

Review Article

Vitamin D deficiency in Bangladesh: A review of prevalence, causes and recommendations for mitigation

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Vitamin D is essential for the maintenance of calcium homeostasis and bone mineralization. Overt deficiency of vitamin D causes rickets in children and osteomalacia in adults. Vitamin D deficiency is an important public health problem worldwide. This review examines the available published data from all peer-reviewed original research articles of community and hospital-based research carried out on vitamin D status in different population groups in Bangladesh. Baseline data of intervention trials are also included. The available selected articles were in English and retrieved from 2002 to January 2022. The paper concentrates on underlying factors for increased prevalence of vitamin D deficiency in Bangladesh. Studies uniformly report very high prevalences of hypovitaminosis D among different population groups. Age and sex-specific comparisons indicate that prevalence is higher for the elderly and women. Hypovitaminosis D ranged from 21 to 75 % for infants, children, and adolescents, 38 to 100 percent for premenopausal women, 66 to 94.2 % for pregnant women, 6 to 91.3 % for adult men and 82 to 95.8 % for postmenopausal women. Important underlying factors related to this silent epidemic include dark skin colour, homebound and sedentariness, insufficient sunlight exposure, atmospheric pollution, clothing style, obesity, use of sunscreen and no supplementation. A comprehensive strategy to alleviate and control the health consequences of vitamin D deficiency is needed. This would include the creation of public awareness, refrain in sunscreen usage, exposure to sunlight, regular exercise, food fortification, and supplementation with vitamin D (bearing in mind potential differences between them and food-based sources).

Key Words: hypovitaminosis D, Vitamin D deficiency, prevalence, determinants, Bangladesh

INTRODUCTION

Vitamin D deficiency has become epidemic worldwide in all age groups of people irrespective of gender, race, and geographical locations. It has been estimated that about one billion people in the world have either vitamin D deficiency or relative insufficiency.¹

Bangladesh is a small country in South-Asia (total area 147,570 km²), with a population of 163 million, the 8th most densely populated country in the world. It is located within a tropical to sub-tropical climate zone (extends from Latitude 20°43' to 26°36'N and Longitude from 88°3' to 92°40'E) with sufficient ultraviolet radiations (290-315 nm). Therefore, it has always been presumed that Bangladeshi people are vitamin D sufficient. However, a few earlier studies uniformly reported that vitamin D deficiency is a silent epidemic in Bangladesh despite plenty of sunshine.²⁻⁵

In Bangladesh, there was scarcity of literature on vitamin D deficiency in different population groups only two decades ago.² In the last few years vitamin D insufficiency or deficiency has been receiving increasing attention as a potential public health concern and become an important area of research. Vitamin D deficiency is associated with different factors such as age, time length of sun exposure, area of skin exposed, time of the day, latitude, atmospheric pollution, season, clothing, melanin pigmen-

tation, use of sunscreen, use of supplementation, dietary and genetic factors.¹

Vitamin D plays an important role in maintenance of bone mineral homeostasis.^{6,7} Vitamin D deficiency can result in rickets in children, osteomalacia and osteoporosis in adults. Rickets is a major public health problem in Bangladesh. More than 8% of children are clinically affected in some areas of the country.^{8,9} Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro architectural deterioration of bone tissue in which the density of bone is reduced with a consequent increase in bone fragility and susceptibility to fracture risk in later life.⁸ Women are four times more likely than men to develop this disease.^{10,11} Osteoporosis represents a major public health issue as the frequency of osteoporotic fracture is rising dramatically in both high and low-income countries because of increasing trend of life exp-

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ectancy. In Bangladesh, the average life expectancy significantly increased from 46 years in 1974 to 73 years in 2017.¹²⁻¹⁴ Due to very high prevalence of vitamin D deficiency, osteoporosis and fracture might be high in elderly people of Bangladesh, but there are no data available.

Optimal vitamin D status is associated not only in maintaining the bone health and physiological functions but also with many chronic conditions including diabetes, cardiovascular diseases (CVD), high blood pressure, different types of cancers, schizophrenia, multiple sclerosis, dementia, impaired immune function, and infectious diseases including tuberculosis (Figure 1).¹⁵⁻²⁶ Several studies highlighted the association of low prenatal vitamin D status and increased risk of adverse neonatal outcomes such as preterm birth, small for gestational age, low birth weight and length.²⁷⁻³⁵ Vitamin D supplementation during lactation could meet the requirements for infants and protect them from the consequences of vitamin D deficiency.^{36,37} Vitamin D status has relevance to infectious disease susceptibility, possibly including SARS-CoV-2 and COVID 19.³⁸⁻⁴⁰

There is a high prevalence of type 2 diabetes and cardi-

ovascular disease in Bangladesh. One in ten adults in Bangladeshi adults has diabetes with more than 10 million people affected in Bangladesh.⁴¹⁻⁴⁴ The high prevalence of vitamin D deficiency may be a contributory factor to the risk of diabetes in Bangladesh.¹

This non-systematic review includes studies with measured serum 25-hydroxyvitamin D concentrations in a range of different population groups in Bangladesh. It identifies putative underlying risk factors for vitamin D deficiency in the country and opportunities for relevant health and nutrition policy.

VITAMIN D DEFICIENCY

Serum 25-hydroxyvitamin D <50 nmol/L is a commonly used identifier for vitamin D deficiency.^{15,45} Earlier vitamin D deficiency was defined as a blood level of 25-hydroxyvitamin D of <25 nmol/L or 30 nmol/L which was mainly increases the risk for development of osteomalacia and rickets.¹ The optimal level of S-25OHD concentration for skeletal health is still debatable. Several studies reported that S-25OHD concentrations <50 nmol/L are suboptimal for bone health and recommend-

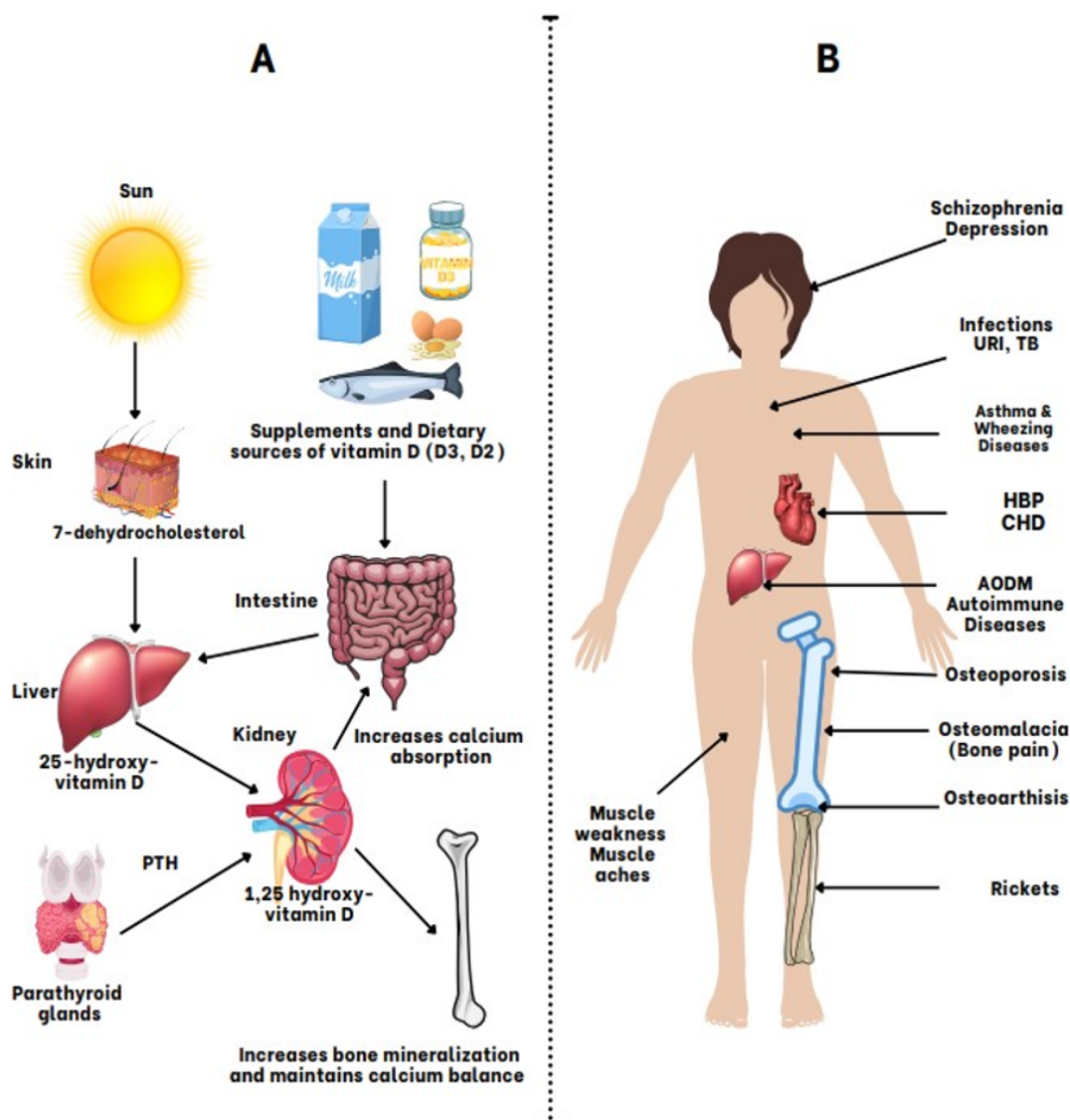


Figure 1. A. Schematic diagram of the synthesis and metabolism of vitamin D for regulating bone mineralization. B. The health consequences of vitamin D deficiency (Adapted from Holick and Chen¹³). URI: Upper respiratory infection; TB: tuberculosis; HBP: high blood pressure; CHD: coronary heart disease; AODM: adult onset diabetes mellitus.

ed 50 to 100 nmol/L as the required S-25OHD level.⁴⁶⁻⁴⁹ According to Hollis, serum vitamin D above 80 nmol/L is required for maintenance of bone health.⁵⁰ Serum 25-hydroxyvitamin D >50 nmol/L was suggested for optimal bone mineral density, bone turnover, muscle strength and S-25OHD >76 nmol/L was recommended for maintaining an adequate immune response.^{51,52}

Some reports suggest a reference range of S-25OHD (135–225 nmol/L) to indicate vitamin D sufficiency in the normal subjects of sunny countries.⁵³ Priemel et al did not observe any evidence of osteomalacia and osteoidosis in German adults with blood level of S-25OHD of at least 75 nmol/L.⁵⁴ The Institute of Medicine (IOM) in 2011 concluded that blood level 25-hydroxyvitamin D >50 nmol/L is adequate to maintain maximum bone health.⁵⁵ Based on the Endocrine Society, vitamin D deficiency was defined as a S-25OHD concentrations <50 nmol/L, insufficiency as 51–74 nmol/L and sufficiency as >75 nmol/L for maximum musculoskeletal health.⁵⁶ They also supported that toxicity is usually absent until S-25OHD concentrations reach at 375 nmol/L. They further reported that blood level of >75 nmol/L was required to reduce the risk of falls in elderly people.^{57,58}

The National Osteoporosis Foundation USA (NOF), International Osteoporosis Foundation (IOF), American Association for Clinical Endocrinologists (AAACE) and American Geriatric Society (AGS) agree with these criteria for vitamin D deficiency, insufficiency, and sufficiency. However, the threshold for S-25OHD which is sufficient for different non-skeletal outcome is higher and still controversial.

The negative relationship between S-25OHD and S-iPTH has more often been used to establish the appropriate S-25OHD level. Substantial studies found that S-25OHD concentrations from about 30 to 125 nmol/L are required to maintain a normal S-iPTH level.^{53,59,60} Some studies observed the relationship between 25-hydroxyvitamin D and serum iPTH concentrations in hospital population and postmenopausal women in USA. The serum iPTH levels continued to decline and plateaued when serum S-25OHD concentrations were at about 75–100 nmol/L.^{61,62} However, the controversy around S-25OHD concentrations, the definitions of vitamin D sufficiency, insufficiency and deficiency are only the matter of approximation. Table 1 shows the different

cut-off values for serum 25-hydroxyvitamin D to identify vitamin D deficiency and sufficiency.

SITUATION ASSESSMENT AND ANALYSIS

Vitamin D deficiency is one of the major public health problems globally in all age groups of the population. Due to lack of diagnosis and treatment, vitamin D deficiency is still epidemic at this time of medical advancement. The prevalence of vitamin D deficiency in different groups of population in Bangladesh was uniformly higher irrespective of age, sex, race, religion, location, and socio-economic status. The data revealed the prevalence of vitamin D deficiency ranged from 27.2 to 100 % in different population groups. Tables 2-6 summarize vitamin D status of different groups of subjects from upper and lower socio-economic groups in both urban and rural settings together with other relevant information.

Infants, children and adolescents

The data on the prevalence of hypovitaminosis D in infants, children and adolescents are summarized in Table 2. The studies indicated predominantly higher prevalence (ranged from 27.2% to 75%) of hypovitaminosis D in this population group. Combs et al. reported that the prevalence of vitamin D deficiency was 27.2% in 1-5 years old children by using a low cut-off value (S-25OHD <37.5 nmol/L).⁵ The corresponding figure was 28.3% in 6-8 months children using even lower cut-off value (S-25OHD <30 nmol/L).⁶³ Ahmed et al. carried out a study among 6 to 24 months old underweight and normal-weight children in urban slum area of the Dhaka city which showed very high prevalence of hypovitaminosis D.⁶⁴ The reported prevalences of vitamin D deficiency and insufficiency; S-25OHD <75 nmol/L) were 76.9% and 85.2% in underweight and normal-weight children, respectively.

Zaman et al. studied the prevalence of hypovitaminosis D in children (from 0 to 16 years of age) living in Dhaka city.⁶⁵ The subjects were divided into four age groups (0-1 year, 2-5 years, 6-11 years and 12-16 years). They indicated very high prevalence hypovitaminosis D and showed an increasing trend of vitamin D deficiency and insufficiency with age. Notably, the prevalence of vitamin D deficiency and insufficiency (S-25OHD <75 nmol/L) were 84.1% and 98.6% in children of 0 to 1 and 12 to 16

Table 1. Different cut-off values for serum 25-hydroxyvitamin D concentrations to identify vitamin D status

References	Cut-off values for S-25OHD	Vitamin D status
Thomas et al. 1998 ⁶¹	>75 nmol/L	Sufficient
Lips 2004 ⁴⁵	<12.5 nmol/L	Severe deficiency
	12.5-25 nmol/L	Moderate deficiency
	25-49 nmol/L	Mild deficiency
	≥50 nmol/L	Sufficient
Hollis 2005 ⁵⁰ ; Grant and Holick 2005 ⁵³	<50 nmol/L	Deficiency
	50-75 nmol/L	Insufficiency
	>75 nmol/L	Sufficient
Holick 2007 ¹	<25 nmol/L	Deficiency
	>375 nmol/L	Toxicity
Holick et al. 2011 ⁵⁷ (Endocrine Society Guideline 2011)	<50 nmol/L	Deficiency
	50-75 nmol/L	Insufficiency
	>75 nmol/L	Sufficient

Table 2. Summary of the prevalence of hypovitaminosis D in Bangladeshi infant, children and adolescents with cut-off values

Reference	Settings	Subjects	Sample size (<i>n</i>)	Cut-off values used	Prevalence of hypovitaminosis D (%)
Combs et al. 2008 ⁵	Chakaria, Cox's Bazar	Children Age: 1-5 years	158	<37.5 nmol/L	27.2
Roth et al. 2010 ⁶⁸	Sylhet district (Rural area)	Infant Age: 1-6 months	29	<40 nmol/L	59
Ahmed et al. 2015 ⁶⁴	Slum area at Mirpur, Dhaka	Children a) Underweight b) Normal weight Age: 6-24 months	468 445	<50 nmol/L	34.6 45.6
ICDDR-B, UNICEF and GAIN 2013 ⁶⁶	The National Micronutrients Status Survey 2011-2012	a) Preschool children b) School children Age: N/A	461 557	<50 nmol/L	39.6 45.5
Zaman et al. 2017 ⁶⁵	Dhaka city	Children 0-1 years 2-5 years 6-11 years 12-16 years	69 76 78 77	<25 nmol/L	31.8 38.2 41 46.8
Tofail et al. 2019 ⁶³	Slum in Dhaka city	Infants Age: 6-8 month	205	<30 nmol/L	28.3
Ahmed et al. 2019 ⁶⁷	Dhaka city and Gazipur district	Primary school children a) Girl b) Boy Age: 5-14 years	137 137	<50 nmol/L	26.3 32.1
Saha et al. 2020 ⁶⁹	Multicentre study	Children Age: 1-10 years	150	<75 nmol/L	75

years of age groups, respectively.⁶⁵

The National Micronutrients Survey (NMS 2011–2012) showed the highest prevalence of vitamin D deficiency (S-25OHD <50 nmol/L) in the poorest and severely food-insecure preschool-age children. Similar situation of vitamin D deficiency was observed in school-age children of the richest and food-secure households. The overall prevalences of vitamin D deficiency were 39.6% and 45.5% for preschool-age and school-age children, respectively. Children living in the slums were found to be the most vulnerable to vitamin D deficiency.⁶⁶

Ahmed et al. found a somehow similar rate of vitamin D deficiency in school children of both urban and rural locations.⁶⁷ Roth et al used a low cut-off value (S-25OHD <40 nmol/L) and showed a remarkably high incidence of vitamin D deficiency (59%) in 1-6 months old children.⁶⁸ Saha et al reported the highest incidence (75%) of suboptimal vitamin D status (S-25OHD <75 nmol/L) in 1-10 years old children.⁶⁹

Adult women

Most literature on vitamin D deficiency is available in this group. Data on the prevalence of hypovitaminosis D in adult women are summarized in Table 3. They indicate that adult women of childbearing age are the most vulnerable to vitamin D deficiency. The studies indicated predominantly higher prevalence (ranged from 38% to 100%) of hypovitaminosis D in this population group. Islam et al. showed that the prevalence of vitamin D deficiency was 38% in 18-40 years old low-income rural women by using a low cut-off value (S-25OHD <37.5 nmol/L).² The corresponding figure was 50 % in high income urban women of the same age and cut-off value.

Islam et al. found that the prevalence of vitamin D deficiency among apparently healthy female young students of the Dhaka University was surprisingly high (77.9%) using the cut-off value of S-25OHD <40 nmol/L.³ Mahmood et al showed that the incidence of sub-optimal vitamin D status (S-25OHD <75 nmol/L) in adult female garment factory workers was at the highest level (100 %).⁷⁰ Islam et al also noticed a high prevalence (70.5%) of vitamin D deficiency (S-25OHD <50 nmol/L) in premenopausal garment factory workers at Mirpur, Dhaka.⁴ According to the NMS 2011-2012 survey, 71.5% of non-pregnant non-lactating women were found to be <vitamin D deficient (S-25OHD <50 nmol/L).⁶⁶ A high prevalence of vitamin D deficiency (S-25OHD <75 nmol/L) was observed among female physicians (64.2%) working in different health centres in Bangladesh and among reproductive aged rural women (81%) in Pubna District in Northern Bangladesh.^{71,72}

Shefin et al showed a high prevalence (71.5) vitamin D deficiency (S-25OHD <50 nmol/L) in adult female wearing the Hijab.⁷³ Mahmood et al found that female outdoor workers not wearing the Hijab were equally vulnerable to suboptimal vitamin D status (S-25OHD <75 nmol/L in 80% of subjects).⁷⁰ Fatema et al showed very high prevalence (71%) of hypovitaminosis D in a hospital-based study among premenopausal women with bone pain.⁷⁴ Jeong et al reported surprisingly higher prevalence (74%) of severe vitamin D deficiency (S-25OHD <30 nmol/L) among reproductive aged women living in Dhaka.⁷⁵ Of

note, the highest prevalence (97%) of suboptimal vitamin D status was shown by Ali et al among reproductive aged women living in Dhaka city.⁷⁶ Few other studies among women of different occupations with a wide age range (10-89 years old) also reported similarly high prevalences (of vitamin D deficiency and insufficiency) varied from 69.6% to 97.8%.^{73,77-80}

In summary, the situation for vitamin D deficiency among non-pregnant non-lactating women has deteriorated. Focused studies are needed to develop action plans.

Pregnant women

Table 4 summarizes the main findings for hypovitaminosis D in pregnant women. Ullah et al showed very high prevalences of suboptimal vitamin D status among normal pregnant women and women with eclampsia or pre-eclampsia.⁸¹ The prevalence rate was 66%, 86.1% and 87.9% for normal pregnant women, women with eclampsia and pre-eclampsia, respectively. Asaduzzaman et al carried out a retrospective study at Crescent Hospital, Dhaka (based on hospital records of 140 healthy pregnant women at different trimesters of pregnancy), showed a remarkably high prevalence (94.2%) of suboptimal vitamin D status. Furthermore, 62.8% of the subjects were found to be vitamin deficient (S-25OHD <50 nmol/L).⁸² Bhowmik et al studied 498 pregnant women (at 6-14 weeks of pregnancy) from Dhaka city showed a prevalence of 46.4% for severe vitamin D deficiency (S-25OHD <30 nmol/L).⁸³ The prevalence of severe vitamin D deficiency was found to be much higher (48.7%) in underweight (BMI <18.5 kg/m²) participants.

Subramanian et al showed the highest prevalence (63.6%) of severe vitamin D deficiency among 1257 subjects in Dhaka city in late pregnancy.⁸⁴ Ahmed et al reported a high prevalence (64.6%) of vitamin D deficiency (S-25OHD <50 nmol/L) among rural pregnant women in four Upazillas of Bangladesh.⁸⁵

Adult men

Table 5 summarizes the data on the prevalence of hypovitaminosis D in adult men in Bangladesh. Islam et al. showed a high prevalence (89.8%) of vitamin D deficiency among physicians working in Specialized Hospitals.⁸⁶ In a retrospective, laboratory-based, observational study (carried out from January 2015 to May 2017) at the Department of Pathology of a diagnostic centre of Dhaka City showed that the prevalences of vitamin D deficiency and insufficiency in men were 57.2% and 24.9%, respectively.⁸⁷ Chowdhury et al reported a high prevalence of hypovitaminosis D (82.8%) in men over a wide age range.⁷⁸ A cross-sectional multicentre study also reported higher prevalence vitamin D deficiency (66.5% had S-25 OHD <50 nmol/L) among male physicians working in different hospitals in Bangladesh.⁷¹

Jeong et al. observed a lower prevalence (only 6% had S-25 OHD <30 nmol/L) of severe vitamin D deficiency in young adult male outdoor workers.⁷⁵ The corresponding figure for the prevalence of vitamin D deficiency was similar (18.6% had S-25 OHD <50 nmol/L) among subjects of similar occupation (Fisherman).⁸⁸ Studies among adult males of different occupations over a wide age range (10-70 years old) also report similarly high preva-

Table 3. Summary of the prevalence of hypovitaminosis D in Bangladeshi adult women with cut-off values

Reference	Settings	Subjects	Sample size (n)	Cut-off values used	Prevalence of hypovitaminosis D (%)
Islam et al. 2002 ²	Dhaka city (Khilgaon and Nakhhalpara area) and Betagair, Nandail, Mymensingh	a) High income urban women	90	≤37.5 nmol/L	50
		b) Low-income rural women Age:18-40 years	99		38
Islam et al. 2006 ³	Dhaka city INFS, Dhaka University	Healthy young women Age: Mean age (22.3±1.9) years	36	<40 nmol/L	77.9
Islam et al. 2008 ⁴	Dhaka city (Standard Garments, Mirpur)	Female garment workers Age:18-40 years	200	<50 nmol/L	70.5
Micka 2009 ⁷²	Pubna District	Women Age:18-33 years	147	<75 nmol/L	81
ICDDR-B, UNICEF and GAIN 2013 ⁶⁶	The National Micronutrients Status Survey 2011-2012	NPNL women Age: N/A	613	<50 nmol/L	71.5
Mahmood et al. 2017 ⁷⁰	Damari Upazila Dhaka	a) Female garment workers	40	<75 nmol/L	100
		b) Female outdoor workers Age: mean age (27.8±5.1) years	40		80
Shefin et al. 2018 ⁷³	An urban endocrine clinic	Adult female using Hijab Age: ≥18 years	353	<50 nmol/L	71.7
Fatema et al. 2018 ⁷⁴	Apollo Hospital, Dhaka	NPNL women Age: NPNL 15-45 years	486	<75 nmol/L	71
Chowdhury et al. 2018 ⁷⁸	Clinic in Dhaka city	Adult female Age: 18-89 years	160	<75 nmol/L	88.8
Rahman et al. 2019 ⁷⁷	NICVD Dhaka	Adult female Age 29 -70 years	22	<75 nmol/L	91
Jeong et al. 2019 ⁷⁵	Maternal and Child Health Training Institute, Dhaka	Adult female Age: 19-34 years	84	<30 nmol/L	74
Acherjya et al. 2019 ⁷⁹	Jashore district	Adult female Age: 10-70 years	91	<75 nmol/L	97.8
Khan et al. 2019 ⁸⁰	Mymensingh Medical College Hospital	Female physician Age: >23 years	23	<75 nmol/L	69.6
Ali et al. 2020 ⁷⁶	BSMMU, Dhaka	Adult Female Age: 21-39 years	73	<75 nmol/L	97
Islam et al. 2021 ⁷¹	Different Hospitals in Bangladesh	Female Physicians Age: N/A	318	<50 nmol/L	64.2

Table 4. Summary of the prevalence of hypovitaminosis D in Bangladeshi pregnant women with cut-off values

Reference	Settings	Subjects	Sample size (<i>n</i>)	Cut-off values	Prevalence of hypovitaminosis D (%)
Ullah et al. 2013 ⁸¹	Dhaka Medical College Hospital, Dhaka	a) Normal pregnant women	76	<75 nmoL/L	66
		b) Women with Eclampsia	79		86.1
		c) Women with pre-eclampsia	33		87.9
		Age: N/A			
Asaduzzaman et al. 2018 ⁸²	Crescent Hospital, Uttara, Dhaka	Healthy women of different trimesters of pregnancy	140	<50 nmoL/L	62.8
		Age: 18-43 years		≥50-<75 nmoL/L	31.4
Bhowmik et al. 2019 ⁶⁹	Dhaka City	Pregnant women	498	<30 nmoL/L	46.4
		Age: mean age±SD (20±2.6) years			
Ahmed et al. 2021 ⁸⁵	Four Upazilas in three regions of Bangladesh	Pregnant women	515	<30 nmoL/L	17.3
		Age: mean age±SD (23.6±4.8)		≥ 30-<50 nmoL/L	47.2
Subramanian et al. 2021 ⁸⁴	Dhaka City	Pregnant women	1257	<30 nmoL/L	63.6
		Age: mean age±SD (23.2±4.2)			

Table 5. Summary of the prevalence of hypovitaminosis D in Bangladeshi adult men with cut- off values

Reference	Settings	Subjects	Sample size (<i>n</i>)	Cut-off values	Prevalence of hypovitaminosis D (%)
Islam et al. 2016 ⁸⁶	Specialized Hospitals Bangladesh	Physicians	157	<50 nmoL/L	89.8
		Age: N/A			
Chowdhury et al. 2018 ⁷⁸	Clinic in Dhaka city	Adult male	29	<75 nmoL/L	82.8
		Age: 18-89 years			
Islam et al. 2019 ⁸⁷	A diagnostic centre of Dhaka city	Adult male	269	<50 nmoL/L	57.2
		Age: 62% of subjects within 21-60 years of age		≥50-<75 nmoL/L	24.9
Jeong et al. 2019 ⁷⁵	Maternal and Child Health Training Institute, Dhaka	Young adult male outdoor workers	84	<30 nmoL/L	6
		Age: 19-34 years			
Haque et al. 2019 ⁸⁸	Cox's Bazar (Coastal region)	Fishermen	140	<50 nmoL/L	18.6
		Age: mean±SD (38.1±11.6)		≥50-<75 nmoL/L	52.1
Acherjya et al. 2019 ⁷⁹	Jashore district	Adult male	69	<75 nmoL/L	91.3
		Age: 10-70 years			
Khan et al. 2019 ⁸⁰	Mymensingh Medical College Hospital, Mymensingh	Male physician	79	<75 nmoL/L	65.8
		Age: 23-60 years			
Islam et al. 2021 ⁷¹	Different Hospitals in Bangladesh	Male physicians	794	<50 nmoL/L	66.5
		Age: N/A			

lence of vitamin D deficiency and insufficiency, from 65.8 % to 90.6%.^{3,78,80}

Elderly women and those with different health problems

Very limited data are available on vitamin D status of postmenopausal women in Bangladesh.

Table 6 summarizes the prevalence of hypovitaminosis D in elderly women and in subjects with different health complications based on common cut-offs. Islam et al showed a remarkably high prevalence (83%) vitamin D deficiency (S-25OHD <50 nmol/L) in urban veiled postmenopausal women.³ Among elderly diabetic women, the prevalence rate was 74.5%. Ahmed et al. carried a study in apparently healthy postmenopausal women with a history of complete cessation of menstruation over a period of at least one year.⁸⁹ The observed prevalences of vitamin D deficiency, insufficiency and sufficiency were 47.4%, 34.6% and 18%, respectively.

A retrospective study among 527 women of 46-70 years old reported surprisingly high prevalence (75%) of hypovitaminosis D.⁷⁴ High prevalences of vitamin D deficiency and insufficiency have been observed among those with various health conditions (such as, diabetes, cardiovascular disease, bone and muscle pain, body aches and pain, and obesity), varying from 39.2% to 95.8%.^{3,77,90-94}

DETERMINANTS OF VITAMIN D DEFICIENCY

Our literature review reveals age and gender to be associated with serum vitamin D with women and the elderly the most vulnerable to vitamin D deficiency. For Bangladesh,^{2-4,65,67,68,70,71,74,80,86,87,89,93-95} there are several possible determinants of vitamin D deficiency. These are as follows:

- 1) Unawareness due to lack of nutritional knowledge
- 2) Traditional and deliberate avoidance of sunlight exposure
- 3) Being homebound
- 4) Covered-up and cultural dress practices (wearing hijab),
- 5) Excessive use of sunscreen
- 6) Inefficient cutaneous production of vitamin D with brown/darker skin
- 7) Inadequate dietary intake of vitamin D
- 8) Increased air pollution,
- 9) Unavailability of D-fortified food items,
- 10) No vitamin D supplementation
- 11) Decreased bioavailability due obesity and malabsorption
- 12) Other health problems (such as gastrointestinal disorders, renal, and liver disease)

DISCUSSION

The definition of vitamin D deficiency is controversial. In fact, there is no universally accepted optimal range for S-25OHD concentration available to define vitamin D deficiency or insufficiency. Furthermore, the demarcation between vitamin D sufficiency and insufficiency is not clearly defined. Yet again, laboratory assessment of serum 25-hydroxyvitamin D is not comprehensively standardised or harmonized. Different approaches to risk assessment and cut-off points for vitamin D deficiency are in evidence, particularly with reference to collateral

measurements and indicators. For fracture risk, other skeletal and different non-skeletal considerations, including iPTH together with S-25OHD concentrations are used to identify vitamin D deficiency or insufficiency.⁵

The Endocrine Society Guideline is perhaps the most used criteria to identify vitamin D status in a population.⁵⁷ If used, virtually all findings reported would be worse.

Vitamin D deficiency is a silent epidemic, an often undiagnosed and untreated nutritional deficiency in Bangladesh. It has been presumed not to be a problem in this region since there is plentiful sunshine all year round in Bangladesh. It now receives growing attention as a public health concern. The available literature about vitamin D status in Bangladesh illustrates the magnitude and trend in vitamin D deficiency. It also identifies determinants of hypovitaminosis D. Hypovitaminosis D has become a public health threat in Bangladesh. Vitamin D deficiency or low vitamin D status is associated with gender, age, personal behaviours, and the food and health systems, notably indoor living, limited physical activity and sunlight avoidance, with consequential obesity. Those most likely to be affected are the overweight and obese, women in the reproductive age group, who are pregnant, postmenopausal or elderly, but also men in general.^{1-3,71,74,89,90,96,97} The decreased ability of pigmented and aged skin to produce vitamin D is complicated by physiological well as behavioural difference. Increased degrees of body fatness, evident with overweight and obesity add complexity to the vitamin D problem. Due to its fat solubility, vitamin D is sequestered in body fat with reduced concentrations in the peripheral circulation. Thus, there is an apparent increase in vitamin D requirements of the order of 2 to 5-fold when body mass index (BMI) is greater than 30 kg/m².^{16,96,97}

Age influences the production of vitamin D in skin. An elderly person, >70 year, requires three times the duration of sun exposure of a child to produce the same amount of vitamin D in skin.¹ Even so, a cross-sectional multicentre study of physicians showed that those aged <35 years were also vulnerable to vitamin D deficiency (70.6%).⁷¹ Lack of sunlight exposure with extended indoor occupations and poor dietary biodiversity can be a major risk factor for deficiency.^{98,99}

Traditional avoidance of sunlight exposure, common use of sunscreen and covered-up dress style of women make them vulnerable to low vitamin D status or suffer from insufficient vitamin D concentration as a whole.¹ Our earlier study among premenopausal garment workers in Dhaka city indicated that nearly 90 % of participants used sunscreen (generally called skin lightening cream) on their face and hands, areas usually exposed to sunlight.⁴ Melanin pigment is a natural sun block. Therefore, individuals with darker skin requires 3 to 5 times longer contact with sunlight than a person with lighter skin.¹⁰⁰ There is a higher prevalence of vitamin D deficiency among dark skinned African Americans than among white Americans.¹⁰¹ However, in Bangladesh, dark or brown skin type might not in itself be associated with lower vitamin D status.^{102,103}

Haque et al reported that outdoor workers who spent much of their time in the sunshine had a lower prevalence

Table 6. Prevalences of hypovitaminosis D in Bangladeshi elderly women and in people with health disorders by cut-off values

Reference	Settings	Subjects	Sample size (<i>n</i>)	Cut-off values	Prevalence of hypovitaminosis D (%)
Islam et al. 2006 ³	Dhaka city Nakhalpara, Tejgaon	Veiled women Age: mean age (47.7±9.4) years	30	<40 nmol/L	83
Islam et al. 2006 ³	Dhaka city BIRDEM	Diabetic women Age: mean age (50.2±5.9) years	55	<40 nmol/L	74.5
Ahmed et al. 2018 ⁸⁹	Hospital in Dhaka city	Post-menopausal women Age: ≥45 years	133	<75 nmol/L	82
Fatema et al. 2018 ⁷⁴	Apollo Hospital, Dhaka	Post-menopausal women Age: 46-70 years	527	<50 nmol/L ≥50-<75 nmol/L	20 75
Hossain et al. 2018 ⁹⁰	Popular Medical College Hospital, Dhaka	Patients with muscle pain Age: ≥18 years	212	<50 nmol/L	95.8
Alam et al. 2018 ⁹¹	Comilla Diabetic Hospital, Comilla	Newly diagnosed diabetic patient Age: N/A	50	<75 nmol/L	66
Rahman et al. 2019 ⁷⁷	NICVD Dhaka	Adult male heart patients Age 29 -70 years	80	<75 nmol/L	68.8
Islam et al. 2019 ⁸⁷	A diagnostic centre in Dhaka city	Adult female Age: 62% of subjects within 21-60 years of age	524	<50 nmol/L	68.4
Eva et al. 2019 ⁹²	Diagnostic centres in Dhaka city	Patients with body aches and pain Age: 18 years and above	1523	<75 nmol/L	85.1
Paul et al. 2020 ⁹³	Specialized Endocrine center, Bangladesh	Obese male and female Age: Mean age (45.8±11.4) years	500	<50 nmol/L	39.2
Selim and Lona 2020 ⁹⁴	Eight diabetic care centres of Bangladesh	Male diabetic (type 2) patients Age: 30-69 years	2860	<75 nmol/L	80.9
Islam et al. 2021 ⁷¹	Different Hospitals in Bangladesh	Male physicians Age: 46-59 years	374	<50 nmol/L	62.6

of vitamin D deficiency.⁸⁸ Islam et al showed higher concentrations of vitamin D in rural women who had a greater exposure to sunlight because of their livelihood rather than that of their urban counterparts.² Together, these studies suggest a relatively large impact of sunlight on vitamin D sufficiency. Due to a feedback mechanism, sunlight exposure does not lead to vitamin D toxicity, but maintains normal reference range of S-25OHD concentrations.³⁷

Symptomatic vitamin D deficiency in population subgroups is evidenced by the prevalence of rickets and osteomalacia in Bangladesh.^{8,79,81}

Vitamin D data in Bangladesh have often been obtained by locality and are not representative for all regions. The majority of studies are based on Dhaka city and areas close to it. Cut-off values are not universal, and the magnitudes of hypovitaminosis D are different. Prevalence was lower when a low cut-off value was used. Different methods of analysis, inconsistent reporting of vitamin D supplementation and limited information about seasonal variation made the reporting, reliance and interpretation of findings complicated. Therefore, uncertainty often remains as to the actual or real prevalence of vitamin D deficiency in any population group. But the overall picture is one of a serious public health nutritional policy challenge.

RECOMMENDATIONS

The following measures could be recommended to mitigate the widespread problem of hypovitaminosis D in vulnerable Bangladeshi populations:

- 1) Public awareness: Raising extensive awareness about health benefit of vitamin D, the health consequences of vitamin D deficiency, importance of sunshine exposure in controlling vitamin D deficiency and existing widespread prevalence of hypovitaminosis D in Bangladesh. The information could be disseminated through mass communication by using multiple mediums like internet communications, radio, television, social networking (Facebook, YouTube), billboards, newspapers, magazines, short film and literature in educational system. Healthcare providers of the government of Bangladesh might play an important role to implement this programme.
- 2) Sunlight exposure: Regular contact with outdoor sunshine for 10–15 min with exposed arm, feet, and face (at least 2 to 3 times per week). Duration of sunshine contact must be increased by 2–3 times (30–45 min) for veiled woman with brown/dark skin compared to those unveiled or having lighter skin.
- 3) Food biodiversification, especially with fish and sundried mushrooms.
- 4) Food fortification with vitamin D, as an efficacious method of correcting vitamin D deficiency. Widely consumed round the year, financially affordable and available foods are commonly used as fortification vehicle. The food items include oil, margarine, milk, cheese, and other dairy products (both regular-fat and low-fat), infant formulas, bread, flour (rice, wheat) and orange juice could be selected as food carriers for vitamin D fortification.

- 5) Providing supplementation: Free distribution of supplements (vitamin d, calcium and multiple micronutrients) to the vulnerable groups of population (children, women and elderly) through the Community Clinics in Bangladesh.
- 6) Strengthening nutrition education: Nutrition education is an important factor for all strategies to eliminate vitamin D deficiency. Active measures need to be taken for strengthening nutrition education programme through schools and health centres to improve knowledge on sources of vitamin D, as well as health consequences of vitamin D deficiency.
- 7) Rapid detection of vulnerable people: Development of simple questionnaire to use in community health centres by nurse or physicians to assess vitamin D status of the people and to take accurate measures on time.
- 8) Speedy diagnostic procedure: Easy and affordable laboratory measurement facilities must be provided to the people in the local health centres to confirm vitamin D deficiency.
- 9) Further research must be funded by the government to monitor the impact of all the actions of elimination of vitamin D deficiency.

CONCLUSIONS

This review draws attention to the magnitude and extent of vitamin D deficiency and insufficiency in Bangladesh among several population groups. Biochemical evidence supports the likelihood that belief systems, prevailing personal behaviors, and livelihoods conducive sunlight avoidance, dietary restriction and limited physical activity are translated into this micronutrient inadequacy. But they also point to the prevalence of these determinants as health risk factors, by way of sedentariness, limited dietary biodiversity, dress preference and sunlight restriction. Public health initiatives to address this problem are challenged to reach different subgroups and localities, including tribal people living in hilly areas.

Nevertheless, Bangladesh is a somewhat homogenous society, and a comprehensive programme is recommendable to deal with the silent epidemic. For example, strategies might include improved and regular judicious exposure to sunshine for at least 10 to 15 minutes per day, refraining from use of sunscreen and improved dietary biodiversity with locally available fish or fungal foods like mushrooms, dried in the sun; and reduced sodium intake on account of its adverse effect on calcium balance. The value of fortification and vitamin D supplementation in disease prevention is controversial, although commercially more and more available.^{16,104,105}

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REFERENCES

- Holick MF. Vitamin D deficiency. *N Engl J Med.* 2007;357:266-81.
- Islam MZ, Lamberg-Allardt C, Karkkainen M, Outila T, Salamattullah Q, Shamim AA. Vitamin D deficiency: a concern in premenopausal Bangladeshi women of two socio-economic groups in Bangladesh. *Eur J Clin Nutr.* 2002;56:51-6.
- Islam MZ, Akhtaruzzaman M, Lamberg-Allardt C. Hypovitaminosis D is common in both veiled and nonveiled Bangladeshi women. *Asia Pac J Clin Nutr.* 2006;15:81-7.
- Islam MZ, Shamim AA, Kemi V, Nevanlinna A, Akhtaruzzaman M, Laaksonen M, Jehan AH, Jahan K, Khan HU, Lamberg-Allardt C. Vitamin D deficiency and low bone status in adult female garment factory workers in Bangladesh. *Br J Nutr.* 2008;104:241-7.
- Combs GF, Jr, Hassan N, Dellagana N, Staab D, Fischer P, Hunt C, Watts F. Apparent efficacy of food-based calcium supplementation in preventing rickets in Bangladesh. *Biol Trace Elem Res.* 2008;121:193-204.
- Christakos S. Recent advances in our understanding of 1,25-dihydroxyvitamin D(3) regulation of intestinal calcium absorption. *Arch Biochem Biophys.* 2012;523:73-6.
- Veldurthy V, Wei R, Oz L, Dhawan P, Jeon YH, Christakos S. Vitamin D, calcium homeostasis and aging. *Bone Res.* 2016;4:16041. doi: 10.1038/boneres.2016.41.
- Craviari T, Pettifor JM, Thacher TD, Meisner C, Arnaud J, Fischer PR. Rickets: an overview and future directions, with special reference to Bangladesh. A summary of the Rickets Convergence Group meeting, Dhaka, 26-27 January 2006. *J Health Popul Nutr.* 2008;26:112-21.
- Ahmed S, Goldberg GR, Raqib R, Roy Sk, Haque S, Braithwaite VS, Pettifor JM, Prentice A. Aetiology of nutritional rickets in rural Bangladeshi children. *Bone.* 2020;136:115357. doi: 10.1016/j.bone.2020.115357.
- Kanis JA, Melton 3rd LJ, Christiansen C, Johnston CC, Khaltsev N. The diagnosis of osteoporosis. *J Bone Miner Res.* 1994;9:1137-41.
- Alswat KA. Gender disparities in osteoporosis. *J Clin Med Res.* 2017;9:382-7.
- Vollset SE, Goren E, Yuan C-W, Cao J, Smith AE, Hsiao T et al. Fertility, mortality, migration and population scenarios for 195 countries and territories from 2017 to 2100: a forecasting analysis for the Global Burden of Disease Study. *Lancet.* 2020;396:1285-306.
- United Nations, Department of Economic and Social Affairs, Population Division. *World Population Prospects: The 2017 revision.* New York: United Nations; 2017.
- WHO methods and data sources for global causes of death 2000-2016. *Global Health Estimates Technical Paper WHO/HIS/IER/GHE/2018.3.* Geneva: World Health Organization; 2018.
- Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *Am J Clin Nutr.* 2008;87(Suppl):1080s-6s.
- Holick MF. Vitamin D: A D-lightful solution for health. *J Invest Med.* 2011;59:872-80.
- Pludowski P, Holick MK, Pilz S, Wagner CL, Hollis BW, Grant WB et al. Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality—a review of recent evidence. *Autoimmun Rev.* 2013;12:976-8.
- Autier P, Boniol M, Pizot C, Mullie P. Vitamin D status and ill health: a systemic review. *Lancet Diabetes Endocrinol.* 2014;2:76-89.
- Grant WB, Wimalawansa SJ, Holick MF, Cannell JJ, Pludowski P, Lappe JM, Pittaway M, May P. Emphasizing the health benefits of vitamin D for those with neurodevelopmental disorders and intellectual disabilities. *Nutrients.* 2015;7:1538-64.
- Mirhosseini N, Vatanparast H, Kimball SM. The association between serum 25(OH)D status and blood pressure in participants of a community-based program taking vitamin D supplements. *Nutrients.* 2017;9:1244. doi: 10.3390/nu9111244.
- McDonnell SL, Baggerly CA, French CB, Baggerly LL, Garland CF, Gorham ED, Hollis BW, Trump DL, Lappe JM. Breast cancer risk markedly lower with serum 25-hydroxyvitamin D concentrations ≥ 60 vs < 20 ng/ml (150 vs 50 nmoL/L): Pooled analysis of two randomized trials and a prospective cohort. *PLoS One.* 2018;13:e0199265. doi: 10.1371/journal.pone.0199265.
- Estébanez N, Gómez-Acebo I, Palazuelos C, Llorca J, Dierssen-Sotos T. Vitamin D exposure and risk of breast cancer: a meta-analysis. *Sci Rep.* 2018;8:9039. doi: 10.1038/s41598-018-27297-1.
- Dawson-Hughes B, Staten MA, Knowler WC, Nelson J, Vickery EM, LeBlanc ES, Neff LM, Park J, Pittas AG. Intratrial exposure to vitamin D and new-onset diabetes among adults with prediabetes: a secondary analysis from the vitamin D and type 2 diabetes (D2d) study. *Diabetes Care.* 2020;43:2916-22.
- Wu G, Xue M, Zhao Y, Han Y, Zhang S, Zhang J, Li C, Xu J. Low circulating 25-hydroxyvitamin D level is associated with increased colorectal cancer mortality: a systematic review and dose-response meta-analysis. *J Biosci Rep.* 2020;31;40:BSR20201008. doi: 10.1042/BSR20201008.
- Acharya P, Dalia T, Ranka S, Sethi P, Oni OA, Safarova MS, Parashara D, Gupta K, Barua RS. The Effects of vitamin D supplementation and 25-hydroxyvitamin D levels on the risk of myocardial infarction and mortality. *J Endocr Soc.* 2021;5:1-11.
- Dai L, Liu M, Chen L. Association of serum 25-hydroxyvitamin D concentrations with all-cause and cause-specific mortality among adult patients with existing cardiovascular disease. *Front Nutr.* 2021;8:740855. doi: 10.3389/fnut.2021.740855.
- Burriss HH, Rifas-shiman SL, Camargo Jr CA, Litonjua A, Huh SY, Rich-Edwards JW, Gillman MW. Plasma 25-hydroxyvitamin D during pregnancy and small for gestational age in black and white infants. *Ann Epidemiol.* 2012;22:581-6.
- Song SJ, Si S, Liu J, Chen X, Zhou L, Jia G et al. Vitamin D status in Chinese pregnant women and their newborns in Beijing and their relationships to birth size. *Public Health Nutr.* 2013;16:687-92.
- Gernand AD, Simhan HN, Klebanoff MA, Bodnar LM. Maternal serum 25-hydroxyvitamin D and measures of newborn and placental weight in a U.S. multicenter cohort study. *J Clin Endocrinol Metab.* 2013;98:398-404.
- Schneuer FJ, Roberts CL, Guilbert C, Simpson JM, Algert CS, Khambalia AZ, Tasevski V, Ashton AW, Morris JM, Nassar N. Effects of maternal serum 25-hydroxyvitamin D concentrations in the first trimester on subsequent pregnancy outcomes in an Australian population. *Am J Clin Nutr.* 2014;99:287-95.
- Aydogmus S, Kelekci S, Aydogmus H, Eris S, Desdicioglu R, Yilmaz B, Saglam G. High prevalence of vitamin D deficiency among pregnant women in a Turkish population and impact on perinatal outcomes. *J Matern Neonatal Med.* 2015;28:1828-32.
- Eckhardt CL, Gernand AD, Roth DE, Bodnar LM. Maternal vitamin D status and infant anthropometry in a US multi-centre cohort study. *Ann Hum Biol.* 2015;42:215-22.

33. Zhu P, Tong S, Hu W, Hao J, Tao R, Huang K, Mou Z, Zhou Q, Jiang X, Tao F. Cord blood 25-hydroxyvitamin D and fetal growth in the China-Anhui Birth Cohort Study. *Sci Rep* 2015;5:14930. doi: 10.1038/srep14930
34. Miliku K, Vinkhuyzen A, Blanken LME, McGrath JJ, Eyles DW, Burne TH et al. Maternal vitamin D concentrations during pregnancy, fetal growth patterns, and risks of adverse birth outcomes. *Am J Clin Nutr*. 2016;103:1514-22.
35. Boyle VT, Thorstensen EB, Mourath D, Jones MB, McCowan LME, Kenny LC, Baker PN. The relationship between 25-hydroxyvitamin D concentration in early pregnancy and pregnancy outcomes in a large, prospective cohort. *Br J Nutr*. 2016;116:1409-15.
36. Taylor SN, Wagner CL, Hollis BW. Vitamin D supplementation during lactation to support infant and mother. *J Am Coll Nutr*. 2008;27:690-701. doi: 10.1080/07315724.2008.10719746.
37. Hollis BW, Wagner CL, Howard CR, Ebeling M, Shary JR, Smith PG, Taylor SN, Morella K, Lawrence RA, Hulsey TC. Maternal versus infant vitamin D supplementation during lactation: a randomized controlled trial. *Pediatrics*. 2015; 136:625-34.
38. Kaufman HW, Niles JK, Kroll MH, Bi C, Holick MF. SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels. *PLoS One*. 2020;17:15:e0239252. doi: 10.1371/journal.pone.0239252.
39. Asghar MS, Yasmin F, Dapke K, Shah SMI, Zafar MDB, Khan AA, Mohiuddin O, Surani S. Evaluation of vitamin-D status and its association with clinical outcomes among COVID-19 patients in Pakistan. *Am J Trop Med Hyg*. 2021; 106:150-5. doi: 10.4269/ajtmh.21-0577.
40. Pal R, Banerjee M, Bhadada SK, Shetty AJ, Singh B, Vyas A. Vitamin D supplementation and clinical outcomes in COVID-19: a systematic review and meta-analysis. *J Endocrinol Invest*. 2021;24:1-16. doi: 10.1007/s40618-021-01614-4.
41. Akter S, Rahman MM, Abe SK, Sultana P. Prevalence of diabetes and prediabetes and their risk factors among Bangladeshi adults: a nationwide survey. *Bull World Health Organ*. 2014;92:204-13.
42. Chaity AJ. Obesity blamed for alarming rise in childhood diabetes, Dhaka Tribune November 13th, 2017. [October 25, 2021]; Available from: <https://www.dhakatribune.com/health/2017/11/13/obesity-childhood-diabetes-alarming>.
43. Mohiuddin AK. Diabetes fact: Bangladesh perspective. *International J Diabetes Res*. 2019;2:14-20.
44. Chowdhury MZI, Haque MS, Farhana Z, Anik AM, Chowdhury AH, Haque SM et al. Prevalence of cardiovascular disease among Bangladeshi adult population: a systematic review and meta-analysis of the studies. *Vasc Health Risk Manag*. 2018;14:165-81.
45. Lips P. Which circulating level of 25-hydroxyvitamin D is appropriate? *J Biochem Mol Biol*. 2004; 89/90:611-4.
46. Chapuy MC, Pamphile R, Paris E, Kempf C, Schlichting M, Arnaud S, Garnero P, Meunier PJ. Combined calcium and vitamin D3 supplementation in elderly women: confirmation of reversal of secondary hyperparathyroidism and hip fracture risk: the Decalys II study. *Osteoporosis Int*. 2002; 13:257-64.
47. Trivedi DP, Doll R, Khaw KT. Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. *Br Med J*. 2003; 326:469-74.
48. Need AG, O'Loughlin PD, Morris HA, Coates PS, Horowitz M, Nordin BEC. Vitamin D metabolites and calcium absorption in severe vitamin D deficiency. *J Bone Miner Res*. 2008;23:1859-63.
49. Sanders KM, Stuart AL, Williamson EJ, Simpson JA, Kotowicz MA, Young D, Nicholson GN. Annual high-dose oral vitamin D and falls and fractures in older women: a randomised controlled trial. *JAMA*. 2010;303:1815-22.
50. Hollis BW. Circulating 25-hydroxyvitamin D levels indicative of vitamin D deficiency: implications for establishing a new effective dietary intake recommendation for vitamin D. *J Nutr*. 2005;135:317-22.
51. Bischoff-Ferrari HA, Giovannucci E, Willet WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. *Am J Clin Nutr*. 2006;84:18-28.
52. Kuchuk NO, Pluijij SM, van Schoor NM, Looman CWN, Smit JH, Lips P. Relationships of serum 25-hydroxyvitamin D to bone mineral density and serum parathyroid hormone and markers of bone turnover in older person. *J Clin Endocrinol Metab*. 2009;94:1244-50.
53. Grant WB, Holick MF. Benefits and requirement of vitamin D for optimal health: a review. *Altern Med Rev*. 2005; 10:94-111.
54. Priemel M, von Domarus C, Katte TO, Kessler S, Schlie J, Mtreichert T, Puschel K, Amling M. Bone mineralization defects and vitamin D deficiency: histomorphometric analysis of iliac crest bone biopsies and circulating 25-hydroxyvitamin D in 675 patients. *J Bone Miner Res*. 2010; 25:305-12.
55. IOM (Institute of Medicine) Dietary reference intakes for calcium and vitamin D. Committee to review dietary reference intakes for calcium and vitamin D. Washington DC: The National Academies Press Institute of Medicine; 2011.
56. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM. Controversy in clinical Endocrinology; guidelines for preventing and treating vitamin D deficiency and insufficiency revisited. *J Clin Endocrinol Metab*. 2012;97: 1153-8.
57. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM. Evaluation, treatment and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96:1911-30.
58. Murad MH, Elamin KB, Abu Elnour NO, Elamin MB, Alkatib AA, Fatourechi MM et al. The effect of vitamin D on falls: a systemic review and meta-analysis. *J Clin Endocrinol Metab*. 2011;96:2997-3006.
59. Chapuy MC, Preziosi P, Maamer M, Arnaud S, Galan P, Hercberg S, Meunier PJ. Prevalence of vitamin D insufficiency in an adult normal population. *Osteoporosis Int*. 1997;7:439-43.
60. Kinyamu HK, Gallagher JC, Rafferty KA, Balhorn KE. Dietary calcium and vitamin D intake in elderly women: effect on serum parathyroid hormone and vitamin D metabolites. *Am J Clin Nutr*. 1998; 67:342-8.
61. Thomas KK, Lloyd-Jones DH, Thadhani RI, Shaw AC, Deraska DJ, Kitch BT, Vamvakas EC, Dick IM, Prince RL, Finkelstein JS. Hypovitaminosis D in medical inpatients. *N Eng J Med*. 1998;338:777-83.
62. Holick MF, Siris ES, Binkley N, Beard MK, Khan A, Katzer JT, Petruschke RA, Chen E, de Papp AE. Prevalence of vitamin D inadequacy among postmenopausal north American women receiving osteoporosis therapy. *J Clin Endocrinol Metab*. 2005;90:3215-24.
63. Tofail F, Islam MM, Mahfuz M, Alam MA, Aktar S, Haque R, Hossain MI, Mondal D, Petri WA, Ahmed T. Association

- of vitamin D nutrition with neuro-developmental outcome in infants of slums in Bangladesh. *PLoS One*. 2016;14:e0221805. doi: 10.1371/journal.pone.0221805
64. Ahmed AMS, Ahmed T, Long KZ, Magalhaes RJS, Hossain MI, Islam MM et al. Prevalence and risk factors of vitamin D insufficiency and deficiency among 6–24-month-old underweight and normal-weight children living in an urban slum of Bangladesh. *Public Health Nutr*. 2015;20:1718-28.
 65. Zaman S, Hawlader MDH, Biswas A, Hasan M, Jahan M, Ahsan GU. High prevalence of vitamin D deficiency among Bangladeshi children: an emerging public health problem. *Health*. 2017;9:1680-88.
 66. International Centre for Diarrhoeal Diseases Research, Bangladesh (ICDDR, B), Global Alliance for Improved Nutrition (GAIN), The United Nations Children's Fund (UNICEF). The National Micronutrients Status Survey 2011-12, Dhaka, Bangladesh: International Centre for Diarrhoeal Diseases Research, Bangladesh; 2013.
 67. Ahmed S, Chowdhury AK, Hossain IA, Yasmin R, Haque MM, Faruquee MH, Salim AFM. Status of serum vitamin D among Bangladeshi Children: urban and rural setting. *Acta Scientific Paediatrics*. 2019;2:3-7.
 68. Roth DE, Shah MS, Black RE, Baqui AH. Vitamin D status of infants in North-eastern rural Bangladesh. Preliminary observations and a review of potential determinants. *J Health Popul Nutr*. 2010;28:458-69.
 69. Saha A, Shakur MS, Laila R, Shakur S, Shomik MS, Habib RB. Risk factors associated with vitamin D status among children of an urban and a rural areas of Bangladesh. *Bangladesh Med Res Council Bull*. 2020;46:134-41.
 70. Mahmood S, Rahman M, Biswas SK, Saqueeb SN, Zaman S, Manirujjaman M, Perveen R, Ali N. Vitamin D and parathyroid hormone status in female garment workers: a case-control study in Bangladesh. *Bio Med Res Int*. 2017; 2017:4105375. doi: 10.1155/2017/4105375.
 71. Islam QT, Reaz MA, Rahman MK, Islam AFMN, Rahman S, Sutradhar SR et al. Evaluation of vitamin d status among the doctors of Bangladesh. *Bangladesh J Med*. 2021;32:31-8.
 72. Micka A. Vitamin D status among Bangladeshi women of reproductive age 2009. Masters Theses 1911 - February 2014. [2021/10/25]; Available From: <https://scholarworks.umass.edu/theses/287>.
 73. Shefin SM, Qureshi NK, Nessa A, Latif ZA. Vitamin D status among Bangladeshi adult Muslim females having diabetes and using hijab. *BIRDEM Med J*. 2018;8:203-9.
 74. Fatema KN, Ibrahim M, Faruk MO, Islam S, Tabassum M, Biswas M et al. Vitamin D status and its relation with bone pain in adult Bangladeshi women: a study at a JCI accredited hospital in Bangladesh. *Eur J Biomed Pharma Sci*. 2018;5:1009-16.
 75. Jeong JH, Korsiak J, Papp E, Shi J, Gernand AD, Mahmud AA, Roth DE. Determinants of vitamin D status of women of reproductive age in Dhaka, Bangladesh: insights from husband-wife comparisons. *Curr Dev Nutr*. 2019;3:1-7.
 76. Ali SMM, Islam MN, Haq SA, Newaz ASMR, Talukder SI, Kabir MH, Mahmood T, Azad MAK. Prevalence of 25-hydroxyvitamin D deficiency: a hospital-based study among healthy Bangladeshi volunteers. *North Bengal Med Coll J*. 2020;6:4-9.
 77. Rahman AU, Karmakar PK, Jabeen S, Nabi S, Khan AM, Shahriar S, Alam I, Chakraborty S, Matin MA, Azam STMA. Association of vitamin D level with severity of angiographically documented coronary artery disease: Observations from Bangladeshi patients. *J Cardiovasc Disease Res*. 2019;10: 52-7.
 78. Chowdhury NA, Hossain MZ, Mia MM, Hoque S, Chowdhury NA, Sultana R, Nizhu LN. Vitamin D status of adults in the outpatient department in Bangladesh. *J Dhaka Med Coll*. 2018;27:94-7.
 79. Acherjya GK, Ali M, Tarafder K, Akhter N, Chowdhury MK, Islam DU, Rahman MH, Miah MT. Study of vitamin D deficiency among the apparently healthy population in Jashore, Bangladesh. *Mymensingh Med J*. 2019;28:214-21.
 80. Khan MAU, Hossain MA, Rahman MA, Rahman HW, Reza MA, Khan MK, Mahmud AA. Estimation of vitamin D levels among physicians working in a tertiary level hospital of Bangladesh. *Mymensingh Med J*. 2019;28:322-7.
 81. Ullah MI, Koch CA, Tamanna, Rouf S, Shamsuddin L. Vitamin D deficiency and the risk of preeclampsia and eclampsia in Bangladesh. *Horm Metab Res*. 2013;45:682-7.
 82. Asaduzzaman M, Basak R, Islam MS, Juliana FM, Ferdous T, Islam MJ, Mamun AA, Sabrina S, Uddin MM, Islam MK. Vitamin D deficiency and insufficiency in healthy pregnant women living in Dhaka, Bangladesh. *IOSR J Dental Med Sciences*. 2018;17:66-73.
 83. Bhowmik B, Siddique T, Majumder A, Mdala I, Hossain IA, Hassan Z et al. Maternal BMI and nutritional status in early pregnancy and its impact on neonatal outcomes at birth in Bangladesh. *BMC Pregnancy Childbirth*. 2019;19:413. doi: 10.1186/s12884-019-2571-5.
 84. Subramanian A, Korsiak J, Murphy KE, Mahmud AA, Roth DE, Gernand AD. Effect of vitamin D supplementation during pregnancy on mid-to-late gestational blood pressure in a randomized controlled trial in Bangladesh. *J Hypertension*. 2021;39:135-42.
 85. Ahmed F, Khosravi-Boroujeni H, Khan MR, Roy AK, Raqib R. Prevalence and predictors of vitamin D Deficiency and insufficiency among pregnant rural women in in Bangladesh. *Nutrients*. 2021;13:449. doi: 10.3390/nu13020449.
 86. Islam SS. Evaluation of vitamin D status among doctors of a specialized hospital in Bangladesh. *J Bangladesh Orthopaedic Soc*. 2016;31:80-4.
 87. Islam AKMM, Hasan MN, Rahman KM, Asaduzzaman M, Rahim MA, Zaman S, Islam MR, Jesmin Hh, Yeasmin L. Vitamin D status in Bangladeshi subjects: a laboratory-based study. *BIRDEM Med J*. 2019;9:202-6.
 88. Haque WMM, Pathan MF, Sayeed MA. Vitamin D status of healthy coastal fisherman of Bangladesh. *IMC J Med Sci*. 2019;13:1-5.
 89. Ahmed AKMS, Haque WMMU, Uddin KN, Abrar FA, Afroz F, Huque HF, Afroze SR, Rahim MA. Vitamin D and bone mineral density status among postmenopausal Bangladeshi women. *IMC J Med Sci*. 2018;12:44-9.
 90. Hossain HT, Islam QT, Khandaker MAK, Ahasan HN. Study of serum vitamin D level in different socio-demographic population-a pilot study. *J Med*. 2018;19:22-9.
 91. Alam MS, Hasan MK, Kalam ST, Selim S, Akter F, Saifuddin M. Vitamin D status in newly diagnosed type 2 diabetes patients attending in a tertiary hospital of Bangladesh. *Mymensingh Med J*. 2018;27: 362-8.
 92. Eva MA, Begum N, Kabir ASM, Ahmed KW, Sharmin M, Saha SK, Bayazid MB, Hasan S. A study on vitamin D level among the patients attending in a private chamber in Dhaka city. *Northern Int Med Coll J*. 2019;10:393-6.
 93. Paul AK, Kamrul-Hassan ABM, Chanda PK, Nondi DC. Vitamin D status of overweight and obese Bangladeshi adults. *J Family Med Prim Care*. 2020;9:3444-9.
 94. Selim S, Lona H. Vitamin D deficiency is associated with erectile dysfunction in men with type 2 diabetes. *Int J Diabetes Endocrinol*. 2020;5:77-82.
 95. Uddin R, Huda NH, Jhanker YM, Jesmeen T, Imam MZ, Akter S. Awareness regarding the importance of calcium and vitamin D among the undergraduate pharmacy students

- in Bangladesh. *BMC Res Notes*. 2013;6:134. doi: 10.1186/1756-0500-6-134.
96. De Pergola G, Martino T, Zupo R, Caccavo D, Pecorella C, Paradiso S, Silvestris F, Triggiani V. 25 Hydroxyvitamin D levels are negatively and independently associated with fat mass in a cohort of healthy overweight and obese subjects. *Endocr Metab Immune Disord Drug Targets*. 2019;19:838-44. doi: 10.2174/18715303196661901220940 39.
97. Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. Decreased bioavailability of vitamin D in obesity. *Am J Clin Nutr*. 2000;72:690-3.
98. Wahlqvist ML. Vitamin D status and food security in North-East Asia. *Asia Pac J Clin Nutr*. 2013;22:1-5.
99. Lee MS, Li HL, Hung TH, Chang HY, Yang FL, Wahlqvist ML. Vitamin D intake and its food sources in Taiwanese. *Asia Pac J Clin Nutr*. 2008;17:397-407
100. Tsiaras WG, Weinstock MA. Factors influencing vitamin D status. *Acta Derm Venereol*. 2011;91: 115-24.
101. Harris SS. Vitamin D and African Americans. *J Nutr*. 2006; 136:1126-9.
102. Lucock MD, Jones PR, Veysey M, Thota R, Garg M, Furst J et al. Biophysical evidence to support and extend the vitamin D-folate hypothesis as a paradigm for the evolution of human skin pigmentation. *Am J Hum Biol*. 2021:e23667. doi: 10.1002/ajhb.23667.
103. Jablonski NG. The evolution of human skin pigmentation involved the interactions of genetic, environmental, and cultural variables. *Pigment Cell Melanoma Res*. 2021;34:707-29. doi: 10.1111/pcmr.12976.
104. Kennel KA, Drake MT, Hurley DL. Vitamin D deficiency in adults: when to test and how to test. *Mayo Clin Proc*. 2010;85:752-8.
105. Behl T, Kumar S, Sehgal A, Singh S, Sharma N, Chirguru-pati S, Aldubayan M, Alhowali A, Bhatia S, Bungau S. Linking COVID-19 and Parkinson's disease: Targeting the role of vitamin D. *Biochem Biophys Res Commun*. 2021; 583:14-21.