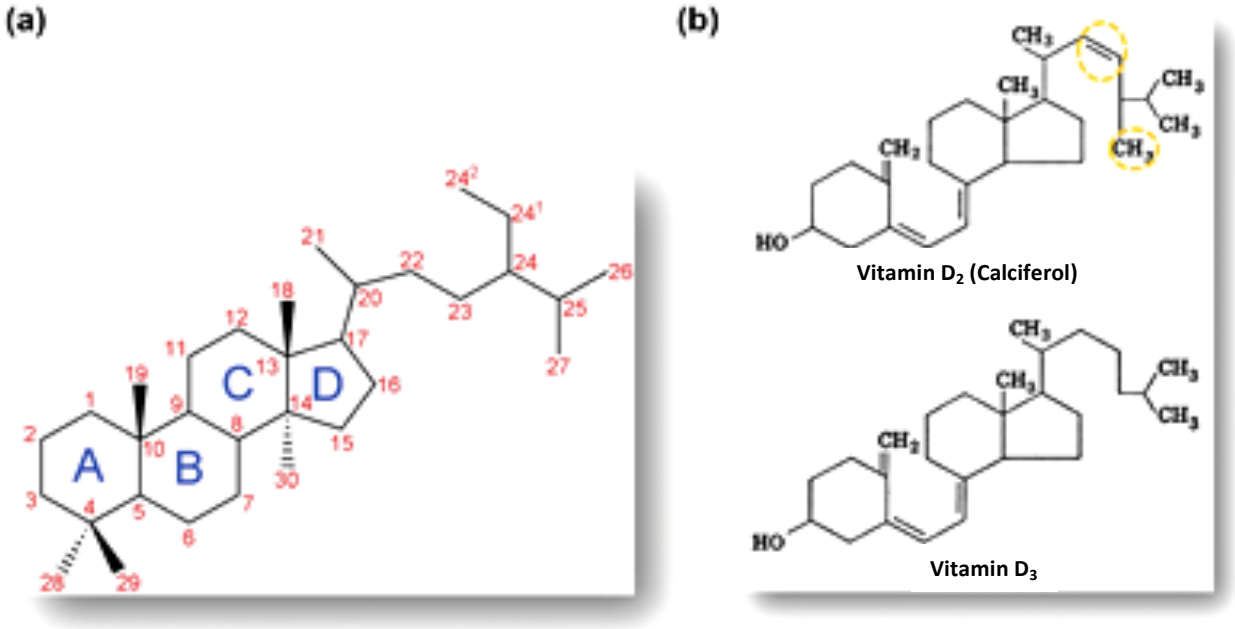


Figure 4: (a) Basic Chemical structure of steroid. (b) The structures of calciferol and cholecalciferol. The structural differences between the two compounds are limited to the side chain; D_2 has one additional methyl group and a double bond.
Adopted from http://www.polarresearch.net/index.php/ljm/article/viewArticle/5648/html_46

Hypovitaminosis D

Hypovitaminosis D is typically diagnosed by measuring the concentration in blood of the compound 25-(OH) D (calcidiol), which is a precursor to the active form 1,25-(OH) D (calcitriol). [35] A review study in 2008 has proposed the following four categories for hypovitaminosis D. [36]

- Insufficient; 50-100 nmol/L (20-40 ng/mL)
- Mild; 25–50 nmol/L (10–20 ng/mL)
- Moderate; 12.5–25.0 nmol/L (5-10 ng/mL)
- Severe; < 12.5 nmol/L (< 5 ng/mL)

Note that 1.0 nmol/L = 0.4 ng/mL for this compound. [37] Other authors have suggested that a calcidiol 25-(OH) D level of 75–80 nmol/L (30–32 ng/mL) may be sufficient, [38,35,39] although a majority of healthy young people with comparatively extreme sun exposure did not reach this level in a study done in Hawaii. [40] In current medical practice, these reference ranges are gradually shifting upward as vitamin D deficiency is increasingly being implicated in the etiology of an expanding list of diseases. [41,42]

Epidemiology of vitamin D deficiency

Vitamin D deficiency is now recognized as a pandemic particularly in the northern hemisphere where winters are severe and sun exposure is minimal. The biomarker of vitamin D status is the level of circulating calcidiol [25(OH)D], which due to its lipophilic nature distributes into the adipose tissue and represents the storage form of vitamin D with a half-life of 15 days. Obvious vitamin D toxicity manifested as hypercalcemia and ectopic calcification does not occur until the calcidiol level is well above 150ng/mL.

The Third National Health and Nutrition Examination Survey (NHANES III) has revealed that a large segment of the American population have low vitamin D levels. The phenomenon of vitamin D deficiency has also been found in many other parts of the world including North Africa and the Middle East where social customs dictate minimal skin exposure. The reasons for vitamin deficiency are multiple and include indoor life style, high latitude, dark skin, insufficient

skin area exposed to UVB, obesity (expanded volume of distribution), aging (reduced capacity for photosynthesis), severe liver disease, and chronic kidney disease.

In addition to bone diseases in both children and adults, vitamin D deficiency has been linked to a wide variety of chronic conditions including diabetes mellitus type 2, hypertension, colorectal cancer, infectious diseases, and autoimmune diseases such as systemic lupus erythematosus and diabetes mellitus type 1. However, in most of these conditions a causal relationship and the pathophysiological mechanisms involved have not yet been established.

Biochemical Pharmacology of vitamin D

Role of vitamin D

Vitamin D, in addition to its role in calcium and bone metabolism, has pleiotropic effects in many cell types in many life forms. Thus, not surprisingly hypovitaminosis D has been linked with hypertension, atherogenic dyslipidaemia and increased cardiovascular (CV) disease risk.

Synthesis of vitamin D

Bioactive vitamin D; 1,25(OH)2D is synthesized in a pathway involving different organs and intermediates as shown in Fig. 5.

Vitamin D receptor

Vitamin D exerts its effects by binding to the nuclear vitamin D receptors (VDRs) and in recent years VDRs have been found in various tissues, including the skeletal muscle and the adipose tissue, which are the main determinants of peripheral insulin sensitivity. [43,44,45]

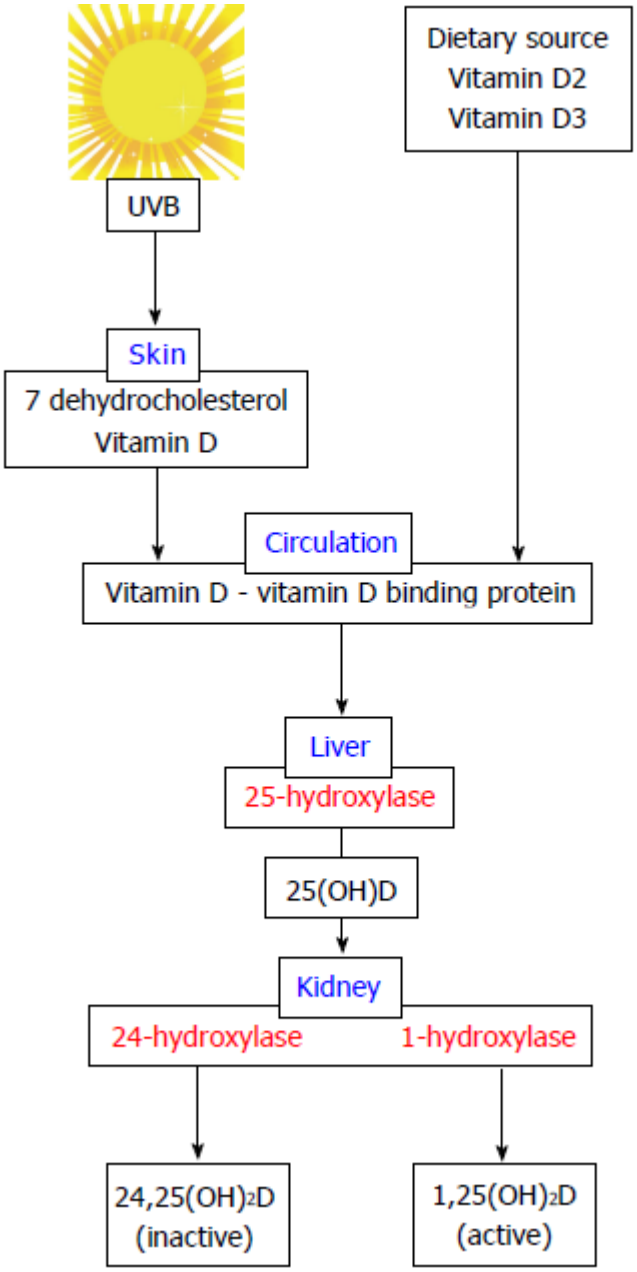


Figure 5: Simplified synthetic pathway leading to the formation of the active metabolite 1,25(OH)2D. UVB: Ultraviolet B. [*Strange RC et al.*] [91]

Skin pigmentation, UV radiation and vitamin D

Vitamin D photosynthesis is long established among animals implying a key role in metabolism. Eumelanin absorbs UV radiation, reducing its penetration and, thereby, formation of potentially harmful free radicals (reactive oxygen species) in the skin. The migration of humans from Africa to environments of often low and highly seasonal UV radiation placed pressure on the original constitutive, dark-skinned phenotype. [46] Thus vitamin D_3 synthetic ability, following movement into higher latitudes, was enabled by polymorphic change in genes that determine skin pigmentation, such as melanocortin 1 receptor, with the resulting development of partially depigmented phenotypes capable of tanning. Thus, the present range of skin pigmentation results from a requirement to promote cutaneous UV radiation induced vitamin D_3 synthesis (depigmented phenotype) and simultaneously prevents UV radiation induced damage (pigmented phenotype. [46] Studying the relationship between UV radiation exposure, vitamin D status, skin type and disease risk is complicated by historical and recent population movements resulting in many people living under solar regimes very different to those in which their ancestors developed mechanisms to balance sunlight's harmful and beneficial effects. [46]

Vitamin D deficiency risk factors

Vitamin D deficiency has been linked with significant complications such as CV events, obesity, metabolic syndrome, type 2 diabetes, various types of cancer, immune disorders and increased mortality. [47,48,49]

Cardiovascular diseases

Calcitriol plays a significant role in the regulation of many genes including those involved in the regulation of renal renin production and the proliferation and growth of cardiac and vascular muscle cells. Also, calcitriol has an anti-inflammatory effect manifested in the down regulation of C-reactive protein and other proinflammatory markers. In a retrospective study focusing on racial differences between black and white Americans, Fiscella and colleagues evaluated data from nearly 15,000 participants in the NHANES III (1988–1994) and cause-specific mortality through 2001 using the National Death Index. Black participants with calcidiol levels in the lowest quartile (mean=13.9 ng/L=34.8 nmol/L) had a 40% greater risk of death due to coronary heart disease, heart failure, or stroke compared with those whose levels were in the three higher quartiles (means: 21.6, 28.4, and 41.6 ng/mL). [50] Several other studies have also shown vitamin D deficiency to be associated with a higher risk for metabolic syndrome, hypertension, and

adverse CV events. [50,51,52] Revved up renin–angiotensin–aldosterone system, insulin resistance, and secondary hyperthyroidism are thought to mediate at least some of the CV effects of vitamin D deficiency.

Diabetes

Previous studies have yielded contradictory findings on the relationship between low vitamin D and impaired glucose homeostasis. However, calcium is necessary to secrete insulin, which indirectly suggests that vitamin D may in fact contribute to maintaining insulin secretion. Among the disorders linking vitamin D deficiency to hyperglycemia, type 2 diabetes mellitus and metabolic syndrome. Type 1 diabetes mellitus and Type 2 DM patients have a higher incidence of vitamin D deficiency in comparison to the healthy population.

Metabolic syndrome

Metabolic syndrome is a cluster of conditions — increased blood pressure, a high blood sugar level, excess body fat around the waist and abnormal cholesterol levels — that occur together, increasing the risk of heart disease, stroke and diabetes.

The relationship between sensitivity to insulin, obesity and glucose homeostasis was first observed by the Swedish physician Eskil Kylin. [53] Accumulating research suggests that circulating concentrations of vitamin D may be inversely related to the prevalence of diabetes, [54-57] to the concentration of glucose, [57-61] and to insulin resistance. [57,58,61,62] In addition, vitamin D deficiency may be a risk factor for the metabolic syndrome, [61,63] a highly prevalent condition among U.S. adults (Fig. 6). [64-66]

Parathyroid hormone (PTH)

Vitamin D deficiency is also an important worldwide public health problem. [67] Although the most-studied and best-known function of vitamin D, together with parathyroid hormone (PTH), is related to bone metabolism, [68] many studies show evidence of the relationship between obesity and low levels of 25(OH)D. [68-73] The frequently observed increases in PTH serum concentrations in obese individuals [74] could be explained by a compensatory mechanism in response to low circulating levels of 25(OH)D.

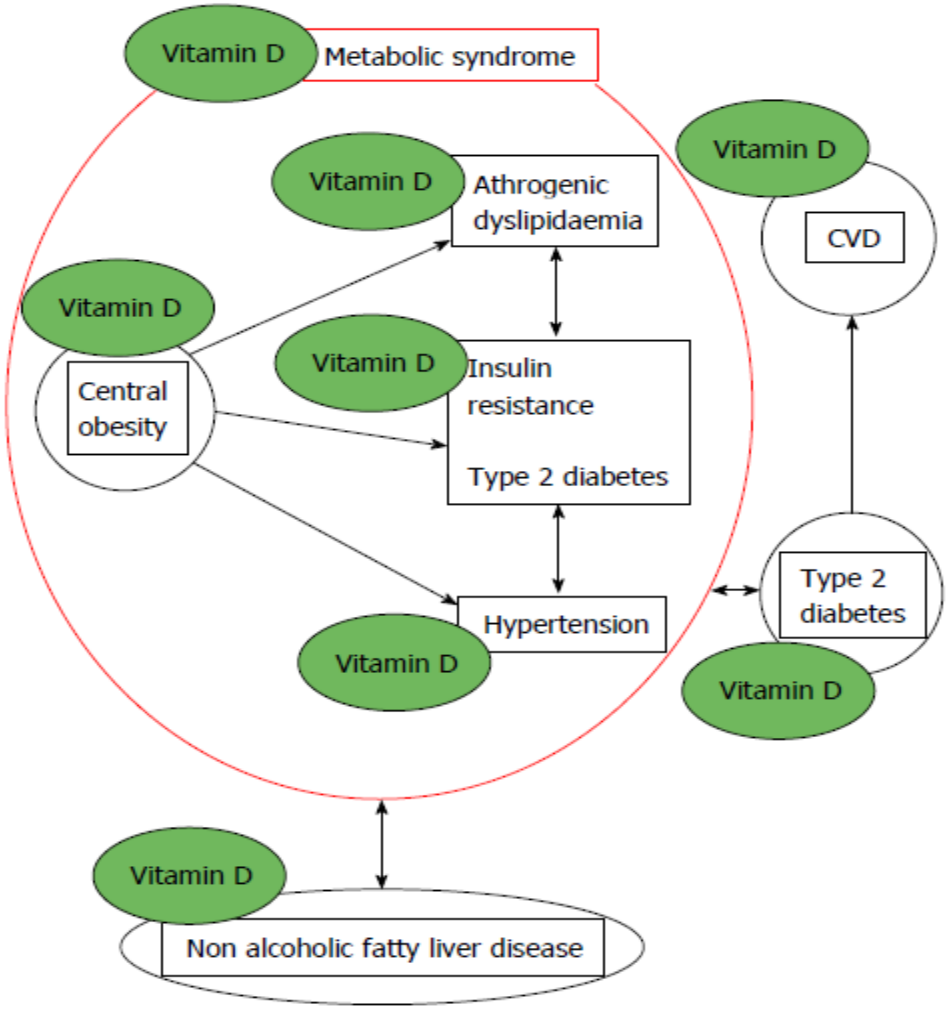


Figure 6: Simplified illustrations of the component risk of metabolic syndrome

The complex relationships between them and the outcomes leading to increased morbidity and mortality. CVD: Cardiovascular disease. [*Strange RC et al.*] [91]

Cancer

The relationship between vitamin D status and the higher incidence of many types of cancer has suggested that vitamin D may play a role in the etiology of these forms of cancer. The results of many studies have corroborated the fact that 1α,25(OH)2D exhibits anti-proliferative, pro-differentiating, anti-inflammatory, and pro-apoptotic functions in a tissue- and cell-specific manner. It has been shown to have a growth inhibitory effect on prostate, colon, breast, lung, liver and pancreatic cancer cells which express VDR. [75,76] In the Women's Health Initiative

Calcium and Vitamin D trial the authors observed no effect of vitamin D and calcium supplementation on mammographic density after one year follow-up.[77] Epidemiological studies have suggested that low vitamin D levels are associated with an increased risk of breast cancer.

Vitamin D and Obesity

The link between obesity and vitamin D deficiency has been observed for years but determining the cause and effect has been difficult. Vimaleswaran et al. suggested that a higher BMI leads to a lower vitamin D status whereas the effects of low vitamin D status on BMI are likely to be marginal. In other words, these findings provide evidence for obesity as the causal factor for the development of vitamin D deficiency but there is no proof that vitamin D deficiency serves as the causal factor for the development of obesity. [78] Nonetheless, experimental studies have demonstrated that 1,25(OH)2D_3 plays an active role in adipose tissue by modulating inflammation, adipogenesis and adipocyte secretion as the key component of metabolic disorders e.g. in the metabolic syndrome. [79] A large study of the genetics underpinning both conditions finds that obesity may decrease vitamin D levels but a predisposition to vitamin D deficiency does not in fact lead to obesity. The findings also suggest that increasing vitamin D levels will not reverse obesity.

The fundamental mechanism that would explain why obesity suppresses vitamin D is still discussed. Since vitamin D is fat soluble, some scientists had assumed that it was sequestered in fatty tissues. If this was the case, less vitamin D would reach the bloodstream. Nevertheless, while the vitamin is indeed stored in the adipose tissue, there is no evidence for sequestration of supplemental or endogenous cholecalciferol. The patients with BMI over 30 may require higher or more frequent doses of vitamin D. [80,81] Nonetheless, Mason et al. found that vitamin D_3 supplementation during weight loss did not translate into higher body mass reduction or associated factors as compared with placebo, however, women who became replete experienced greater improvements. [82]

In obese people, low levels of 25(OH)D can be attributed mainly to:

- The lower bioavailability of the vitamin, due to its sequestration by adipose tissue. [71]
- The dilution of ingested or cutaneously synthesized vitamin D in the enlarged fat mass.[72]
- Low sun exposure, due to mobility limitations or the low sun exposure of large areas of the body.[73]
- A low intake of calcium and vitamin D.

There is a growing evidence that obesity and vitamin D deficiency are related, although the cause-effect relationships remains unclear.

Objectives of the study

Main objective of this work was to find out whether obesity alters vitamin D level in obese adults in the eastern region of Libya.

Chapter II
Materials and methods

Data collection

Data was collected during the period 7th -16th September 2015 questionnaire from a total of 120 patients visiting nutrition clinics both Benghazi and Tobruk.

Data collection tool

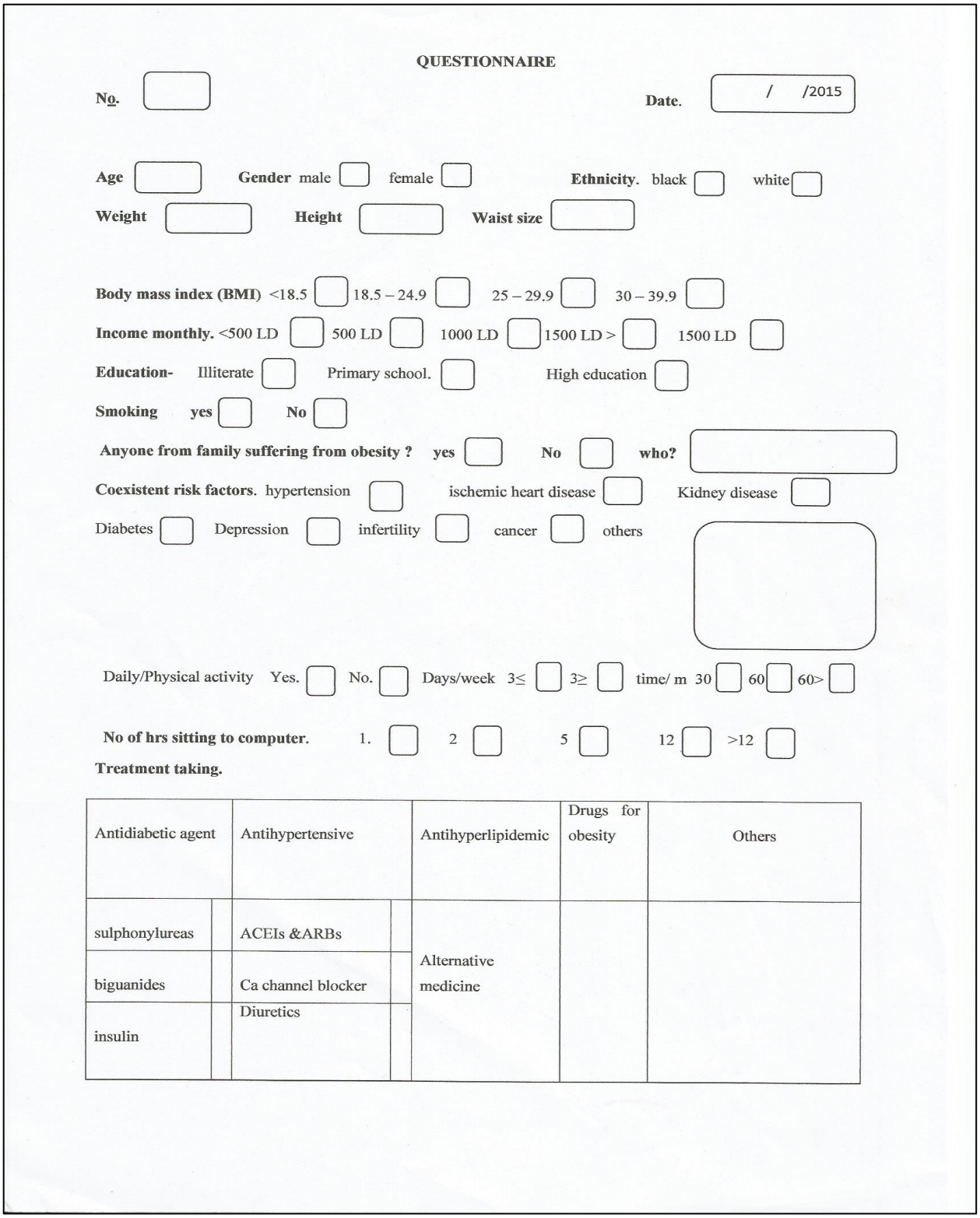
The investigators interviewed each subject with the aid of a structured questionnaire (Fig. 7a&b). The questionnaire included basic information regarding the study subjects as follow:

Information gathered included: age, gender, ethnicity, weight, height, waist size, body mass index, income monthly, education, smoking, family history, coexistent risk factors, hour of daily sport, hour sitting to the computer and any drug treatment taking by patients in addition to clinical investigations (Fig. 7a).

Clinical investigations tests results collected included: fasting blood glucose, HbA1c, lipid profile, renal function, complete blood count, vitamin D; 25(OH)vitamin D (calcidiol), calcium and TSH (Fig. 7b).

Data analysis and statistics

All data was presented as mean ± SEM(n) or percentage (%) as required. Excel was used for statistical analysis of data.



QUESTIONNAIRE

No. ☐ Date. ☐ / /2015

Age ☐ Gender male ☐ female ☐ Ethnicity. black ☐ white ☐

Weight ☐ Height ☐ Waist size ☐

Body mass index (BMI) <18.5 ☐ 18.5 – 24.9 ☐ 25 – 29.9 ☐ 30 – 39.9 ☐

Income monthly. <500 LD ☐ 500 LD ☐ 1000 LD ☐ 1500 LD > ☐ 1500 LD ☐

Education- Illiterate ☐ Primary school. ☐ High education ☐

Smoking yes ☐ No ☐

Anyone from family suffering from obesity ? yes ☐ No ☐ who? ☐

Coexistent risk factors. hypertension ☐ ischemic heart disease ☐ Kidney disease ☐

Diabetes ☐ Depression ☐ infertility ☐ cancer ☐ others ☐

Daily/Physical activity Yes. ☐ No. ☐ Days/week 3≤ ☐ 3≥ ☐ time/ m 30 ☐ 60 ☐ 60> ☐

No of hrs sitting to computer. 1. ☐ 2 ☐ 5 ☐ 12 ☐ >12 ☐

Treatment taking.

Antidiabetic agent	Antihypertensive	Antihyperlipidemic	Drugs for obesity	Others
sulphonylureas ☐	ACEIs &ARBs ☐	Alternative medicine		
biguanides ☐	Ca channel blocker ☐			
insulin ☐	Diuretics ☐			

Figure 7a: Questionnaire used (page 1)

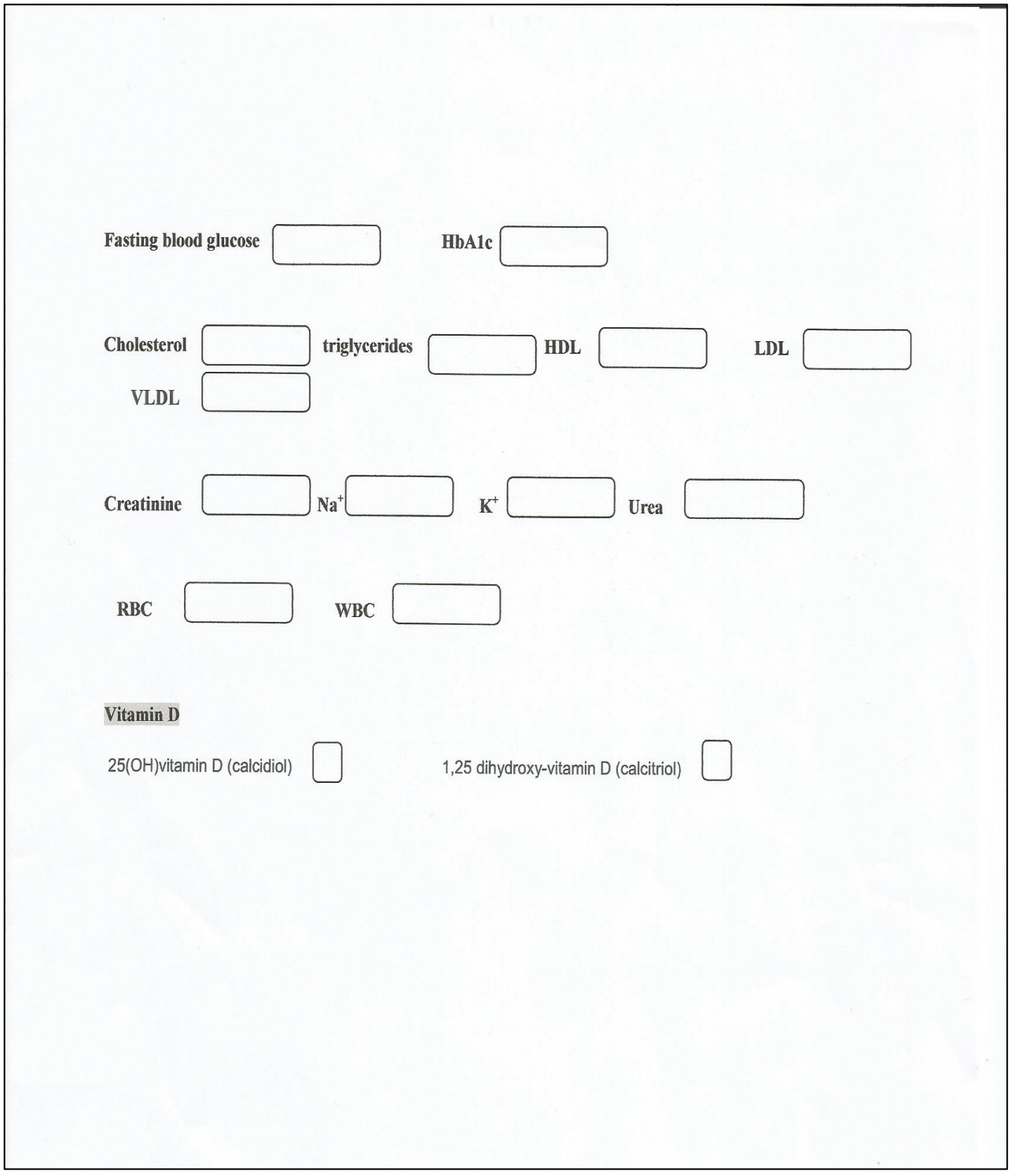


Figure 7b. Questionnaire used (page 2)

Chapter III
Results

Baseline criteria of study subjects

Mean age (years) ± SEM of study sample was 30.93 ± 1.05 (n=118) (Table 1). Females represented 95% (n=114) of study sample, meanwhile males represented 5% (n=6) of study sample (Table 1). Subjects with white ethnicity represented 95% (n=114) of study sample, meanwhile subjects with black ethnicity represented 5% (n=6) of study sample (Table 1).

Mean weight (kg) ± SEM of study sample was 86.79 ± 1.47 (n=120), mean height (cm) ± SEM of study sample was 161.94 ± 0.65 (n=120), mean waist size (cm) ± SEM of study sample was 99.38 ± 2.93 (n=32) (Table 1).

Illiterate subjects represented 6.67% (n=8) of study sample, primary school attendants represented 28.33% (n=34) and higher education attendants represented 65% (n=78) (Table.1). All study subjects were non-smokers (Table 1).

Monthly income of 8.33% (n=10) of study sample was <500 LD, monthly income of 35.00% (n=42) of study sample was 500 LD, monthly income of 18.33% (n=22) of study sample was 1000 LD, monthly income of 3.33% (n=4) of study sample was 1500 LD, monthly income of 2.50% (n=3) of study sample >1500 LD, noting that 32.5% (n=39) of study sample has no income (Table 1).

Out of whole study sample 55.83% (n=67) had a family history of obesity and in about 80% of them this family history was from either mother side alone or father side alone or from both mother and father (Table 1).

Out of whole study sample adult 60% used to exercise at once a week for 30-6 min (Table1). Also, Out of whole study subjects about 60% used to sit to computer at least 1hrs/day (Table 1).

Table 1: Baseline characteristics of study subjects

	Mean ± SEM	n	%
Age (Years)	30.93±1.05	118	
Gender			
Females		114	95.00
Males		6	5.00
Ethnicity			
White		114	95.00
Black		6	5.00
Weight (Kg)	86.79±1.47	120	
Height (cm)	161.94±0.65	120	
Waist size (cm)	99.38±2.93	32	
Education			
Illiterate		8	6.67
Primary school attendant		34	28.33
Higher education attendant		78	65.00
Monthly income (LD)			
No income		39	32.50
<500		10	8.33
500		42	35.00
1000		22	18.33
1500		4	3.33
>1500		3	2.50
Smoking habbits			
Smokers		0	0.00
Non-smokers		120	100
Family history of obesity			
With family history		67	55.83
Father side		15	22.39
Mother side		25	37.31
Father & mother side		14	20.90
Father, mother & brothers		2	2.10
Mother & brothers		5	7.50
Brother & sister		6	8.10
With No family history		53	44.17
Daily sport activity (30-60min)			
Yes		71	59.17
>3d/week		50	41.7
<3d/week		21	17.5
No		49	40.83
Hour/day sitting to computer:			
0		51	42.50
1hr		21	17.50
2hr		15	12.50
5hr		25	20.83
12hr		8	6.67
>12		0	0.00

Body mass index distribution over study sample

Adult obese subjects represented 63.33% of study sample, adult overweight subjects represented 25.83% of study sample, adult healthy subjects represented 3.33% of study sample and children represented 7.50% of study sample (Fig. 8).

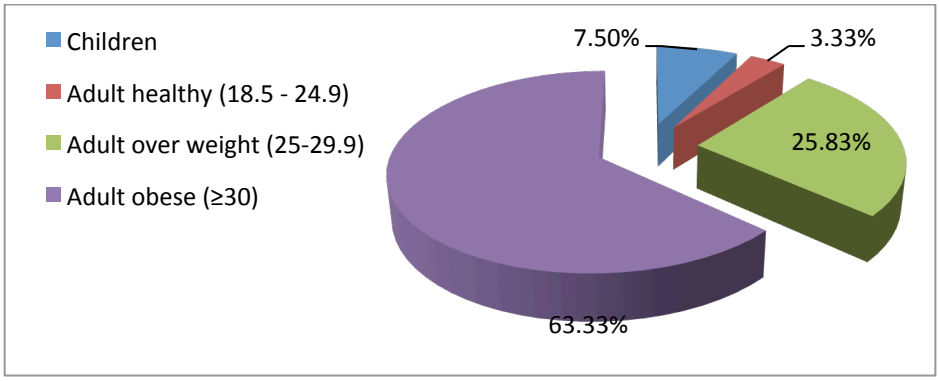


Figure 8: Body mass index distribution over study sample

Risk factors to study sample

Regarding risk factors to study sample, depression, hypertension and diabetes, represented 0.83%, 5.00% and 5.83% of all risk factors. Cancer, infertility, kidney disease and IHD as common risk factors of obesity were not found at all among study sample. Noting that 10.83% of study sample had some other health complaints rather than those mentioned above. Most interestingly 80.83% of study sample did not suffer any health problem at least from their point of view (Fig 9).

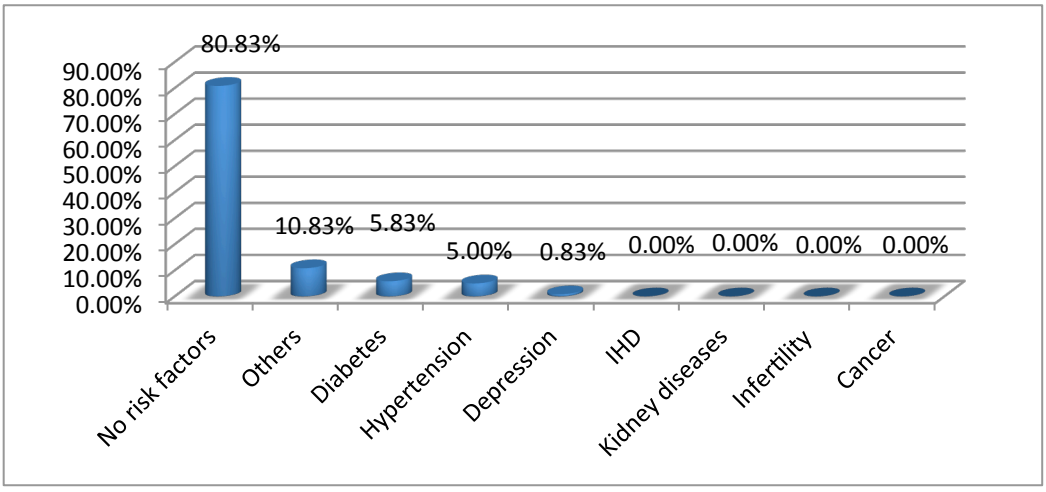


Figure 9: Risk factors among study population

Drug(s) treatment consumed by study population

Regarding number of drugs taken by study subjects, 67.50% were taking no drugs, 18.33% were taking 1 drug, 10.83% were taking 2 drugs, and 3.33% were taken 3 drugs (Fig.10)

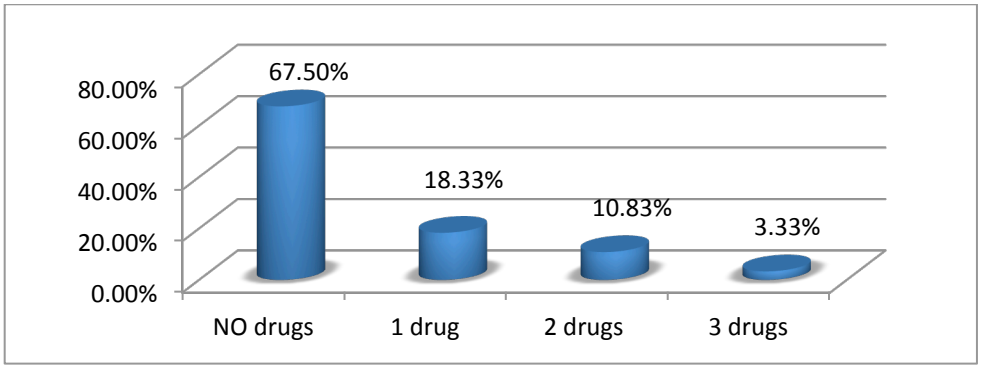


Figure 10: Number of drugs consumed by study population

Regarding types of treatment, 28.33% were taking vitamin D, 18.30% were taking other drugs, 11.67% were taking antidiabetic drugs, 11.67% were taking levothyroxine, 8.33% were taking contraceptives, 6.67% were taking antihypertensive drugs, 6.67% were taking calcium, 6.67% were taking omeprazole, 1.67% were taking drugs for obesity, and interestingly none of the study subjects was taking any drugs or alternative medicines (Fig.11).

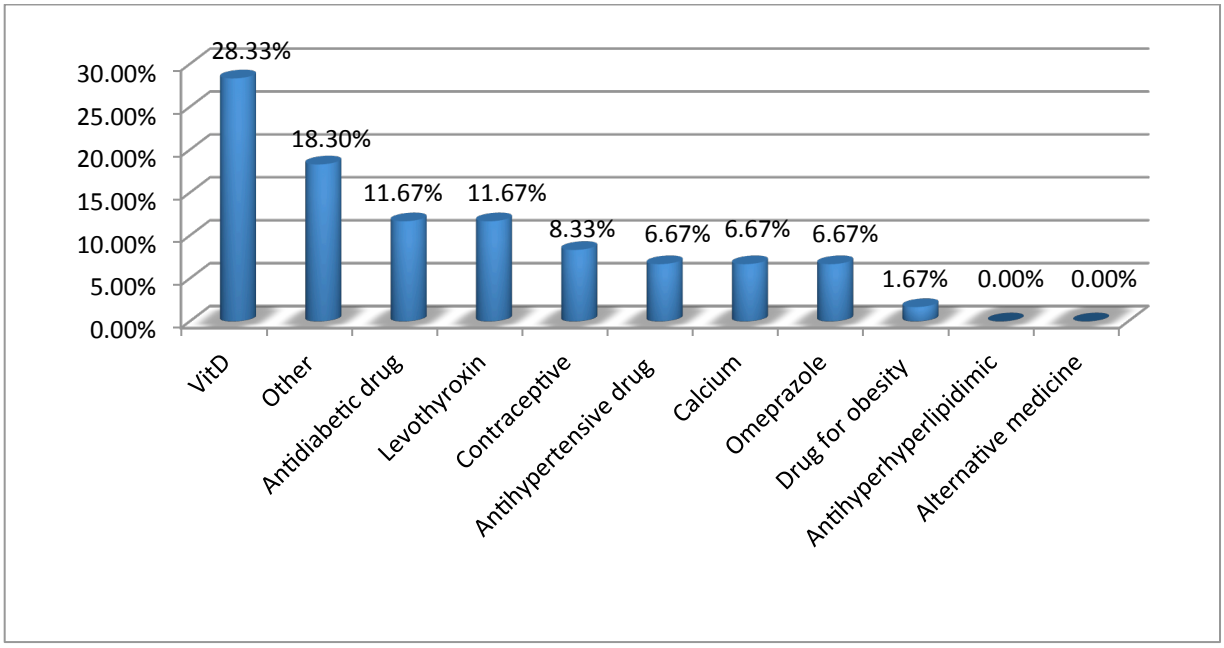


Figure 11: Most commonly used drugs by study population

Clinical investigations data

Clinical investigations data collected included vitamin D, calcium, lipid profile (Cholesterol, Triglycerides, HDL, LDL, VLDL) fasting blood glucose, HbA1c, complete blood count (CBC), creatinine, Na^+, K^+, urea and TSH levels measurement. Mean vitamin D level in obese and overweight adults was 9.91 ± 0.63 (103), in healthy weight adults was 11.11 ± 1.72 (4) and in children was 9.98 ± 1.63 (9) (Table 2). Mean ± SEM level of all other clinical investigations results are listed in (Table 2).

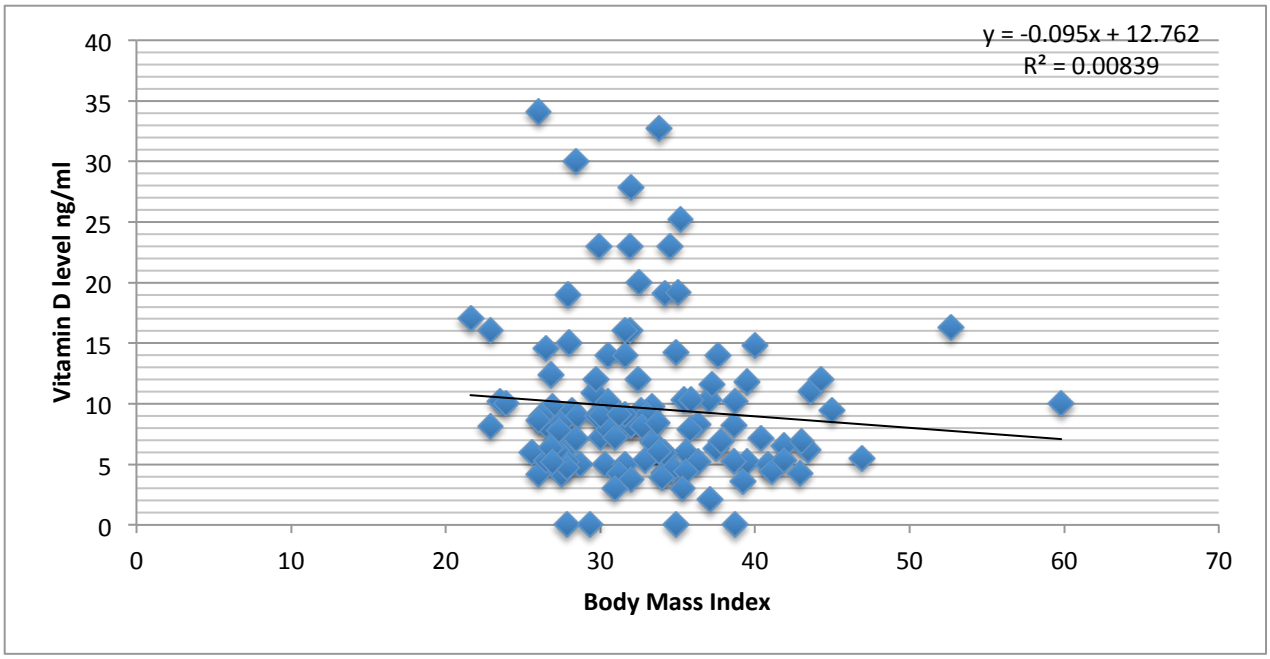
Table 2: Clinical investigations data of study sample

	Mean ± SEM(n) Obese and over weight adults	Mean ± SEM(n) Healthy weight adult	Mean ± SEM(n) Children	Reference value
Vitamin D (ng/ml) Calcidiol	9.91±0.63(103)	11.11±1.72(4)	9.98±1.63(9)	30-80 ng/ml
Calcium (mg/L)	9±0.08(62)	6.58±2.19(3)	7.29±1.39(7)	8.1 – 11.0 mg/L
Cholesterol (mg/dl)	176.96±4.56(98)	169.75±15.67(4)	118±24.08(7)	50 – 200 mg/dl
Triglycerides (mg/dl)	120.65±6.06(96)	93.75±17.96(4)	93.78±22.48(7)	50 – 200 mg/dl
HDL (mg/dl)	50.45±1.35(87)	36.75±12.79(3)	32.65±7.32(7)	40 – 110 mg/dl
LDL (mg/dl)	107.27±4.17(87)	75±28.29(3)	75.36±16.97(7)	55 – 130 mg/dl
VLDL (mg/dl)	24.50±1.44(70)	16.55±6.38(3)	18.51±4.50(7)	10 – 40 mg/dl
Fasting blood glucose (mg/dl)	97.27±3.19(82)	65.25±22.48(3)	80.33±15.54(7)	70 – 115 mg /dl
HbA1c(%)	0.06±0.0038(24)	_____	_____	4.5 – 6 %
RBC (Millions/ul)	4.54±0.05(100)	4.12±0.07(4)	3.69±0.703(7)	3.80 -5.80 Millions/ul
WBC (10^3/ul)	7.15±0.17(98)	6.53±2.46(3)	6.12±1.24(7)	4-11 10^3/ul
Creatinine (mg/dl)	0.61±0.05(16)	_____		0.5 – 1.3 mg/dl
NA^+ (mmol/L)	138.84±2.09(11)	_____	2- 141	135 – 145 mmol/L
K^+ (mmol/L)	4.20±0.13(9)	_____	2- 4.1	3.5 – 5.3 mmol/L
Urea (mg/dl)	24.56±2.42(16)	_____		10 – 50 mg/dl
TSH (ulU/ml)	2.02±0.41(9)	_____	4- 5.635	0.27 – 4.2 ulU/ml

HDL; High-density lipoprotein, LDL; Low-density lipoprotein, VLDL Very-low-density lipoprotein, HbA1c; Glycohemoglobin, RBC; Red blood cell, WBC; White blood cell, TSH; thyroid - stimulating hormone.

Distribution of obese and non-obese subjects across the vitamin D range

Most of study subjects experienced a deficiency in vitamin D with level < 20ng/ml. Much less subjects experienced insufficiency in vitamin D with level 21-29ng/ml. Very few subjects experienced a sufficient vitamin D level with concentration > 30ng/ml (Fig. 12).



Groups	BMI (Kg/m^2)	Vitamin D [Mean ± SEM(n)]
Children		9.98 ± 1.63(9)
Healthy adults	(18.5-24.9)	11.11 ± 1.72(4)
Overweight adults	(25-29.9)	9.92 ± 1.37(29)
Obese adults	(≥30)	9.38 ± 0.70(74)

Figure 12: Distribution of study population across the vitamin D range

Chapter IV
Discussion and conclusion

Discussion

This study was conducted in the eastern region of Libya during the period 7th –16th September 2015. Most of this study sample that has been presenting in nutritional clinics was females, which could be because females are more interested in controlling their weight, more aggressively than male. [83,84] Although current study revealed that zero% of the study sample are smokers, but this does not mean that it reflects the truth Libya is a conservative society which does not accept smoking habit among females who in turn will never admit that they are smokers. Also, more than 80% of obese cases in current study did not expose any of the common risk factors and this may be because the average age of sample was around thirties.

Most (67%) of the study sample was with family history of obesity and most of the family history of this study sample was from either mother or father side. This is in agreement with previous research results in other countries. The risk of obesity is determined by not only specific genotypes but also gene-gene interactions. However, there are still challenges associated with detecting gene-gene interactions for obesity. [85] Like many other medical conditions, obesity is the result of interplay between genetic and environmental factors. [86]

Sample study was classified into four groups (children, healthy adults, over weight adults and obese adults) based on BMI and according to the WHO criteria. We could not keep balanced number of the 4 groups as not all clinics inside Benghazi due to current security situation in the city. The number of healthy individuals and children in this study was small compared to the other 2 groups and we could not hire healthy individuals from outside the clinics because it is difficult to convince them to do clinical investigation tests including measurement of vitamin D level just for doing research, especially that the vitamin D level measurement is expensive.

Most obese patients of this study sample were taking vitamin D noting that most of other clinical investigation tests reported were within the normal range compared to reference values. The four study groups had a severe lack of vitamin D. Exact reason is not known. It may be due to environmental factors, inadequate exposure to sunlight, menopause in women, age that reduces the base material consisting of vitamin D in the skin, mal-absorption of vitamin D in the small intestine because of the presence of disease in the intestine, weight gain leading to collection of vitamin D in fat, as well as malnutrition, liver disease and kidney disease, patients taking epilepsy drugs or even some genetic diseases in children.

The WHO has projected that there should be approximately 2.3 billions over weight adults worldwide and that obesity should affect among more than 700 million in 2015. [87] Taking into account the association between vitamin D deficiency and obesity, these two morbid events may constitute important current health issues during this period.

Different theories can be proposed to explain the relationship between obesity and vitamin D deficiency. First because of issues of low social acceptance, it is suggested that obese individuals reduce their exposure to sunlight, perform fewer outdoor activities and/or use clothes that cover more of the body, which limits exposure to the sun and, consequently, cutaneous vitamin D synthesis. However, in a study based on the Framingham cohort, which evaluated the association between obesity and vitamin D, it was reported that after adjustments for practicing outdoor physical activities, this theory was insufficient to explain the relationship between obesity and vitamin D deficiency. [88] Thus different level of sun exposure seems to be an unlikely explanation for the relationship between vitamin D deficiency and adiposity. This may apply as well for Islamic wear by majority of Libyan females

On the other hand, some experimental data have suggested that vitamin D deficiency can favour greater adiposity by promoting increased parathyroid hormone levels and greater inflow of calcium into adipocytes, thereby increasing lipogenesis. [89] Accumulated evidence suggests that 1.25(OH)D inhibits adipogenesis through action modulated by vitamin D dependent receptors. Thus depletion of vitamin D can lead to excessive differentiation of pre-adipocytes to adipocytes. [90]

Results from current study emphasize the prevalence of vitamin D deficiency in obese and overweight, however, the impact of several confounding factors, such as diet intake, physical activity, educational level, season of the year and presence of secondary hyper-parathyroidism, should be recognized as to the decrease in vitamin D level.

Conclusion

Vitamin D deficiency in common among Libyans living in the Eastern region regardless their BMI. This study should be extended to measure vitamin D level among different ages and in all main cities within the country.

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