Original Article

Role of Vitamin D Deficiency on The Microscopic Structure of Pancreas and Potential Induction of Diabetes in Albino Rats

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ABSTRACT

Background: Vitamin D3 has the potential to modulate both endocrine and immune system. Evidence increased on non-classical role of vitamin D (Vit. D) in many autoimmune diseases. Vitamin D deficiency is considered as a global health problem and has been suggested -based on animal studies- to be associated with prevalence of glucose intolerance.

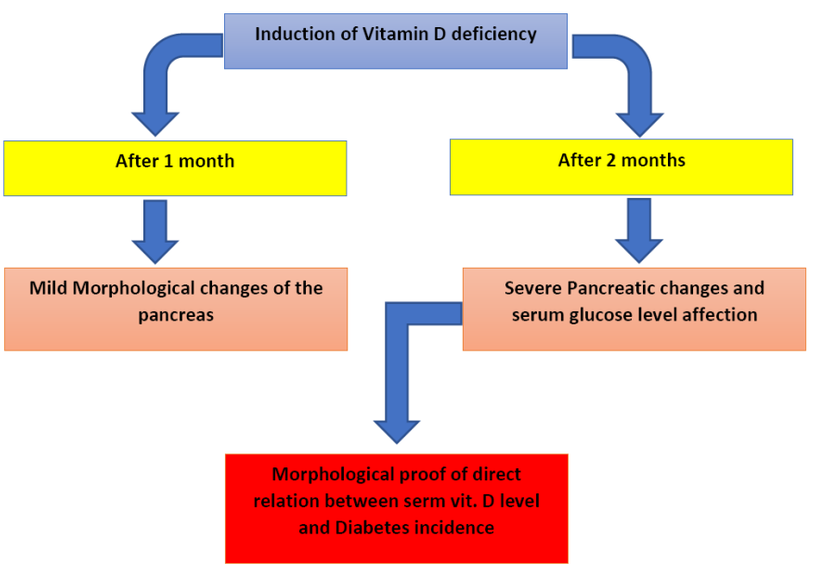
Aim: To investigate the effect of vitamin D deficiency on blood glucose level and microscopic structure of pancreas of albino rat.

Material and Methods: Thirty adult male Wistar albino rats were used in the current study and were divided into two groups. Group I (Control) was fed vit. D balanced diet and exposed to sun light, and Group II was fed vit. D deficient diet and deprived from sun light exposure. Group II was further subdivided into subgroup (IIa) which was sacrificed after 1 month, and subgroup (1Ib) which was sacrificed after 2 months. Pancreata were collected from all rats of all groups and were prepared for histopathological examination. Morphometric measurements were done using image analyzer and blood glucose level was measured and all data were statistically analyzed.

Results: Subgroup IIa showed fewer and smaller islets of Langerhans compared with those of the control group, while Subgroup IIb showed disfigurement of the islets, with marked decrease in their number and size. Highly significant increase in blood glucose level was detected in rats of subgroup IIb compared to the control group.

Conclusion: There is an inverse correlation between serum vitamin D and insulin resistance. Persistent vitamin D deficiency status may lead to metabolic disorders including insulin resistance and raised blood glucose.

Graphical Abstract



Effect of Induced Vitamin D Deficiency on the Pancreas of Albino Rats

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Key Words: Diabetes, pancreas, vitamin D.

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INTRODUCTION

The molecular structure of vitamin D resembles that of classic steroid hormones as both contain the same root ring structure and so classified as a secosteroid[1]. Wide recognition of vitamin D role in many functions has been reported aside from its classic function in mineral absorption and skeletal remodeling. The steady-state serum concentration of 25 (OH) D is proved to be associated with enhanced health[2]. The known biological function of vitamin D is to maintain normal serum calcium and phosphorus concentrations levels, facilitating their small intestinal absorption from diet[3]. Vitamin D receptors (VDR) are ligand-inducible nuclear receptors. They are involved in several physiological processes, including bone metabolism, immune regulation, cell proliferation and differentiation. VDR-ligand complex play an important role in the pathogenesis and therapy of different pathologies such as osteoporosis, arthritis, psoriasis, and cancers[4]. Owing to its biological importance, serum level of vit. D concentration had to be followed up, and the best indicator for its intake is serum 25 (OH) D concentration. Serum 25 (OH) D concentrations below 20ng/mL indicates sever vit. D deficiency[5].

Globally, vit. D deficiency is reported to be associated with increased risk of sepsis, cardiovascular and metabolic disorders (e.g. hyperlipidemia, type 2 diabetes mellitus, acute vascular events, dementia, stroke, and heart failure). Also, vit. D inadequacy was reported to increase the risk of several cancer morbidities[6].

Several in *vivo* studies reported the possible influence of long term vit. D deficiency in inducing type 1 diabetes mellitus (T1DM) in a mouse model. The 1, 25 (OH) 2 D3 or its non-hypercalcemic analogues were reported to inhibit the pancreatic inflammations and were protective against diabetes. Also, vit. D deficiency was reported to affect β -cell function, impair glucose tolerance, and increase mortalities from type 2 diabetes mellitus (T2DM) across age and ethnic groups. Vit. D deficiency has been correlated to impaired glucose clearance and insulin secretion in rat and rabbit models, with improvement after vitamin D repletion independently of dietary intake and calcium homeostasis[7].

1, 25-dihydroxyvitamin D plays an important role in glucose homeostasis by different mechanisms. It not only improves insulin sensitivity of the target cells (liver, skeletal muscle, and adipose tissue), but also enhances and improves β-cell function. In addition, 1, 25-dihydroxyvitamin D protects β-cells from detrimental immune attacks, directly by its action on β-cells, and indirectly by acting on different immune cells, including inflammatory macrophages, dendritic cells, and a variety of T cells. Macrophages, dendritic cells, T- lymphocytes, and B-lymphocytes can synthesize 1,25 dihydroxy vitamin D, hence contributing to the regulation of local immune responses[8].

Vitamin D is an important field of investigation of the pathophysiology of DM, since its deficiency is commonly discovered in patients with diabetes compared to normal population. Recent studies suggested that it can improve peripheral insulin sensitivity and glucose metabolism, and the exact pathophysiological mechanism needs to be further investigated[9]. Hence, the present study aimed to investigate the effect of vitamin D deficiency on blood glucose level and microscopic structure of pancreas of albino rat.

MATERIAL AND METHODS

Ethical Statement

The present study was approved by the Research Ethics Committee of the Faculty of Medicine, Ain Shams University (FMASU-REC). FMASU-REC is organized and operated according to guidelines of the International Council of Harmonization (ICH) Anesthesiology, the United States Office for Human Research Protections and the United States Code of Federal regulations and operates under Federal Wide Assurance No. FWA 00017585 (approval number 281/2015).

Study design

The current experiment aimed to induce dietary vitamin D deficiency to the experimental animals for a duration of two months. Then, after reaching the target duration, animals were sacrificed, and target organs (pancreata) were extracted and prepared for histopathological examination using different techniques.

Animals

The experiment was carried according to the guidelines of the Committee of the Animal Research Ethics (CARE) at Ain Shams Faculty of Medicine. Thirty adult male, Wistar albino rats, weighing “160-200 gm” were obtained from the Animal House of medical research unit (MASRI), Faculty of Medicine, Ain Shams University, Cairo, Egypt.

Animals housing and husbandry

Prior to be utilized for the experimental purposes, rats were left for two weeks allowing them to acclimatize to the new environment. Rats were housed in metallic cages one rat per cage. The rats were allowed free water access with suitable environmental conditions.

Animals grouping

Group I: (control group) Formed of twelve rats that were fed Purified (AIN) 93M diet[10]. Rats in this group were exposed to the sun freely and a 12-hr light/dark cycle was maintained. Six rats were sacrificed after one month and the others were sacrificed after two months.

Group II: Formed of eighteen rats that were fed Purified (AIN) 93M diet deficient of vitamin D and were kept away from direct sun light to avoid any effect of the hyperparathyroidism secondary to vit. D deficiency, 2% Ca (carbonate) was added to the diet[11].

Rats in this group were further subdivided into 2 subgroups:

Subgroup IIa: Formed of nine rats that were sacrificed after one month.

Subgroup IIb: Formed of nine rats that were sacrificed after two months.

Diet

Diet composition

*AIN-93M mineral mix was formed of (Calcium carbonate, Potassium phosphate, Sodium chloride, Potassium sulfate, Potassium citrate, Magnesium oxide, Ferric citrate, Zinc carbonate, Manganous carbonate, cupric carbonate, Potassium iodate, Sodium selenite, Ammonium paramolybdate) (Table 1).

Table I: The composition of Purified (AIN) 93M diet

Ingredient	g/kg diet
Corn starch	465.5
Dextrin	155
Sucrose	100
Powdered cellulose (fiber)	50
Soybean oil	40
L-Cystine	1.8
AIN- 93M mineral mix* 35	
AIN- 93M vitamin mix** 10	
Casein	140

**AIN-93 vitamin mix was formed of (vitamin E, A, D3, K, nicotinic acid and B complex)[10].

Diet preparation

The dietary ingredients were obtained from El-Gomhouria® Co. for trading chemicals and medical appliances, Cairo, Egypt, and were mixed according to the required concentrations mentioned in table (I) using tap water as a mixing media. The fat-soluble vitamins (e.g., vit. A, E, K) were mixed in Maize oil then added to the diet. Diet was stored at 4°C in plastic containers.

Tissue preparation

At the beginning of the experiment and at the end of each month blood samples were obtained from the orbital venous plexus and sent to the laboratory for estimation of blood glucose level and vitamin D level.

At the end of the experiment, all rats were sacrificed by an overdose of ether inhalation. The abdomen was opened to dissect the pancreas. The pancreata were collected from all groups. All pancreata were cut longitudinally into two halves. One half of each pancreas was put in 10% formalin fixative solution for 24 hours, dehydrated in ascending grades of ethanol, cleared in xylol, and embedded in paraffin. Sections of 5 µm thick were cut and stained with Hematoxylin & Eosin and Masson's trichrome then examined by light microscope.

Other half of each pancreas was immediately cut into very small pieces and fixed in 2% glutaraldehyde solution for 3 hours washed with 0.1% phosphate buffer PH 7.3. Specimens were further cut into 1 mm3 pieces and left in the fixative for another 24 hours in the refrigerator at 4°C. Specimens were then post fixed in osmium tetroxide for 1 hour. After dehydration, the specimens were embedded in Epon; semi thin sections (1 µm) were cut and stained by Toluidine blue.

All sections were examined by an Olympus light microscope (CX31) in Anatomy department, ASU, and photographed.

Morphometric analysis The measurements were done by using the image analyzer (TS View ® program) in Anatomy Department, Faculty of Medicine, Ain Shams University. The image analyzer was first calibrated automatically to convert the measurement units (pixels) produced by the image analyzer program into actual micrometer units. Each field was enclosed inside the standard measuring frame, and then the areas of islets of Langerhans were masked by a blue binary color to be measured. The area percentage of these islets was measured in H&E stained sections at total magnification of 400 in five non overlapping fields from five serial sections from five animals of each group[12].

Statistical analysis The data were analyzed by Graphpad prism, software program, version 5.0 (2007) (Inc., CA, and USA). Statistical difference among groups was determined using ANOVA followed by post hoc "Tukey Test". *P values* were obtained and interpreted as follows; $p>0.05$ were considered statistically insignificant, $p<0.05$ were considered statistically significant and $p<0.001$ were highly significant.

RESULTS

Biochemical results

Mean blood glucose level was non significantly increased ($P>0.05$) after one month of vit. D deficiency in subgroup IIa as compared to the control group. However, it was significantly ($p<0.001$) increased after two months of vit. D deficiency in comparison to control group and one-month deficiency subgroup (Bar chart I).

Light microscopic examination

Group I (control)

Examination of the paraffin sections of pancreas of this group, stained with hematoxylin and eosin showed that the pancreas was formed of exocrine tissue and endocrine islets of Langerhans (Figure 1). The exocrine part consisted of closely packed acini with very small lumen and very little connective tissue in-between (Figures 1,2).

The acinar cells were pyramidal in shape with basal deeply basophilic cytoplasm, rounded basally located nuclei and apical acidophilic zymogen granules. Blood capillaries were seen in-between the pancreatic acini (Figure 2). The endocrine part of the pancreas -represented by the islets of Langerhans- was seen as pale areas of non-encapsulated, highly demarcated variable-sized clusters of cells, scattered in-between the acini, and were most numerous in the tail of pancreas. The islets exhibited closely packed cells, with intervening blood capillaries with pale-stained Beta cells with large rounded central vesicular nuclei, and smaller Alpha cells with deeply stained nuclei (Figures 2,3). Masson's trichrome stain showed some collagen fibers surrounding the blood vessels in-between the acini. No collagen fibers were seen surrounding the islets of Langerhans (Figure 4). Toluidine blue stained semithin sections of the pancreas of this group clearly showed the pancreatic acinar cells were seen studded with their secretory granules. The islets of Langerhans clearly showed the Beta cells with large pale nuclei and apparently smaller Alpha cells with dark nuclei (Figure 5).

Subgroup IIa (vit. D deficient diet for one month)

Examination of the hematoxylin and eosin-stained paraffin sections of pancreas of this subgroup, showed no apparent change in the structure of pancreatic acini. Fewer and apparently smaller islets of Langerhans were seen as compared with those of the control group (Figure 6). However, a non-statistically significant decrease ($P>0.05$) in the mean area percentage of islets was detected as compared to the control group (Bar chart II). Separations between the cells inside some islets were obvious (Figure 7). Some islet cells exhibited karyolitic nuclei, and many others demonstrated vacuolated cytoplasm (Figure 8). Masson's trichrome stain showed the collagen fibers in the exocrine and endocrine components comparable to that of the control group (Figure 9). Semithin sections showed some Beta cells with dark nuclei dispersed in the islets. Apparently few Beta cells with pale vesicular nuclei were encountered (Figure 10).

Subgroup IIb (vit. D deficient diet for two months)

Examination of the paraffin sections of pancreas of this group, stained with hematoxylin and eosin showed marked decrease in the number and size of islets of Langerhans, with disfigurement in the shape of most of them (Figures 11,12). This was also documented by a statistically significant decrease ($p<0.001$) in the mean area percentage of islets as compared to the control group and to subgroup IIa (Bar chart II). Most of the islet cells showed cytoplasmic swelling, and cytoplasmic vacuolations in many cells (Figures 13,14). There were wide separations between the islet cells, and congestion of most of the capillaries inside the islets (Figure 14), and in-between the pancreatic acini (Figures. 11,14). Ill-defined demarcation was noticed between some islets and the surrounded exocrine tissue (Figure 14). Masson's trichrome stain showed apparent increase in the collagen fibers content surrounding the blood vessels in-between the pancreatic acini, as compared to that of the control group and subgroup IIa (Figure 15). Semithin sections of the pancreas of this subgroup showed the pancreatic acinar cells comparable to the control group. The islets were seen were small and disfigured in focal areas. Fewer cells were observed in some of the islets as compared to the control group and subgroup IIb. Pyknotic features were obvious in nuclei of some islet cells, while other cells were hyperactive showing multiple prominent nucleoli (Figures 16,17). Cytoplasmic swelling was seen in most of the cells in some islets (Figure 18).

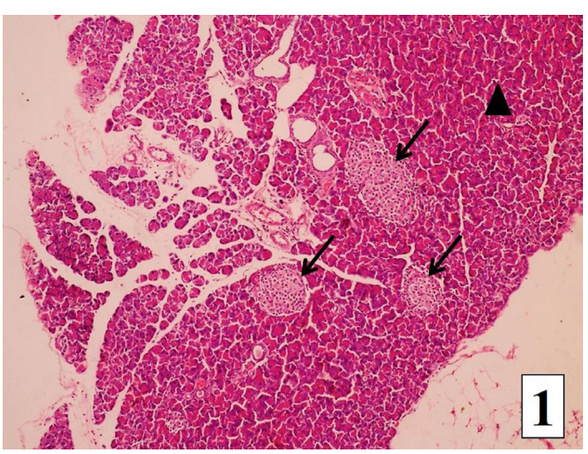


Fig. 1: Showing rounded to oval islets of Langerhans (↑) surrounded by apparently normal pancreatic acini of the exocrine tissue (▲). (Control group, H&E x 100)

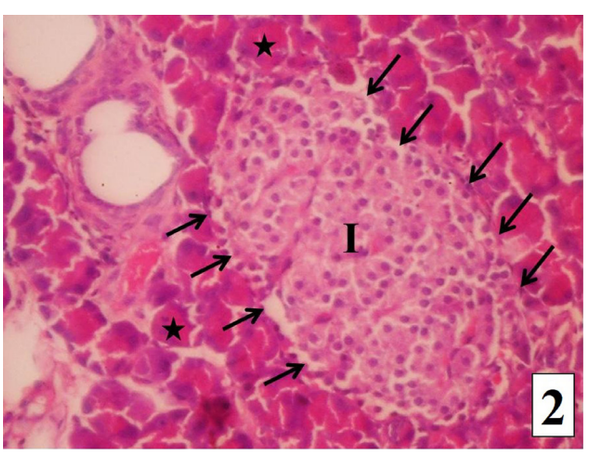


Fig. 2: Showing islet of Langerhans (I) surrounded by pancreatic acini (stars) with well-defined demarcation between them (↑). (Control group, H&E x 400)

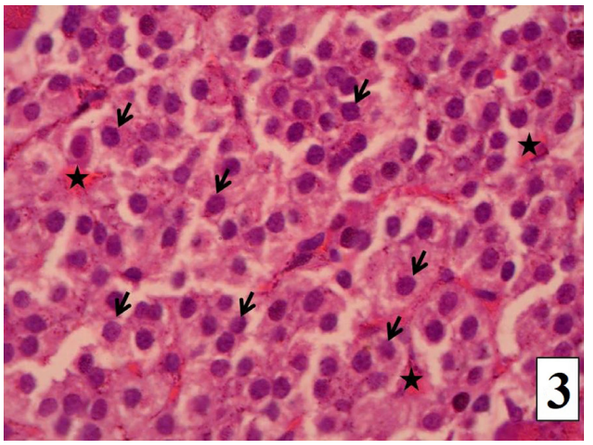


Fig. 3: Showing numerous cells with rounded nuclei (↑). Note many capillaries between the islet cells (stars). (Control group, H&E x 1000).

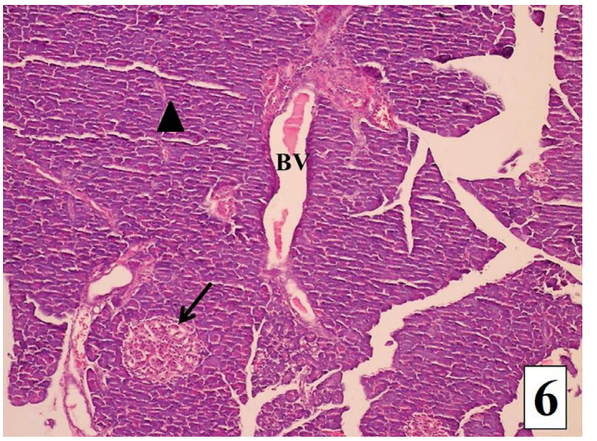


Fig. 6: Showing the exocrine acini (▲), Blood vessel (BV), and few small islets of Langerhans (↑). (Vit. D deficient diet for one month, H&E x 100).

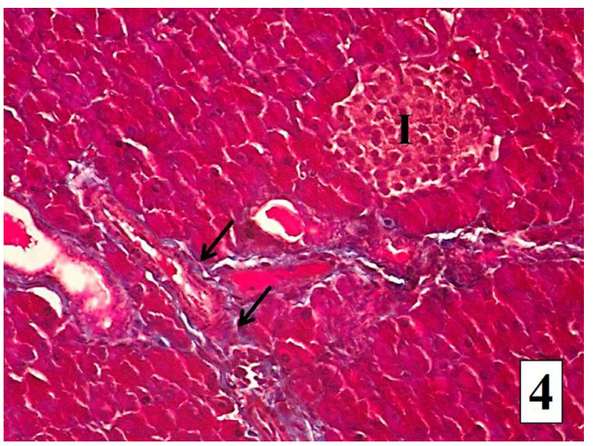


Fig. 4: Showing the collagen fibers surrounding the blood capillaries (↑). No collagen is seen surrounding the islet (I). (Control group, Masson's trichrome x 400).

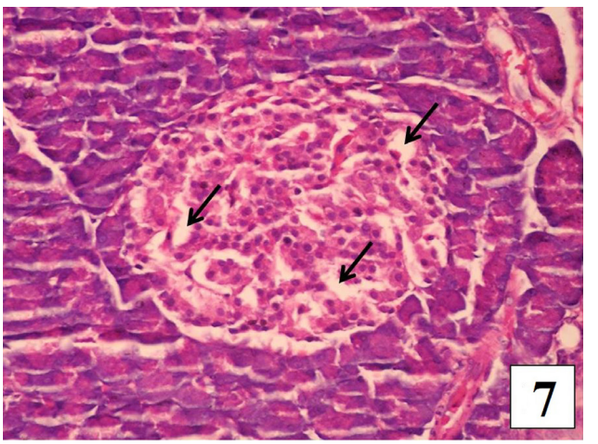


Fig. 7: Showing islet of Langerhans with wide spaces between its cells (↑). (Vit. D deficient diet for one month, H&E x 400).

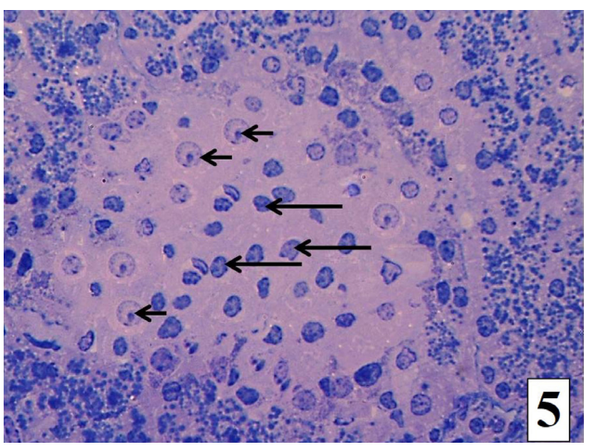


Fig. 5: Showing islets cells with large rounder vesicular nuclei (short ↑), and the small apparently darker nuclei in others (long ↑). (Control group, Toluidine Blue x 1000).

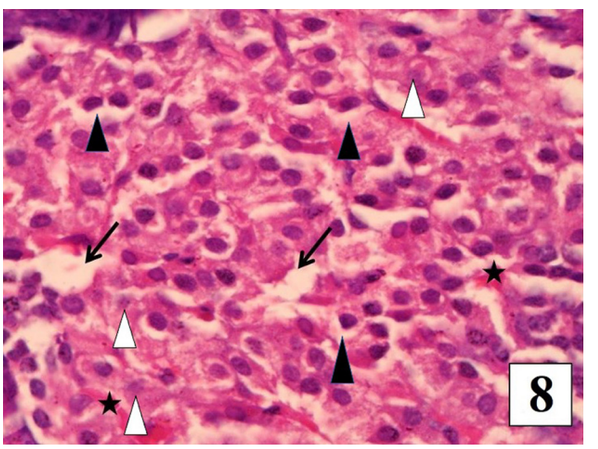


Fig. 8: Showing karyolytic nuclei in some cells of the islet (Δ). Cytoplasmic vacuolations can be also seen in some cells (▲). Notice the separation (↑) between the islets' cells, and the intervening blood capillaries (stars). (Vit. D deficient diet for one month, H&E x 1000).

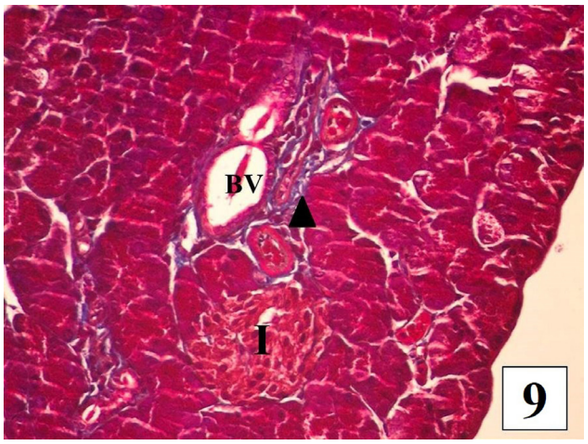


Fig. 9: Showing the collagen fibers (▲) surrounding the blood vessels (BV). No collagen fibers are seen in or surrounding the islet of Langerhans (I) (Vit. D deficient diet for one month, Masson's trichrome x 400)

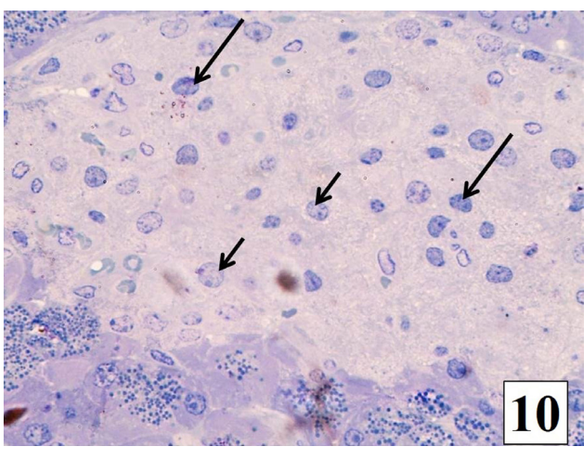


Fig. 10: Showing Few Beta cells with vesicular nuclei (Short ↑). Beta cells with deeply stained nuclei are seen dispersed inside the islet (Long ↑). (Vit. D deficient diet for one month, Toluidine Blue x 1000).

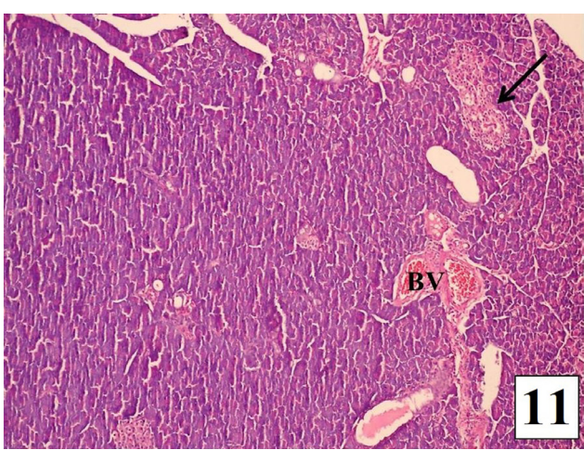


Fig. 11: Showing disfigured islet of Langerhans (↑). Notice the congested blood Vessel (BV). (Vit. D deficient diet for two-months, H&E x 100).

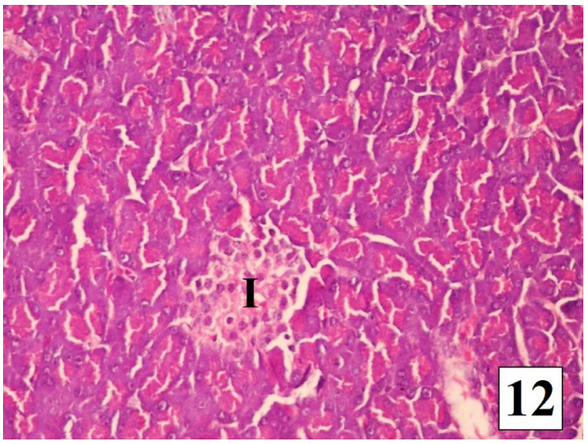


Fig. 12: Showing single small islet of Langerhans (I). (Vit. D deficient diet for two-months, H&E x 400).

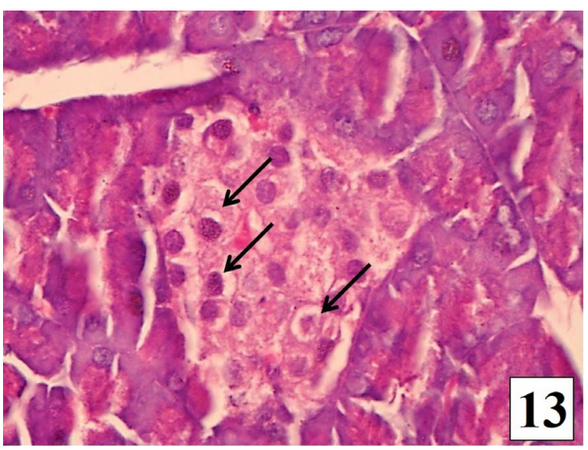


Fig. 13: Showing small disfigured islet with cytoplasmic swelling and vacuolations of most of its cells (↑). (Vit. D deficient diet for two-months, H&E x 1000).

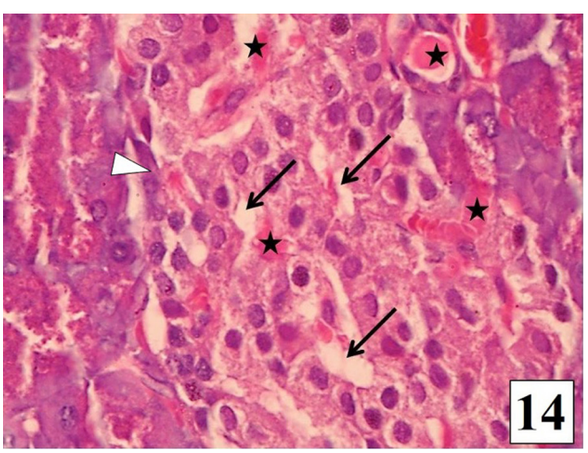


Fig. 14: Showing wide separation (↑) between the islet cells, and congested capillaries (stars). Notice the ill-defined demarcation between the islet and the pancreatic acini (Δ). (Vit. D deficient diet for two-months, H&E x 1000).

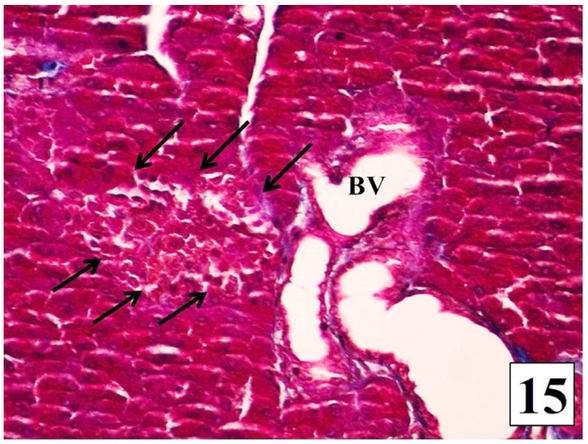


Fig.15: Showing the collagen fibers surrounding the blood vessels (BV). A small islet with irregular outline can be seen (↑). (Vit. D deficient diet for two-months, Masson's trichrome x 400).

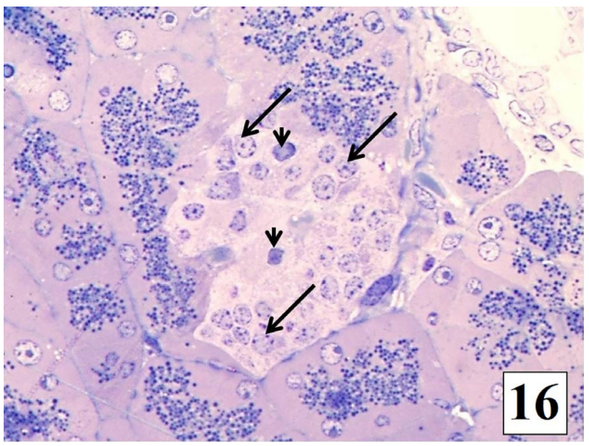
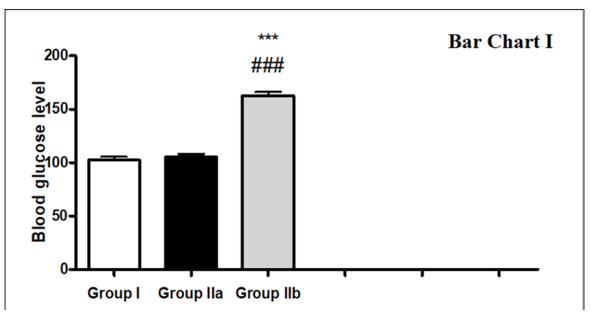


Fig.16: Showing a disfigured islet containing large vesicular hyperactive nuclei with multiple nucleoli in some cells (long ↑), and small darker nuclei of other cells (short ↑). (Vit. D deficient diet for two-months, Toluidine Blue x 1000).



Bar chart 1: Blood glucose level was significantly (p<0.001) increased after two months in comparison to control and one-month deficiency groups. ***p<0.001; in relation to control group, ### p<0.001; in relation to one-month deficiency group. Data are presented as mean± SEM. Analysis by one-way ANOVA, post hoc: tukey's test.

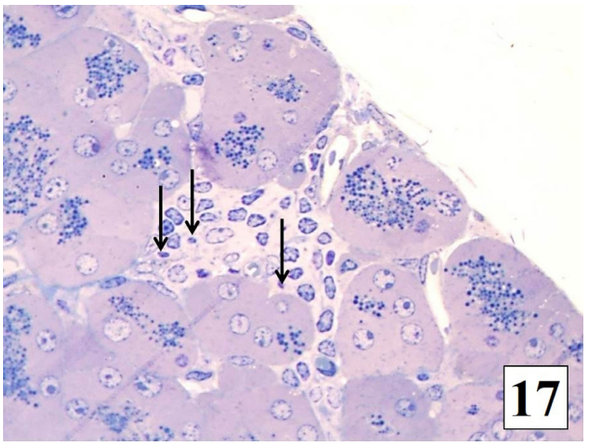


Fig.17: Showing disfigured islet with some pyknotic nuclei (↑). (Vit. D deficient diet for two-months, Toluidine Blue x 1000).

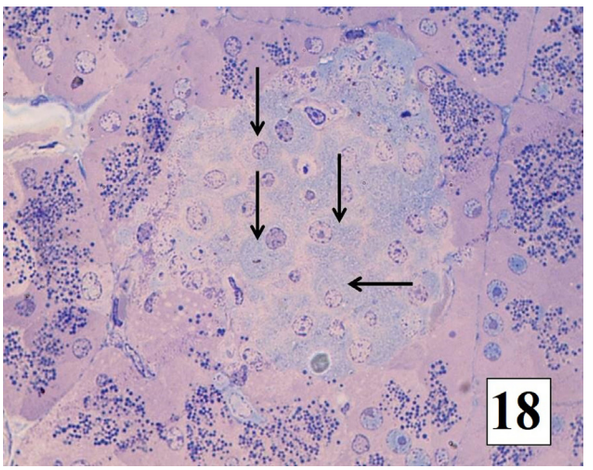
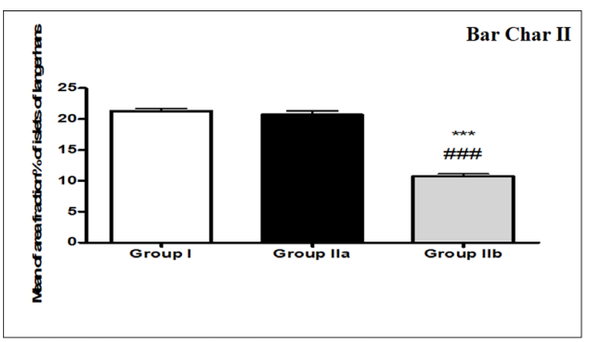


Fig.18: Showing an islet containing apparently swollen cells (↑). (Vit. D deficient diet for two-months, Toluidine Blue x 1000).



Bar chart II: Mean area of percentage of islets of Langerhans was significantly (p<0.001) decreased after two months in comparison to control and one-month deficiency groups. ***p<0.001; in relation to control group, ### p<0.001; in relation to one-month deficiency group. Data are presented as mean± SEM. Analysis by one-way ANOVA, post hoc: tukey's test.

DISCUSSION

Previous studies concerned with vitamin D deficiency in relation to Diabetes Mellitus focused on blood insulin levels, blood glucose levels and vitamin D receptors gene expression, while the current study focused on the histological impact of this deficiency, and on the microscopic structure of the pancreas itself, with special emphasis on the islets of Langerhans.

The current work revealed that dietary deficient in vitamin D and sun deprivation for one month slightly affected the histological structure of the islets. However, the blood glucose level showed non-significant changes compared with those of the control group. This agreed with a previous study which stated that induction of hypovitaminosis D, taking in consideration the precautions to prevent hyperparathyroidism, can be established after three weeks of vitamin D deficient diet[11]. In addition, vitamin D deficient diet and sun deprivation for two months in the present work produced marked effect on the histological structure of the islets of Langerhans, regarding their number, size and cells' structure. These findings were consistent with the observation of previous researches[13,14] which reported that T1DM (type 1 diabetes mellitus) led to a significant reduction in pancreatic islet size. However, it was observed that some islets in diabetics might be very large in diameter because of edema and deposition of amyloid[15]. Besides that, significant reduction of islets of Langerhans' area percentage was detected after two months of vit. D deficiency in the present study. Same finding was also previously reported in diabetic rats, where the number of islets were much lower than in non-diabetic rats[16]. This was also proved by another study which noted that a reduction in total islet mass in diabetic pancreas in T2DM (type 2 diabetes mellitus)[17].

In the present work, some of the islets were disfigured, and after one or two months of vit. D deficiency, the number of the cells inside each islet appeared reduced. These findings were documented earlier by other researchers who found that the islets of non-diabetic rats were oval while in diabetic rats were irregularly shaped with fewer total endocrine cells in the islets in diabetic rats[18].

Evidence of inflammation of the islets in T2DM was previously reported[19] and was even extensive in some cases (insulitis)[20]. This was attributed to increased level of cytokine or chemokine expression[19]. However, in the present study, no mononuclear cellular infiltration was observed.

In the current study, some of the cells showed apoptotic nuclear picture in the form of pyknosis. Similar observation was found in the form of a shrunk structureless nucleus characteristic for pyknotic cells in T1DM rats[21], and T2DM rats[22].

Insulin resistance in T2DM (type 2 diabetes mellitus) was reported to induce hyper-production of insulin (hyperinsulinemia) in the β-cell, and this explained the presence of some cells with hyperactive nuclei in some islets in focal areas in subgroup IIb the present work[23].

Many studies revealed that the pathogenesis of both types of diabetes mellitus is strongly related to the endoplasmic reticulum (ER) stress. This was proved in these studies by electron microscopic examination of the endoplasmic reticulum (ER) in β-cells that showed disruption and dilation as a sign of ER stress[21,24]. This might explain the cytoplasmic vacuolations which were seen in most cells of the islets in vit. D deficient subgroups of the present study. ER is a cellular compartment responsible for many important cellular functions including the biosynthesis and folding of newly synthesized proteins destined for secretion, such as insulin[23]. Overproduction of secretory proteins as in case of insulin resistance (hyperinsulinemia), leads to ER stress and if this stress exceeds the adaptive capacity of the ER, apoptosis and cell death will develop[25]. In this view, it was found that vit. D suppressed ER stress in monocytes and macrophages from diabetic patients and diet-induced vitamin D deficiency in mice increases macrophage ER stress[26]. So, this strongly suggests that the deficiency may have the same effect on the ER of the β-cell.

In the current study there was marked increase in the blood glucose levels associated with vit. D deficiency. Similarly, a study conducted with the help of healthy nondiabetic individuals, found that participants with vitamin D deficiency had significantly higher levels of glucose compared with those with normal vitamin level[27]. The elevation of blood glucose levels was considered as an evidence that vitamin D may stimulate pancreatic insulin secretion both directly and indirectly. The direct effect is exhibited when vitamin D binds to the nuclear VDR (vitamin D receptors) which was found in different tissues, including the pancreatic islet cells. The VDR activate the protein biosynthesis in pancreatic islets, therefore increasing the insulin secretion. The indirect effects of vitamin D may be mediated by regulating extracellular calcium and calcium flux through the cell. Insulin secretion is a calcium dependent process; therefore, alterations in calcium flux can have adverse effects on β-cell secretory function[27]. Prolonged treatment by vitamin D in Osteomalacia might also increase insulin secretion and improve glucose tolerance[28].

On one hand, accumulating evidence that a link between vitamin D levels and insulin sensitivity was observed and there was an inverse correlation between serum vitamin D and insulin resistance[29]. On the other hand, increased circulating vit. D resulted in significant decrease in systemic inflammation biomarkers. Considering the anti-inflammatory effects of vitamin D, persistent vitamin D deficiency status may lead to systemic inflammation and thereby other metabolic disorders including insulin resistance and raised blood glucose[30].

Vitamin D deficiency prevalence was proved to be higher in obese children compared to normal and

overweight children. Serum 25 (OH) D levels showed a negative correlation with insulin and insulin resistance independently of obesity[31]. Other studies added that vitamin D may stimulate the expression of the insulin receptor in peripheral tissues and thus increase glucose transport. Insulin-mediated processes are calcium dependent and therefore may be indirectly influenced by vitamin D level; also, vitamin D deficiency might be involved in the pathogenesis of insulin resistance[32].

Recent studies recommended injection of vitamin D3 for improving insulin resistance and beta-cell function. Intramuscular vitamin D replacement may play a key factor for promotion of glucose metabolism and lowering the risk of diabetes in vitamin D-deficient individuals[33].

CONCLUSION

There is an inverse correlation between serum vitamin D and insulin resistance. Persistent vitamin D deficiency status may lead to metabolic disorders including insulin resistance and raised blood glucose.

COMPLIANCE WITH ETHICAL STANDARDS

Ethical approval: All applicable international (International Council of Harmonization), national, or institutional guidelines (Committee of the Animal Research Ethics) for the care and use of animals were followed.

ABBREVIATIONS

1,25(OH)2D: 1,25 dihydroxyvitamin D, **24,25(OH)2D:** 24,25 dihydroxyvitamin D, **25(OH)D:** 25-hydroxyvitamin D, **AIN:** American Institute of Nutrition, **ANOVA:** Analysis of variance, **Ca:** Calciumion, **DBP:** D binding protein, **ER:** Endoplasmic Reticulum, **Fig:** Figure, **H&E:** Hematoxylin and Eosin, **HbA1c:** Glycated hemoglobin, ***P value:*** Probability value, **PP:** Pancreatic polypeptide, **SS:** Somatostatin, **T1DM:** Type 1 Diabetes Mellitus, **T2DM:** Type2 Diabetes Mellitus, **TPV:** Total pancreatic volume, **UV:** Ultraviolet, **UV-B:** Ultraviolet medium wavelength, **VDR:** Vitamin D receptor.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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الملخص العربى

دور نقص فيتامين د في التركيب المجهري للبنكرياس والتحريض المحتمل لمرض السكري في الجرذان البيضاء

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يُعتبر فيتامين (د) من الحقول الأكثر أهمية لعمل الأبحاث لما له من دور هام في كثير من جوانب الصحة. سابقاً كان يُعتقد أنه مسؤول فقط بتوازن الكالسيوم ولكن الآن ثبت أنه له دور كبير في تنظيم عمل الغدد الصماء وجهاز المناعة. عندما يصل مستوي الفيتامين (د) الي اقل من ٢٠ نانو جرام/ مل نصل الي حالة نقص فيتامين (د) .

يُعتقد ان فيتامين (د) يساهم في التسبب في كلا نوعي داء السكري ,فهو ليس فقط مهم لافراز الانسولين و لكنه ايضا يُحسن حساسية الخلايا المستهدفة للانسولين. لذلك كان الهدف من هذه الدراسة الكشف عن تأثير نقص فيتامين (د) على مستوى السكر في الدم وتركيب البنكرياس.

تم إستخدام ٣٠ من ذكور الفئران سبراج داولي بهذه الدراسة, والتى تم تقسيمها إلي مجموعتين, تتألف المجموعة الاولي من ١٢ فأر كمجموعة ضابطة, والمجموعة الثانية تكونت من ١٨ فأر التي تم تقسيمها الي مجموعتين داخليتين ,الاولي تضم ٩ فئران تم تعرضهم الي نقص فيتامين (د) الغذائي لمدة شهر أما الثانيه تضم ٩ فئران تم تعرضهم الي نقص فيتامين (د) الغذائي لمدة شهرين.

اوضح الفحص المجهري بالميكروسكوب الضوئي لعينات البنكرياس المصبوغه بكل من صبغات الهيماتوكسلين وإيوسين, ماسون ترايكروم و التوليودين الأزرق تغيرات في تركيب جزر لانجارهانز. هذه التغيرات كانت اكثر وضوحا في الفئران التي تعرضت لنقص الفيتامين الغذائي لمدة شهرين عن الفئران التي تعرضت فقط لشهر واحد. كان هناك نقص في عدد و حجم والكتله الاجماليه للجزر. كما قل عدد الخلايا بداخل الجزيره نفسها. اظهرت بعض النوي ملامح تغليظيه بينما اظهر اخرون انتفاخ في السيتوبلازم.

واظهر التحليل الاحصائي لمستويات السكر في الدم زياده غير كبيره في فئران الشهر الاول مقارنة بمستويات المجموعة الضابطة, بينما اظهرت فئران الشهر الثاني زياده كبيره .

و ختاما, اظهرت الدراسة الحالية ان نقص فيتامين (د) لاكثر من شهر يؤثر علي تركيب البنكرياس و يؤدي إلي داء السكري.