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Original Article

Effect of Vitamin D Supplementation on Glucose Homeostasis among Type 2 Diabetic Patients: A Randomized Clinical Trial

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Background: Type 2 diabetes mellitus (T2DM) is a major endocrine and metabolic disorder that has become highly prevalent due to unhealthy diet and sedentary lifestyle. Worldwide by 2030 it will be double from 171 million to an astonishing 366 million people.Among them,90% with T2DM. **Materials and Methods:** A randomized clinical trial was conducted among 124 vitamin D Deficient Type 2 diabetic patients (n=61 for treatment group and n=63 for Placebo) of aged 30-70 years in between 2020 to 2021. Treatment group was given 20,000 IU vitamin D capsule (D-Rise, Beximco Pharmaceuticals) and control/placebo group received 'placebo' (Crystalline) at every 5th day for 12 weeks with follow-up at 6 weeks simultaneously. Collection of socio-demographic data, anthropometric data, laboratory analysis of blood specimens all were carried out at the same schedules. **Results:** Present study showed end line 25-hydroxyvitamin D levels were significantly higher in the treatment group compared to placebo (35.8 ±7.5 ng/mL; 20.05±5.2 ng/mL, p=0.001).Mean FBG (P<0.001) and HbA1c (P=0.004) were gradually decreased significantly from 10.9 mmol/l (±3.5) to 8.42 mmol/l (±1.7) and (8.97±1.9) to (8.5±1.6) respectively at the end line in treatment compared to placebo. All biochemical indices by P- trend like HbA1C, FBG, HOMA-β%, HOMA-IS%, HOMA-IR%, and vitamin D differed significantly (P<0.05). When vitamin D, HbA1C, HOMA-β, HOMA-IS were considered, increased significantly (P<0.05) and FBG, HOMA-IR decreased significantly (P<0.05) in treatment group as compared to placebo except Fasting Plasma Insulin and calcium. However, Vitamin D supplementation showed no significant impact on socio demography variables, BMI (Kg/m2) and vitamin D-related characteristics. Multivariate analysis revealed that FBG (P<.05) was inversely associated with vitamin D levels.In contrast calcium, which was positive predictors of changing Vitamin D level over 3-months intervention. But it was observed that important glycemic indices like FBI, HbA1C and derived-parameters (HOMA β, HOMA-IS, HOMA-IR) were not significant. **Conclusion:** Vitamin D Deficient Type 2 diabetic patients had shown a favorable effect on glycemic control over a period of 12 weeks in treatment group as compared to placebo. **Trial Registration**: UMIN Clinical Trial Registry No: UMIN000048031.

INTRODUCTION

Diabetes mellitus is an endocrine gland disorder, which is responsible for rising of blood glucose level due lack of insulin secretion or inadequate insulin action or both.[1] So that there is disturbance of metabolism of carbohydrate, fat and protein in the body.[2]Now-a-days diabetes especially Type 2 diabetes mellitus (T2DM), a non-communicable diseases and vitamin D deficiency are ubiquitous and more prevalent among both urban and rural population of Bangladesh despite having abundant sunshine at this latitude.[3] As per definition of WHO Diabetes is a non -communicable disease which is chronic in nature responsible for high rise glucose in blood causes detonation of cardiovascular system, renal system and so on. It is due to insufficient secretion of insulin from β- cell of pancreas, nonresponse to insulin and cells are not able to convert glucose into energy.[4] Globally DM is proving to be a global public health burden as this number is expected to rise to another 200 million by 2040. Majority (over 3 in 4) live in low middle-income countries.6.7 million deaths in 2021(1 every 5 seconds) due to.[5]Vitamin D deficiency is a silent and neglected global public health issue. Surprisingly in South Asia, 80% of the apparently healthy population is deficient in vitamin D (<20ng/mL) and up to 40% of the population is severely deficient (< 9ng/mL).[6] It is observed in Ghana (2018) that 92.2% (both Deficiency and insufficiency) of the diabetic women presented with vitamin D inadequacies.[7] In Qatar estimated that 87% severely deficient (D level <20ng/L.[8] Among Sudanese women showed majority (82.6%) had levels of 25 (OH) D below 20 ng/ml (deficient).[9] In Bangladesh in 2019 among 793 respondents (86%) had hypovitaminosis D, 61.4% had deficiency and 24.1% had insufficiency.[10]In 2019 among 102 doctors revealed that 66.6% had Vitamin D deficiency.[11] In 2019 despite having an abundant exposure to the sun, among healthy fishermen 71% had low vitamin D in terms of levels mentioned in the guideline of Endocrine.[12] In 2018 among 353 Muslin women 253(71.67%) had vitamin D deficiency and 80 (22.66%) subjects were insufficient.[13] In 2018 there was another study among 264 respondents showed the prevalence of hypovitaminosis was 84.84%.[14]

Methods and Materials

A single blind randomized clinical trial was conducted among 124 vitamin D Deficient Type 2 diabetic patients (n=61 for treatment group and n=63 for Placebo) in between January 2020 to Decenber 2021. The study was over seen after ethical clearance was approved from the review committee of the Faculty of Biological Science, University of Dhaka (Ref.No. 92/Biol.Scs). Data (Socio-demographic, Anthropometric, Dietary, Physical activity and bio-chemical) were analyzed by SPSS (Version 26). For calculation of -cell function, Insulin sensitivity (IS), and Insulin resistance (IR) used HOMA2-calculator (V2.2.3).

Patient's allocation following CONSORT:

A list of items from existing quality assessment and reporting tools, with Consolidated Standards of Reporting Trials guidelines. Patients assigned with serial number of regular counting order from 1 to 157. A total of 124 random counting numbers with minimum value of 1 through maximum value of 157 are determined (88, 68 ...130, 98) from online random number generator by calculator random number generator 1-100.

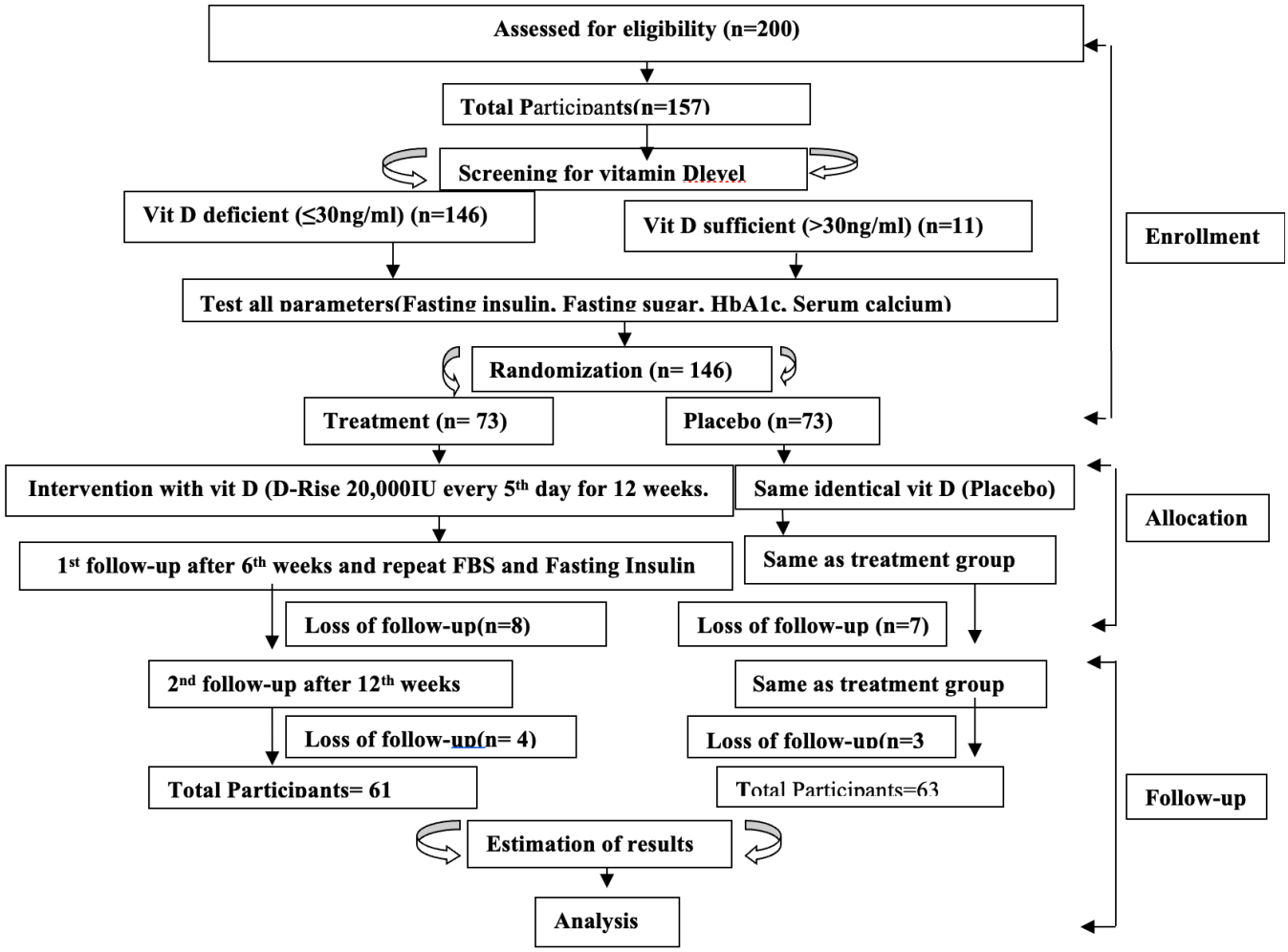

Figure 1. *Consort Flow Diagram*

Outcome measures and testing methods:

Blood analysis	Method	Reference
Serum Fasting Insulin	Chemiluminescence Microparticle Immunoassay (CMIA) by 8K41 ARCHITECT Insulin Reagent Kit. (Brand Architect TM, Abbott Laboratories, Japan) through Architect 4100 machine	Moriyama etal.2006[15]
Plasma Fasting Blood Glucose	Enzymatic method (Hexokinase-mediated reaction) by Hexokinase(Roche Diagnostics, Switzerland) through Roche/Hitachi Cobasc 311/501 Analyzer machine	T.A. Alaidarous.2020[16]
Serum Calcium	Photometric estimation by The Calcium Gen. 2 test system through Roche/Hitachi Cobas C Analyzer machine	W. Alan.2006[17]
Serum Vitamin D	Chemiluminescence Microparticle Immunoassay (CMIA) by ARCHITECT (Abbott Laboratories, Lake Forest, IL, USA) through Architect4100 machine	K. Hutchinson.2017[18]
HbA1c	Ion-exchange high performance liquid chromatographic method by Bio-Rad D-10TM Haemoglobin A1c (Bio-Rad Laboratories, USA through HPLC Analyzer(Fully automated) machine	M. Thevarajah et al.2009[19]

Table 1. *Outcome measures and testing methods*

Results

Table 2 showed the changes of different biochemical variables (Weight, BMI and sun-exposed time etc.) among 'within groups' and in 'between groups' (treatment versus placebo) following (3-months) vitamin D supplementation. Here, no significant differences (P>0.05) were observed for weight, BMI, sun-exposed time between baseline and end line in the treatment and placebo group. It is important to notify that'sun-exposed time' showed significant differences(P<0.05) at baseline between treatment and placebo but at the endline these variables remained independent(P>0.05) (table 3).

Socio-economic profile	Total (N=24)	Treatment % (n=61)	Placebo % (n=63)	P-value
Age in years (Mean±SD) (Minimum-maximum) 30-40 41-50 ≥51	(46.2±9.9) (30-72)	(46.4±9.6) (30-68)	(46.1±10.3) (30-72)	P=.861
	39(31.5)	17(27.9)	22(34.9)	
	57(46.0)	28(45.9)	29(46.0)	
	28(22.6)	16(26.2)	12(19.0)	
Sex Male Female				P=.576
	56(45.2)	26(42.6)	30(47.6)	
	68(54.8)	35(57.4)	33(52.4)	
Education Illiterate Primary (1-5y) Secondary(6-12y) Masters				P=.790
	42(33.9)	21(34.4)	21(33.3)	
	41(33.1)	18(29.5)	23(36.5)	
	31(25.0)	16(26.2)	15(23.8)	
	10(8.0)	06(9.9)	4(6.3)	
Occupation Services Business Housewives Others				P=.129
	45(36.3)	17(27.9)	28(44.4)	
	23(18.5)	10(16.4)	13(20.6)	
	29(23.4)	18(29.5)	11(17.5)	
	27(21.8)	16(26.2)	11(17.5)	
Marital status Married Unmarried				P=.578
	121(97.6)	60(98.4)	61(96.8)	
	03(2.4)	01(1.6)	02(3.2)	
Religion Muslim Hindu				P=.528
	110(88.7)	53(86.9)	57(90.5)	
	14(11.3)	08(13.1)	06(9.5)	
Income (BDT) (Mean±SD) ≤20000 20001-30000 ≥30001	(31,967.7±10150.8)(15 ,000-60,000)	(31,098.4±10738.9) (15,000-60,000)	(32,809.5±9557.7) (15,000-55,000)	P=.350
	22(17.7)	11(18.0)	11(17.5)	
	48(38.7)	27(44.3)	21(33.3)	
	54(43.5)	23(37.7)	31(49.2)	
BMI(Kg/m2) Normal (18.5-24.9) Overweight (25-29.9) Obese (≥30)				P=.321
	45(36.3)	23(37.7)	22(34.9)	
	65(52.4)	32(52.5)	33(52.4)	
	14(11.3)	06(9.8)	08(12.7)	
Duration of diabetes <5-years ≥5-years				P=.611
	82(66.1)	39(63.9)	43(68.3)	
	42(33.9)	22(36.1)	20(31.7)	
Sun-exposed time <One-hour ≥One-hour				P=.046
	94(75.8)	51(83.6)	43(68.3)	
	30(24.2)	10(16.4)	20(31.7)	

Table 2. *Socio-economic Profile (SEP) of respondents*

Different variables	Treatment (n=61)			Placebo (n=63)			
	Baseline	End- line	P-value Within-Treatments	Baseline	End-line	P-value Within placebos groups	P-value Between-groups/ (B-G)+ Effect-size
(Mean± SD) Weight (w1 & W3)	59.5.5±6.6	59.3±6.4	P>0.05	59.9±7.6	59.6±7.4	P>0.05	P>0.05(All-timelines)
(Mean± SD) BMI (BMI1, BMI3)	25.2±3.4	25.1±3.3	P>0.05	24.4±2.7	24.3±2.6	P>0.05	P>0.05(All-timelines)
Having Sun-exposure (yes, N=118, 95.2%)	58 (95.1)	58 (95.1)	P>0.05	60 (95.1)	60 (95.1)	P>0.05	P>0.05(All-timelines)
Sun-exposed-time (n %)(base vs. end)							
<1-hour ≥1-hours	51 (83.6)	47 (77.0)	P>0.05	43 (68.3)	44 (69.8)	P>0.05	P=.046 in Baseline but
	10 (16.4)	14 (23.0)		20 (31.7)	19 (30.2)		P=.364 in End-line

Table 3. *Changes of different non-biochemical variables (Weight, BMI, sun exposed time and Blood pressure etc.) within groups and between groups following (3-months) vitamin D supplementation*

Student's t-test was used for Continuous variables and chi-square for categorical variables. 'Within groups' denoted as comparison among 2 time-periods for both treatment and placebo group (Bonferroni-adjusted pairwise comparisons across repeated time levels). 'Between groups' denoted as comparison between vitamin D-treated group and Placebo.

Mean Indices	Treatment (n=61)				Placebo (n=63)				P-value for Between-groups
	Baseline	6-weeks follow-up	End- line	P-value for Within-Treatments groups	Baseline	6-weeks follow-up	End-line	P-value for Within placebos groups	
Vitamin D (25-OH)2 (ng/ml)	14.5±6.1	-	35.8±7.5	P=.000	19.4±8.8	-	20.5±5.2	P=0. 965	P=.001
HbA1C (%)	8.97±1.9	-	8.5±1.6	P=.004	7.9±2.1	-	7.7±0.60	P=.587	P<.01(All timelines)
Fasting Blood Glucose(mmol/L)	10.9±3.5	9.98±3.3	8.42±1.7	P<0.001	10.6±2.4	9.1±3.6	11.5±2.3	P<.001 (All pairs)	P=000 (End-line)
Fasting Plasma Insulin (µU/ml)	9.8±2.28	9.2±1.0	10.2±1.9	P<0.05	10.1±1.5	9.4±1.0	9.9±1.4	P<0.05	P>0.05 (All-timelines)
HOMA-β (%)	34.0±21.7	36.9±21.1	48.2±24.7	P<0.05	30.5±11.7	48.6±26.9	25.5±8.0	P=.000 (all pairs)	P<.01 (Follow-up, End-line)
HOMA-IS (%)	66.1±16.4	72.6±10.6	69.7±11.6	P<0.01	65.9±11.7	71.3±11.6	64.9±11.4	P=0.01	P=.023 (End-line)
HOMA-IR (%)	1.62±0.45	1.42±0.24	1.48±o.25	P<0.05	1.57±0.33	1.44±0.26	1.58±0.3	P<0.05	P=.030 (End-line)
Serum Calcium(mg/dl)	9.7±0.57	-	9.8±0.46	P=0.295	9.8±0.56	-	9.4±1.42	P=.080	P=0.086 (End-line)

Table 4. *Changes of different bio-chemical indices across three or two time-points following (3-months) vitamin D supplementation*

Table 4 showing baseline to end line (mainly 2 timelines) changes of eight bio-chemical indices by P-trends. All biochemical indices like HbA1C, FBG, HOMA-β%, HOMA-IS%, HOMA-IR%, and vitamin D, were significantly different (P<0.05).Whenever consider between groups vitamin D, HbA1C, HOMA- β, HOMA-IS increased (P<0.05) and FBG, HOMA-IR decreased significantly (P<0.05) in treatment group as compared to placebo except Fasting plasma Insulin and calcium which remain independent (P>0.05).

Bio-chemical Variables	β - c efficient (Unstandardized)	Standard error	P-value	R^2 -change**	Interpretation (One-unit change in vitamin D, decreases/Increase)
HbA1C (%)	-0.291	.351	0.408	Only treatment group (model 1)	↓HbA1C by 0 .291 unit
FBG (mmol/L)	-0.650	.447	0.010	=6.2%	↓FBS by 0 .650 unit
FBI (µIU/mL)	0.232	.623	0.711	Including 10 bio-chemical-parameters	↑Insulin by 0 .232 unit
HOMA- β (%)	0.034	.056	0.542	(model-2)=50.6%	↑HOMA- β by 0.034 unit
HOMA-IS (%)	0.064	.157	0.683	R^2-change=44.4%	↑HOMA-IS by 0.064 unit
HOMA-IR (%)	-5.366	4.778	0.263	(F=19.17P<0.001)	↓HOMA-IR by 5.366 unit unit
Calcium	1.386	.574	0.017		↑Calcium by1.386 unit

Table 5. *"Fixed-Effect multiple Regression Model" describing the association of glycemic indices andother biochemical parameters with Vitamin D (ng/ml) by R2-changes across timelines*

Table 5 describes the association of glycemic indices (A1C, FBG, FBI, HOMA-β, OMA-IS, HOMA-IR and calcium) with vitamin D level by R2-changes across timelines. It outlines that FBG (β = -.650, Std. error =.447, p0.05) predictors of variation in Vitamin D level over 2 timelines.

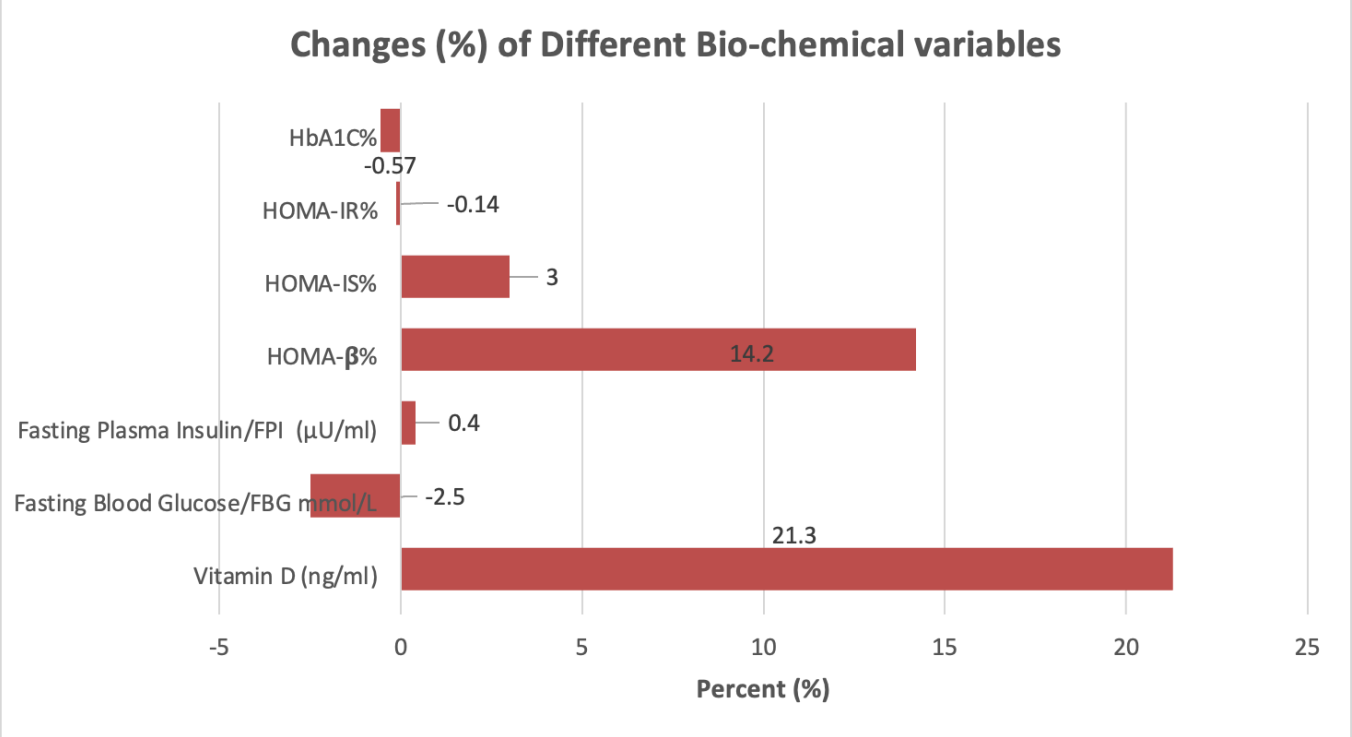

Figure 2. *Percent (%) changes of different biochemical parameters among treatment group from baseline to the end line*

Figure 2 showed percent (%) changes of different biochemical parameters among treatment group from baseline to the end line. The highest changes of variation were observed in Vitamin D (21.3%) followed by HOMA- β (4.2%), and HOMA-IS (3.0%).

Pairs	Biochemical Parameters	Mean± SD	P value
Pair 1	Fasting Insulin (Popular Diagnostic center)	9.52 ± 4.45	0.415
	Fasting Insulin (BIRDEM)	9.98 ± 2.52	
Pair 2	Vitamin D (Popular Diagnostic center)	16.84 ± 6.94	0.055
	Vitamin D (BIRDEM)	18.24 ±1.47	

Table 6. *Validity Test for different biochemical indices*

Table 6 shows Validity test for different biochemical indices like Fasting Insulin (FI) and Vitamin D showed that no significant differences (P>0.05).

Discussion

This randomized clinical trial was conducted among 124 vitamin D Deficient Type 2 diabetic patients with 20,000 IU 25-hydroxy cholecalciferol (vitamin D3) supplementation at every 5th day for 12 weeks with 1st follow-up after 6th weeks. Study showed strongly significant(P=.000) level of 25 (OH) D3 from deficient (baseline: 14.5±6.1 ng/mL) to sufficient levels (end line 35.8±7.5 ng/mL) (i.e. deficient≤ 30 ng/ml, sufficient ≥30 ng/ml) as defined by the American Endocrine society(Holick et al., 2011;Waterbury, 2018)[20.21]End line 25-hydroxyvitamin D levels were significantly higher in the treatment group as compared to placebo (treatment: 35.8 ±7.5ng/mL and placebo: 20.05±5.2 ng/mL, p=0.001). Similar results also reported by couple of studies [(Tang etal.,2018 and)[22] baseline: 41.16 nmol/L and end line: 82.22 nmol/L;(Ryu et al., 2014)[23];35.4 ± 8.5 ng/mL vs. 18.4 ± 7.3 ng/mL, p < 0.001); (Anyanwu et al.,2017)].[24]

Vitamin D and glucose homeostasis: Present study showed significant correction in vitamin D status among the T2DM patients along with correction of FBG. There was some similar findings in different studies by Al-Zahrani M K et al.,2014; Haidari F,2016 and Hu Z et al.,2019.[25-27] Opposite relation also observed by Krul-Poel YHM,2017.[28] There are several studies by Al-Sofiani et al.,(2015); Anyanwu et al.(2017); Dhillon et al.(2016); Safarpour et al.(2020); Hu et al.(2019)[29 24,30 31,27] supporting this idea that vitamin D is an important nutrient in control of glucose homeostasis. However, showed opposite finding by Al Thani et al.(2019); Anastassios G. Pittas et al. (2019); Davidson et al.(2013); Kampmann et al.(2014); Sadiya et al.(2015); Wagner et al.(2016); Yvonne H.M. Krul-Poel et al(2015) [8,32-37] elucidated that there is no effect of intermittent vitamin D3 supplementation on glycemic control in diabetic patients (including pre-diabetic and T2DM) and also for overweight and obese individuals (Jamka et al., 2015). and also for overweight and obese individuals by Jamka et al. (2015).[38]

Study showed 3-timelines (baseline, follow up, and end line) for all glycemic indices (e.g., FBG, FBI, HOMA-β, HOMA-IR, HOMA-IS) except vitamin D, HbA1C, and Calcium had two timelines (baseline verses end line).Bivariate analysis of this study revealed that mean FBG gradually decreased (P<0.001) from baseline 10.9 mmol/l (±3.5) to the end line 8.42mmol/l (±1.7) in treatment group as compared to placebo (P>0.05) due to 12-weeks vitamin D supplementation. Moreover, a study by Haidari et al.(2016)[39] showed multiple regression analysis asserted that FBG is negatively associated with vitamin D level among T2DM patients. Similar findings have also been observed in other studies by Anyanwu et al., (2017); Dhillon et al.(2016); Haidari et al.(2016); Shivaprakash &

Joseph,(2014), Foroughi et al.,(2016).[24,30,39-41].

Overall R2-change (F=19.17, P<0.001) in multivariate analysis showed 44.4% variation for different biochemical predictors of vitamin D and revealed that FBG (P<.05) are inversely associated with vitamin D levels. In contrast, important glycemic indices like HbA1C, FBI and derived-parameters (HOMA-β, HOMA-IS, HOMA-IR) remained significant (P<0.05) only in bivariate analysis but not in multiple regression analysis. Non-significant changes in the mean FBS and HbA1c level after 12 weeks of Vitamin D3 supplementation also reported in other studies by Anyanwu et al.(2017); Rashidi et al.(2016).[24,42]

A study by Al Thani et al.(2019)[8]showed measures of glucose tolerance or insulin sensitivity, with respect to baseline did not differ between the placebo and treatment following 24-weeks Vitamin D supplementation. However, 6-months supplementation with vitamin D and calcium may improve insulin sensitivity but not for adults with low vitamin D status at risk of type 2 diabetes also reported by Gagnon C et al,(2014).[43]There was another study by Dhillon et al. (2016)[30]showed insulin sensitivity is inversely proportional to insulin resistance in treatment group and significant reduction in HOMA-IR levels suggests improved insulin sensitivity due to 12-weeks vitamin D supplementation. Another study outlined by Anyanwu et al.(2017)[24]revealed that 12-week of vitamin D3 supplementation results in a reduction in insulin resistance but has no effect on pancreatic beta-cell function in T2DM patients. Vitamin D repletion for 12 weeks increased serum vitamin D concentrations and improved ß-cell (ability of insulin secretion) but no significant changes in HbA1c or insulin sensitivity or insulin resistance also reported by Al-Sofiani et al.(2015).[29]A study by Ryu et al., (2014)[23] observed after supplementation of vitamin D (4,000IU daily) improved insulin sensitivity (HOMA-IS %) and HOMA-IR% and decreased fasting blood insulin (FBI) in insulin-resistant Asian females compared to placebo. Contrarily,a study by Tang et al. (2018)[22]reported that after vitamin D supplementation no significant differences between treatment and placebo in terms of HOMA-%B and HOMA-IR by Mabhala et al., 2017; Ryu et al., 2014.[44,23]

Socio-demography and vitamin D related characteristics: In this study vitamin D supplementation showed no significant impact on socio-demography, BMI (Kg/m2), co-morbidity, and vitamin D related Characteristics between treatment and control groups (p>0.05). There was a study by Hossain et al.(2018) showed Vitamin D status was associated with a number of socio-demographic variables in vitamin D deficient subjects in Bangladesh.[45]However, several studies by Alam et al. (2018);Shivaprakash & Joseph(2014)[46,47]also showed that age, sex,BMI, family history of DM ,sun exposed time and barriers of sun exposure due to clothing or covering by Al-Zahrani et al. (2014)[25]were not found to influence vitamin D level independently.

Vitamin D and bone mineral Calcium: Multivariate analysis of this study showed calcium is a significant positive predictors of changing Vitamin D level over 3-months intervention while bivariate analyses revealed that calcium level were became higher in the treatment group (baseline: 9.7 ±0.57 ng/mL vs. end line: 9.8±0.56 ng/mL, p = 0.295) compared to placebo group (baseline: 9.8 ± 0.56 ng/mL vs. end line: 9.4 ± 1.52 ng/mL, p = 0.080). Slight increment of serum calcium in treatment group due to vitamin D supplementation [0.70 mmol/L (95% CI: 0.06, 1.3), P = 0.03] also observed by Thani et al. (2019).[8]Regarding validity test for different biochemical indices like Fasting Insulin(FI) and Vitamin D showed that no significant differences (P>0.05). These were estimated from two different laboratories (i.e. Popular Diagnostic center and BIRDEM). Thus, test results did not varies for different laboratory diagnosis and thus null hypothesis was accepted.

Conclusion

Vitamin D deficiency has become epidemic worldwide. Vitamin D Deficient Type 2 diabetic patients had shown a favorable effect on glycemic control in terms of vitamin D, A1C, HOMA-β, HOMA-IS) increased (P<0.05) and some decreased (FBG and HOMA-IR) significantly (P<0.05) in treatment group as compared to placebo except FBI and calcium remain independent (P>0.05). Also, on socio-

demography, BMI (Kg/m2) and vitamin D related characteristics there was no significant impact of vitamin D supplementation between treatment and control groups. Effective educational campaigns would increase awareness about adequate intake of vitamin D (Vitamin D2 (ergocalciferol) or D3 (choleclalciferol) according to the recommendations for Endocrine society and calcium containing food. Additionally, exposing to sun rays is an effective way of enhancing vitamin D status. Last but not the least routine supplementation and monitoring of serum vitamin D levels should be considered since this may help reduce the risk of glucose metabolism disorders.

Strength and Limitation

Validation of biochemical parameters (e.g. vitamin D and Fasting) have been done from another laboratory (e.g. BIRDEM). Advanced Statistical analysis ('Fixed effect regression analysis using dummy variables') and latest version of software were used (SPPSS version 26). As limitation, difficult to maintain time framework because the patients flow was out of control due to COVID-19 situation.

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Conflict of interest: Thesis copy has been submitted to Bangabandhu Science and Technology Fellowship Trust (BSTFT).

References

1. Amirasgari F et al. No Title. Current Research in Diabetes ObesityJournal.2019;11(02).Availablefrom: RL:https://doi.org/http://dx.doi.org/10.19080/CRDOJ.2019.11.555810
2. WHO (2019). Classification of diabetes mellitus. Geneva: World Health Organization; 2019Available from: URL:http://apps.who.int/iris.
3. Mohiuddin AK. Diabetes Fact: Bangladesh Perspective. International Journal of Diabetes Research.2019;2(1):14–20.Available from: URL https://doi.org/10.17554/j.issn.2414-2409.2019.02.12
4. Galicia-garcia, U et al.Pathophysiology of Type 2 Diabetes Mellitus. 1-34.
5. Islam A et al. Vitamin D status in Bangladeshi subjects: a laboratory based study. BIRDEM Medical Journal,(2019);9(3):202–206. Available from : URL: https://doi.org/10.3329/birdem.v9i3.43081.
6. Zaman S et al. High Prevalence of Vitamin D Deficiency among Bangladeshi Children: An Emerging Public Health Problem. Health.2017; 09(12):1680–1688. Available from : URL: https://doi.org/10.4236/health.2017.912123.
7. Fondjo L A et al. Evaluating Vitamin D status in pre-And postmenopausal type 2 diabetics and its association with glucose homeostasis. BioMed Research International, 2018. Available from :URL: https://doi.org/10.1155/2018/9369282.
8. Al Thani M etal.The effect of vitamin D supplementation on the glycemic control of pre-diabetic Qatari patients in a randomized control trial. BMC Nutrition. 2019;5(1): 1–10. Available from : URL: https://doi.org/10.1186/s40795-019-0311-x.
9. Hossain H T et al.Study of Serum Vitamin D Level in Different Socio-Demographic Population - A Pilot Study.2018; 22–29.
10. Islam, A et al. Vitamin D status in Bangladeshi subjects: a laboratory based study. BIRDEM Medical Journal.2019;9(3):202–206. Available from : URL: https://doi.org/10.3329/birdem.v9i3.43081.
11. Khan AU. Estimation of vit D levels among Physicians working in a Tertiary Level Hospital in Bangladesh. Mymensing Medical Journal. 2019;28(2):322–327.
12. HaqueP, Sayeed Ul, FaruqueM.Vitamin D status of healthy coastal fishermen of Bangladesh.2019;13(02).
13. Shefin SM, Qureshi NK, Nessa A. Vitamin D Status among Bangladeshi Adult Muslim

Females Having Diabetes and Using Hijab. BIRDEM Med J, May 2019. Available from: URL: https://doi.org/10.3329/birdem.v8i3.38122
14. Rahman AHMH, Zafreen F, Nazneen L, W. M. (2018). Socio-demographic Determinants of Hypovitaminosis D. JAFMC Bangladesh, 14(02). https://doi.org/DOI: https://doi.org/10.3329/jafmc.v14i2.45902
15. Moriyama M, Hayashi N, Ohyabu C, Mukai M, Kawano S, Kumagai S. Performanceevaluation and cross-reactivity from insulin analogs with the ARCHITECT insulin assay.Clin Chem. 2006 Jul; 52(7):1423-6. doi: 10.1373/clinchem.2005.065995. Epub 2006May11. PMID: 16690737.
16. Thuraya A et al.Impact of the Glycemic Control and Duration of Type 2 Diabetes on VitaminD Level and Cardiovascular Disease Risk. Hindawi Journal of Diabetes Research. 2020; Article ID 8431976:10 pages.
17. Wagner H,Alvarsson M, MannheimerB,Degerblad M. No Effect of High-Dose Vitamin D Treatment on b -Cell Function , Insulin Sensitivity , or Glucose Homeostasis in Subjects With Abnormal Glucose Tolerance : A Randomized Clinical Trial. 2016 March: 345–352.Available from:URL: https://doi.org/10.2337/dc15-1057
18. Hutchinson K, Healy M, Crowley V, Louw M, Rochev Y. Verification of Abbott 25-OH-vitamin D assay on the architect system. Practical Laboratory Medicine.7(2017):27–35.Available from:URL:http://dx.doi.org/10.1016/j.plabm.2017.01.001
19. Thevarajah M et al. Interference of hemoglobinA1c (HbA1c) detection using ion-exchange high performance liquid chromatography (HPLC) method by clinically silent hemoglobin variant in University Malaya Medical Centre (UMMC) – a case report. ClinBiochem. 2009 Mar.
20. Holick MF et al. Evaluation , Treatment , and Prevention of Vitamin D Deficiency : an Endocrine Society Clinical Practice Guideline.2011 25(July):1911–1930.Available from:URL:https://doi.org/10.1210/jc.2011-0385
21. Waterbury S. Implications of & vitamin D toxicity deficiency. The Nurse Practitioner.2018;33(05).
22. Tang H, Li D, Li Y, Zhang X, Song Y, Li X. Effects of Vitamin D supplementation on glucose and insulin homeostasis and incident diabetes among nondiabetic adults: A meta-analysis of randomized controlled trials. International Journal of Endocrinology, 2018.Available from:URL:https://doi.org/10.1155/2018/7908764
23. Ryu C et al. The effect of high-dose vitamin D supplementation on insulin resistance and arterial stiffness in patients with type 2 diabetes.2014;29:620–629.
24. Anyanwu AC, Fasanmade OA, Coker HAB, OhwovorioleAE.Vitamin D supplementation improves insulin resistance in type 2 diabetes subjects in Lagos, Nigeria. African Journal of Diabetes Medicine. 2017;25(1):14–17.
25. Al-Zahrani M K et al. A 3-month oral vitamin D supplementation marginally improves diastolic blood pressure in saudi patients with type 2 diabetes mellitus. International Journal of Clinical and Experimental Medicine.2014;7(12):5421–5428.
26. Haidari F, Zakerkish M, Karandish M, Saki A, Pooraziz S. Association between serum vitamin D level and glycemic and inflammatory markers in non-obese patients with type 2 diabetes. Iranian Journal of Medical Sciences.2016;41(5):367–373.
27. Hu Z et al.Efficacy of vitamin D supplementation on glycemic control in type 2 diabetes patients. Medicine. 2019;98(14(e14970)).Availablefrom:URL:https://doi.org/http://dx.doi.org/10.1097/MD.000000000014970
28. Krul-Poel YHM, Ter Wee M M, Lips P, Simsek S. The effect of Vitamin D supplementation on glycaemic control in patients with type 2 diabetes mellitus: A systematic review and meta-analysis. European Journal of Endocrinology. 2017; 176(1): R1–R14.Available from:URL: https://doi.org/10.1530/EJE-16-0391
29. Al-SofianiME et al.Effect of Vitamin D Supplementation on Glucose Control and Inflammatory Response in Type II Diabetes: A Double Blind, Randomized Clinical Trial. International Journal of Endocrinology and Metabolism 2015;13(1): 1–5. Available from:URL:https://doi.org/10.5812/ijem.22604
30. Dhillon P. K, Rai J, Bal B S, Singh NR.A study to assess the effect of vitamin D

supplementation on insulin resistance and glycaemic control in type 2 diabetes mellitus patients.International Journal of Basic & Clinical Pharmacology.2016;5(2):466–472.
31. Safarpour Pet al.Vitamin D supplementation improves SIRT1 , Irisin , and glucose indices in overweight or obese type 2 diabetic patients : a double- blind randomized placebo-controlled clinical trial.2020:1–10.
32. Pittas,Anastassios G.B. D.-H et al. Vitamin D Supplementation and Prevention of Type 2 Diabetes. New England Journal Medicine Th e o F 2019;381(06). Available from:URL:https://doi.org/10.1056/NEJMoa1900906
33. Davidson,MayerB,Martin L. High-Dose Vitamin D Supplementation in People With Prediabetes and Hypovitaminosis D.2013:36. Available from:URL:https://doi.org/10.2337/dc12-1204.
34. Kampmann U et al. Effects of 12weeks high dose vitamin D3 treatment on insulin sensitivity, beta cell function, and metabolic markers in patients with type 2 diabetes and vitamin D insufficiency - a double-blind, randomized, placebo-controlled trial. Metabolism. 2014;63(9): 1115–1124.Available from:URL:https://doi.org/10.1016/j.metabol.2014.06.008
35. Sadiya A et al. Vitamin D supplementation in obese type 2 diabetes subjects in Ajman, UAE: A randomized controlled double-blinded clinical trial. European Journal of Clinical Nutrition.2015;69(6):707–711.Availablefrom:URL:https://doi.org/10.1038/ejcn.2014.251
36. Wagner H,Alvarsson M, Mannheimer B,DegerbladM.No Effect of High-Dose Vitamin D Treatment on b -Cell Function , Insulin Sensitivity , or Glucose Homeostasis in Subjects With Abnormal Glucose Tolerance : A Randomized Clinical Trial. 39(March)2016:345–352. Available from:URL: https://doi.org/10.2337/dc15-1057
37. Yvonne HM et al. Effect of Vitamin D Supplementation on Glycemic Control in Patients With Type 2 Diabetes (SUNNY Trial): A Randomized Placebo-Controlled. 38(February). 2015:1420–1426. Available from:URL:https://doi.org/10.2337/dc15-0323
38. Jamka M, Woźniewicz M, JeszkaJ,Mardas M. The effect of vitamin D supplementation on insulin and glucose metabolism in overweight and obese individuals : systematic review with meta-analysis. Nature Publishing Group, February 2015:114–116.Available from:URL:https://doi.org/10.1038/srep16142
39. Haidari F et al.Association between serum vitamin D level and glycemic and inflammatory markers in non-obese patients with type 2 diabetes. Iranian Journal of Medical Sciences. 2016;41(5):367–373.
40. Shivaprakash NC,Joseph RB. Relationships between Serum 25-Hydroxy Vitamin D Levels and Plasma Glucose and Lipid Levels in Pediatric Patients in a Rural. International Journal of Scientifi c Study.2014;1(4);24–31.
41. Foroughi M,Maghsoudi Z, Askari G. The effect of Vitamin D supplementation on blood sugar and different indices of insulin resistance in patients with non-alcoholic fatty liver disease (NAFLD). Iranian Journal of Nursing and Midwifery Research 2016; 21(1):100–104.Available from:URL: https://doi.org/10.4103/1735-9066.174759
42. Rashidi H et al. The effect of vitamin d supplementation on insulin resistance and glycemic control in patients with type 2 diabetes. International Journal of Pharmacy and Technology.2016;8(2):11634–11642.
43. Gagnon C et al.Effects of Combined Calcium and Vitamin D Supplementation on Insulin Secretion , Insulin Sensitivity and b -Cell Function in Multi-Ethnic Vitamin D-Deficient Adults at Risk for Type 2 Diabetes : A Pilot Randomized.PLoS ONE,2014; 9(10):Available from:URL:https://doi.org/10.1371/journal.pone.0109607
44. Mabhala MA, Babanumi A, Olagunju A, Akata E, Yohannes A. Evaluating the Use of Vitamin D Supplementation to Improve Glycaemic Outcome in Type 2 Diabetes Mellitus Patients:A Systematic Review of Evidence. Journal of DiabetesMellitus.2017;07(04):22 3–240.Availablefrom:URL:https://doi.org/10.4236/jdm.2017.74018
45. Hossain H T, Islam Q T, Khandaker A K, Ahasan H A M N. Study of Serum Vitamin D Level in Different Socio-Demographic Population - A Pilot Study.2018: 22–29.
46. Alam MS et al.Vitamin D Status in Newly Diagnosed Type 2 Diabetes Patients Attending a Tertiary Hospital of Bangladesh. [Mymensingh Med J. 2018;27(02):362–368.
47. Shivaprakash N C, Joseph R B. Relationships between Serum 25-Hydroxy Vitamin D Levels and Plasma Glucose and Lipid Levels in Pediatric Patients in a Rural. International Journal of Scientifi c Study.2014;1(4):24–31.