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Original Article

Age-specific improvements in impaired fasting glucose and vitamin D status using a lifestyle intervention programme in overweight and obese Saudi subjects

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Abstract: The present study aimed to determine the health benefits of a 3-month lifestyle interventional programme with emphasis on lowering dietary fat content and increasing sunlight exposure in overweight and obese hyperglycemic subjects according to age. Saudi overweight and obese subjects (n=221) with fasting blood glucose between 5.6-6.9 mmol/l underwent a 3-month self-monitoring lifestyle intervention programme. Subjects were divided based on age into 3 groups: 1 (12-17 yr), 2 (18-45 yr) and 3 (46-70 yr). Overall, the 3 month follow up data identified significant improvement in fasting blood glucose, systolic and diastolic blood pressure and vitamin D levels as compared to baseline values (*P* values 2.2×10^{-4}, 8.6×10^{-4}, 0.001 and 7.6×10^{-5} respectively). Analysis by age groups determined significant improvement in fasting blood glucose in both group 1 (P=0.003) and 2 (P=0.035); systolic and diastolic blood pressure also reduced significantly in group 1 (P=0.029 and 0.006) and group 2 (P=0.001 and 0.006) respectively. Group 2 also showed a significant increase in vitamin D levels ($P=3.6\times10^{-6}$) whilst group 3 appeared to only reduce their BMI significantly (P=0.008). Analysis within groups revealed 27.3%, 25% and 17.6% of group 1, 2 and 3 were able to improve their fasting blood glucose levels. In conclusion, a 3 month intervention in lifestyle can lead to improved fasting blood glucose and vitamin D status in younger people whilst older people only appear to substantially improve their BMI. As such, these studies highlight that intervention in the young could provide benefits for long-term health whilst these benefits would appear to be reduced with age.

Keywords: Impaired fasting glucose, fasting blood glucose, vitamin D, life-style intervention, T2DM, obese

Introduction

The current prevalence of diabetes mellitus (DM) for all age-groups worldwide has dramatically increased to 8.3% as compared to 2.8% in 2000 [1, 2]. If the prevalence of DM continues to rise at the current rate, the total number of people with DM is expected to increase from 387 million at present to 592 million in 2035 [2]. The global health expenditure on type 2 diabetes mellitus (T2DM) alone is expected to increase from US$376 billion in 2010 to US$490 billion in 2030 [3]. The co-operation council for the Arab states of the Gulf (GCC) have some of the highest rates of T2DM in the world and Saudi Arabia is no different with the crude prevalence of T2DM at 23.1% [4]. Furthermore, T2DM is no longer a disease of adults alone, abnormal glucose metabolism is highly prevalent among Saudi children and adolescents, exceeding 10%, and more than 90% of them unaware of their metabolic condition [5, 6].

Saudi Arabia has one of the highest prevalence of overweight and obesity in adults as well as in children [7]. Overall, 28.7% Saudis aged 15 years or older are noted to be obese

[6]. Childhood obesity is strongly associated with adult obesity [8, 9] and adult obesity, in turn, is associated with a significant increased risk of morbidity, including T2DM and cardiovascular diseases [10]. This ultimately places the population at higher risk for mortality secondary to non-communicable diseases.

Impaired fasting glucose (IFG) [fasting blood glucose (FBG) =100 mg/dl to 125 mg/dl or 5.6 to 6.9 mmol/l] is also referred to as a state of 'intermediate hyperglycemia', and puts an individual at a high risk not only of developing DM but also its associated complications as well [11-13]. Vascular complications such as ophthalmopathy, nephropathy, and neuropathies have been reported in people with pre-diabetes during follow up periods [14]. Furthermore, around 5%-10% of people with prediabetes reach the clinical criteria for T2DM annually and this is alarming [14]. Worldwide, the number of people with pre-diabetes is estimated to be 314 million and is projected to reach 418 million in 2025 [15, 16]. The combination of traditional Saudi cultural practices, rapid modern cultural changes and economic prosperity has created an obesogenic environment that promotes unhealthy eating, sedentary lifestyles, and weight gain [7].

Studies have shown that people with pre-diabetes who lose weight and increase their physical activity can prevent or delay T2DM and in some cases return their blood glucose levels to normal [15, 16]. Intensive glycemic management has also been shown to have beneficial effects on cardiovascular disease (CVD) complications, suggesting that maintaining normoglycemia is a must in patients with pre-diabetes [17]. Persistent efforts are thus needed to educate the people in general, and overweight and obese persons who have IFG in particular about the benefits of losing weight and increasing physical activity. This approach should be the first to achieve appropriate glycemic control and reduce cardiovascular risk factors, mainly hypertension and hyperlipidemia. There has also been accumulating evidence from our previous studies on the beneficial effects of improving vitamin D status in T2DM subjects [18, 19] and non-diabetic subjects [20]. However there is little evidence on the benefits of increasing vitamin D in subjects with IFG, specifically in this region where the prevalence of both diabetes and vitamin D deficiency are high.

Therefore the aim of the current study was to evaluate the health benefits of a 3-month self-monitoring lifestyle intervention programme which included increased sunlight exposure. In particular, this study examined the effective beneficial impact on overweight and obese subjects with IFG and whether there are age-specific responses to the lifestyle modification programme.

Methods

Subjects

A total of 221 overweight and obese Saudi subjects with fasting blood glucose of 5.6-6.9 mmol/l and age range of 12-70 years agreed for this interventional study. They were selected from the already existing data on Riyadh 2 cohort [4]. They were recruited from different public schools and health centers associated with Biomarkers Research Program (BRP) at King Saud University (KSU), Riyadh, Saudi Arabia. For adolescents, parental consent was also obtained. Pregnant subjects, and anyone with complications such as renal, neurologic, hepatic and pulmonary diseases, and acute conditions that require immediate medical attention, were excluded from the present study. Those taking any sort of medication including vitamin D supplements as well as those who have already been part of other nutrition and lifestyle programs were also excluded from the study. Based from the questionnaire, all subjects had a sedentary lifestyle prior to inclusion as noted in the presence or absence of physical activity. The study was performed in accordance with the ethical principles in the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of the College of Medicine, KSU, Riyadh, Saudi Arabia.

Clinical assessment

Participating subjects were requested to return to their respective schools and primary health care centers (PHCCs) after an overnight fast for anthropometry and blood withdrawal. Anthropometry was measured and included height (to the nearest 0.5 cm), weight (to the nearest 0.1 kg) utilizing a standardized measuring tape in cm; and BMI (calculated as kg/m^2). Resting blood pressure was measured twice by the standard procedure and the average was recorded. Blood was transferred im-

Table 1. Anthropometric and metabolic changes of all subjects in 3-month of follow up

N		221	
Age (years)		33.8 ± 15.7	
Female/Male		147/74	
	Baseline	3-Months	*P*-value
BMI (Kg/m^2)	32.94 ± 5	32.77 ± 5.1	0.07
Systolic BP (mmHg)	126 ± 19.6	124 ± 18.5	8.6×10^{-4}**
Diastolic (mmHg)	77 ± 14	75 ± 12.7	0.001**
Total Cholesterol (mmol/l)	4.29 ± 1.2	4.17 ± 1.4	0.157
Glucose (mmol/l)	6.2 ± 0.4	6.01 ± 0.7	2.2×10^{-4}**
HDL-Cholesterol (mmol/l)	0.98 ± 0.2	0.93 ± 0.3	0.003**
Triglycerides (mmol/l)	1.59 ± 0.8	1.58 ± 0.7	0.953
LDL-Cholesterol (mmol/l)	3.04 ± 1.1	2.95 ± 1.2	0.23
25(OH) D (nmol/l)	33.87 ± 17.3	36.63 ± 20.3	7.6×10^{-5}**

Note: Values are presented in terms of Mean ± Standard Deviation. **P*-value <5% significance level, ***P*-value <1% significance level.

mediately to a non-heparinized tube for centrifugation.

Laboratory parameters

Fasting blood glucose and lipid profile were measured using a chemical Analyzer (Konelab, Vantaa, Finland). Total 25(OH) vitamin D was measured using COBAS e-411 automated analyzer (Roche Diagnostics, Indianapolis, IN, USA). All sample measurements were done in BRP, a participating laboratory for DEQAS (vitamin D External Quality Assessment Scheme) based in UK. All the measurements were repeated after 3 months of follow up.

Lifestyle intervention

The subjects recruited were educated at baseline visit about lifestyle modifications from successful intervention programs done elsewhere [21, 22] like total intake of fat less than 30% of energy consume and increased fiber intake to at least 15 g/1000 kcal. These subjects also received individual guidance on increasing their level of physical activity. They were advised to focus on self-monitoring, eating behaviors, reducing refined carbohydrate and sugar intake, and increasing protein intake. In addition, they were given verbal advice to increase their access to sunlight for 5 to 30 minutes at least twice a week either before 10:00 am and/or after 3:00 pm. The orientation and intervention was conducted by certified nutritionist, physician, nurse and physical therapists that reinforced instructions to the subjects on regular basis. The methodology of the intervention programme is already published in detail [23].

Data analysis

Collected data was analyzed using SPSS version 16.5 for windows (Chicago, Illinois, USA). Descriptive statistics were summarized as the mean ± standard error for continuous variables and as frequencies for categorical variables. Paired T-test was done to determine intervention effects in anthropometric and metabolic parameters at baseline and at 3 months follow up. Pearson correlation coefficients between vitamin D concentration and all other variables were calculated. Prevalence of the cardiometabolic risk factors was shown as frequencies (%) and Chi-square (McNemar test) was used to determine differences. All *P* values were based on two-sided tests of significance and a value of <0.05 was considered significant.

The subjects were divided into 3 groups based on the age. Group 1 (adolescent group) with age range from 12-17; Group 2 (young adults) with age range from 18-45 and Group 3 (Older subjects) with age range from 46-70.

Results

Table 1 highlights the characteristics of all subjects recruited for the study. A total of 221 subjects completed the study. There was a significant improvement in FBG, systolic and diastolic blood pressure, and vitamin D levels with *P*-values of 2.2×10^{-4}, 8.6×10^{-4} and 0.001, and 7.6×10^{-5} respectively. There is no significant improvement in BMI and lipid levels. However HDL-cholesterol has decreased significantly in 3 months of study period (*P* value =0.003). **Table 2** highlight the changes in metabolic parameters in individual age groups at 3 months of follow up compared to the baseline. Significant improvement was seen in FBG with a decrease noted in both group 1 (P=0.003) and group 2 (P=0.035). Systolic and Diastolic pressure also showed an improvement in group 1 (P=0.029 and 0.006) and 2 (P=0.001 and

Table 2. Anthropometric and metabolic changes of subjects in three age groups in 3-month of follow up

	Group 1			Group 2			Group 3		
N (% of total subjects)	77 (34.8)			76 (34.4)			68 (30.8)		
Age (years)	15.2 ± 1.6			36.3 ± 5.1			51.9 ± 6.0		
Female/Male	43/34			59/17			45/23		
	Baseline	3-Month	*P*-value	Baseline	3-Month	*P*-value	Baseline	3-Month	*P*-value
BMI (Kg/m^2)	32.31 ± 5	31.99 ± 5.4	0.109	33.73 ± 5.3	33.8 ± 5.3	0.459	32.77 ± 4.5	32.49 ± 4.5	0.008**
Systolic BP (mmHg)	130 ± 18.1	127 ± 17.1	0.029*	122 ± 15.7	119 ± 14.6	0.001**	126 ± 23.9	125 ± 22.9	0.526
Diastolic BP (mmHg)	74 ± 11.7	71 ± 9.7	0.006**	78 ± 13.3	76 ± 13.3	0.05*	80 ± 16.3	79 ± 13.6	0.332
Total Cholesterol (mmol/l)	3.55 ± 1	3.09 ± 0.8	0.003**	4.77 ± 1.2	4.83 ± 1.3	0.685	4.59 ± 1.1	4.65 ± 1.2	0.735
Glucose (mmol/l)	6.16 ± 0.3	5.9 ± 0.7	0.003**	6.22 ± 0.4	6.02 ± 0.7	0.035*	6.24 ± 0.4	6.1 ± 0.7	0.188
HDL-Cholesterol (mmol/l)	0.87 ± 0.2	0.83 ± 0.2	0.071	1.01 ± 0.3	1 ± 0.3	0.545	1.07 ± 0.2	0.97 ± 0.3	0.057
Triglycerides (mmol/l)	1.33 ± 0.7	1.34 ± 0.6	0.897	1.6 ± 0.8	1.71 ± 0.7	0.278	1.86 ± 0.9	1.73 ± 0.7	0.294
LDL-Cholesterol (mmol/l)	2.45 ± 1	2.03 ± 0.7	0.002**	3.43 ± 1.2	3.52 ± 1.1	0.533	3.29 ± 1	3.35 ± 1.1	0.679
25(OH) D (nmol/l)	28.1 ± 11.8	28.6 ± 15.8	0.702	34.8 ± 19.3	40. 9 ± 21.4	3.6×10^{-6}**	39.3 ± 18.3	40.97 ± 21	0.116

Note: Values are presented in terms of Mean ± Standard Deviation. **P*-value <5% significance level. ***P*-value <1% significance level. Group 1 (12-17 years); Group 2 (18-45 years) and Group 3 (46-70 years).

Table 3. Associations of 25(OH) vitamin D to metabolic parameters according to age groups

Parameters	All (N=221)		Group 1 (N=77)		Group 2 (N=76)		Group 3 (N=68)	
	Baseline	3-Month	Baseline	3-Month	Baseline	3-Month	Baseline	3-Month
BMI (Kg/m^2)	-0.02	-0.05	-0.09	-0.16	0.02	-0.01	-0.05	-0.14
Systolic BP (mmHg)	-0.02	0.01	0.10	0.18	-0.09	-0.01	0.02	0.001
Diastolic BP (mmHg)	-0.18*	-0.25**	-0.23*	-0.26*	0.18	-0.27*	-0.09	-0.26*
Total Cholesterol (mmol/l)	-0.06	-0.09	-0.03	-0.03	-0.05	-0.14	-0.14	-0.08
Glucose (mmol/l)	0.11	-0.17*	0.07	-0.09	0.07	-0.31**	0.14	-0.18
HDL-Cholesterol (mmol/l)	0.09	0.15*	-0.06	0.03	0.04	0.18	-0.08	-0.03
Triglycerides (mmol/l)	0.09	0.12	-0.01	0.03	0.06	0.02	-0.004	0.09
LDL-Cholesterol (mmol/l)	-0.05	-0.18	0.03	0.03	-0.07	-0.12	-0.03	-0.10

Note: Data presented as correlation coefficient (R); *denotes significance at P<0.05. **denotes significance at P<0.01. Group 1 (12-17 years); Group 2 (18-45 years) and Group 3 (46-70 years).

0.05) respectively. Group 2 showed an increase in vitamin D levels ($P=3.6\times10^{-6}$) whilst group 3 appeared to only reduce their BMI significantly (P=0.008). Total cholesterol and LDL-cholesterol showed a significant decrease in only group 1 (*P*-values 0.003 and 0.002 respectively).

Table 3 shows the association of serum vitamin D levels to anthropometric and metabolic parameters at baseline as well as after 3 months. Glucose was significantly associated with vitamin D at 3 months in all subjects (inverse correlation, R=-0.17); and in group 2 at 3 months (R=-0.31). Diastolic blood pressure was significantly associated in all subjects and group 1 at baseline as well as 3 months (inverse correlation, R =-0.18 and -0.25 respectively in all subjects, and R=-0.23 and -0.26 respectively in group 1); and in group 2 and group 3 at 3 months (R=-0.27 and -0.26 respectively). **Table 4** shows the decrease in weight and changes in cardiometabolic risk factors over the study period of 3 months when compared from baseline. Prevalence of hypertension decreased significantly in all subjects (from 29.4% to 23.5%); and in group 1 (from 31.1% to 22.1%) and group 2 (from 22.4% to 15.8%). Prevalence in vitamin D deficiency reduces significantly in group 2 (from 77.6% to 67.1%). Also, 4.1% of overall subjects had a decrease of their weight by at least 5% (from baseline weight) in the three months of study.

Figure 1 shows the improvement in prevalence of glycemic status after three months of follow up. 23.6% of all subjects were able to normalize their FBG levels after 3 months. Almost the same phenomenon was observed in individual age groups with 27.3%, 25% and 17.6% of group 1, 2 and 3 respectively able to normalize their FBG levels.

Table 4. Changes in weight and in risk factors over time

	All subjects		Group 1		Group 2		Group 3	
	Baseline	3-month	Baseline	3-month	Baseline	3-month	Baseline	3-month
1-4.9% decrease in weight		24.4		16.9		21		36.8
5-10% decrease in weight		3.6		6.5		0		4.4
>10% decrease in weight		0.5		1.3		0		0
Obesity	66.9	66.5	53.2	52.9	71.1	69.7	77.9	76.5
Hypertension	29.4	23.5**	31.1	22.1**	22.4	15.8**	35.3	33.8
Hypertriglyceridemia	36.2	38.9	24.7	27.3	31.6	43.2	54.4	47.1
Vitamin D Deficiency	79.6	75.1	94.8	88.3	77.6	67.1*	64.7	69.1

Note: Data presented as percentages (%); Decrease in weight is in 3 months of follow up compared to baseline weight. Group 1 (12-17 years); Group 2 (18-45 years) and Group 3 (46-70 years); *denotes significance at P<0.05 for prevalence after follow up compared to baseline; **denotes significance at P<0.01 for prevalence after follow up compared to baseline; Obesity taken as BMI ≥30 kg/square meter; Hypertension taken as Systolic BP>145 mmHg and/or diastolic BP>85 mmHg; Hypertriglyceridemia taken as serum triglyceride ≥1.7 mmol/l; and Vitamin D deficiency taken as serum 25(OH) vitamin D <50 nmol/l.

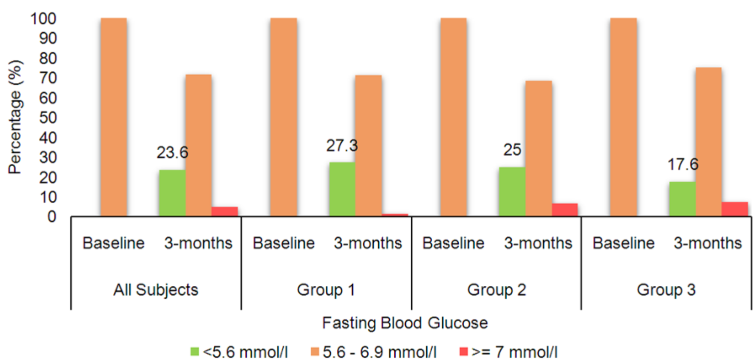

Figure 1. Glycemic status at baseline and after 3 months of self-monitoring. Group 1 (12-17 years); Group 2 (18-45 years) and Group 3 (46-70 years). At baseline, all subjects had IFG (FBG 5.6-6.9 mmol/l). At follow up, 23.6% of all subjects, 27.3% of group 1 subjects, 25% of group 2 subjects and 17.6% of group 3 subjects were able to normalize their FBG levels.

Discussion

To the best of our knowledge, this is the first report on Middle Eastern population that studied the importance of self-monitored lifestyle modifications exclusively on overweight and obese subjects with impaired fasting glucose. The significant finding in this interventional study was that FBG, vitamin D levels, systolic and diastolic blood pressure improved significantly only in younger people whilst in older subjects there was a significant decrease in BMI, not observed in younger subjects. Also, almost 1/4th of the all subjects (23.6%) were able to normalize their FBG in three months of this interventional study.

When the data was analyzed in all subjects, there was an improvement in the glycemic status, vitamin D levels, systolic and diastolic blood pressure at 3 months of follow up compared to the baseline. Al-Zahrani and colleagues [24] reported no significant change in glycemic status and systolic blood pressure in a vitamin D supplementation study of same duration. However, the increase in vitamin D levels in that study was much higher than our study. This may be because in the study referenced, the investigators have used an oral vitamin D supplementation (45000 IU/week for 2 months and a single 45000 IU in the last month) while in our study the subjects were advised to increase the sun exposure, apart from other adjustments in their lifestyle including diet and physical activity.

When the changes in metabolic parameters and risk factors were compared in the three individual age groups, a marked difference was noted. Glycemic status improved significantly in the younger people (group 1 and 2) whilst the older people (group 3) benefitted only from the reduction of their BMI. However, the significant decrease in BMI in the older age group (group 3) did not translate into marked changes in other metabolic factors assessed in our study. FBG decreased significantly in young adult group (P=0.035) and adolescents (P=0.003) while for group 3 subjects, the reduction in fasting blood glucose levels at 3 months of follow up was insignificant (P=0.188). This indicated that weight loss through dietary changes and increasing physical activity may not be the only factor when it comes to lifestyle intervention programmes and should not be generalized for all age groups. Individualized programmes for different age groups might hold the key for effective lifestyle modification programmes. More lifestyle modification based studies are needed though to add to this idea.

Systolic and diastolic blood pressure reduced significantly in groups 1 and group 2 only. This was also seen in the change in prevalence of hypertension where a significant reduction was observed in both these groups. A possible explanation may come from improved vascular and endothelial function. Total cholesterol levels also decreased significantly in group 1 subjects. Epidemiological investigations have found that hypertensive patients frequently have a concomitant increase in serum total cholesterol levels [25], whilst the endothelium plays a role in the regulation of blood pressure. For group 2, the significant decrease in blood pressure might be due to the parallel increase in vitamin D levels. Many observational and interventional studies have focused on role of vitamin D metabolites in the development of hypertension, the most notable mechanism being its role as a negative regulator of renin angiotensin system [26].

Another important finding is the significant decrease in HDL-cholesterol for all subjects overtime, though this significance was lost when individual age groups were considered. Low HDL-cholesterol is already the most common metabolic syndrome component among Saudis with 90% of adults [27] and almost 80% of adolescents [28] harboring this condition. This lack of improvement in lipid profile especially HDL-cholesterol may be in line with some of the recent published articles questioning the role of vitamin D status correction in a meaningful clinical change in lipid profile [29]. It may otherwise be simply because of the short duration of this study and 3 months may not be enough to see apparent changes in lipid profile. A longer duration, probably 6-12 months, of self-monitoring of lifestyle modifications, including possible manipulation of gut flora [30], is warranted to achieve better results.

The authors acknowledge some limitations of this study and findings should be interpreted with caution. The short duration (3 months) of this study, as mentioned above, may have influenced the results. Also the study was not designed to test the relative contributions of dietary changes, increased physical activity, and increased sunlight exposure in reducing the cardiometabolic risk factors, and the effects of these components remain to be determined. Nevertheless, the study has merits in being the first to observe effects of self-monitoring of lifestyle modifications in Saudi adolescents and adults in an age specific manner, and in its recruitment of high risk overweight and obese subjects suggesting overweight and obese people, if properly guided via intervention programs, are willing to participate and possibly change a sedentary lifestyle.

In summary, the present study showed differences in age-specific benefits to a lifestyle intervention programme of 3 months in overweight and obese Saudi subjects with IFG. An improved FBG and vitamin D status was found in younger people whilst older people only appear to substantially improve their BMI at 3 months of follow up. As such these studies highlight that intervention in the young could provide benefits for long-term health whilst these benefits would appear to be reduced with age. Further interventional studies with a longer duration and with a larger cohort in individual age groups is warranted to elicit better clinical conclusions.

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Disclosure of conflict of interest

None.

Author's contribution

MA and HA conceived the study, oversaw study execution, and contributed to manuscript writing. MA, MSA and OSA recruited subjects and collected data. KW analyzed samples. NMA and KW performed data analysis. KW wrote the manuscript. NJA and OSA reviewed/edited the final version of the manuscript. All authors approved the final manuscript.

Abbreviations

T2DM, Type 2 diabetes mellitus; IFG, impaired fasting glucose; Yr, Year; FBG, Fasting blood glucose; BMI, Body mass index; BRP, Biomarkers Research Programme (laboratory at King Saud University, Saudi Arabia); 25(OH) Vitamin D, 25-hydroxy Vitamin D. In this article wherever Vitamin D is mentioned, it means 25-hydroxy Vitamin D.

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