Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 23s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

A Short Of Review On Pancreatic β- Cell Function In Diabetes Mellitus Patients

Dr. Hariballav Mahapatra[1], Dr. Jaydeep Kumar Sahu[2], Dr. Akanksha Pandey[3], Danish Javed[4], Ramya.P[5], Dr. Dinesh Tripathi[6]

[1]MBBS, MHSc, PGD Clin Endo, DipDiab, FDRC, FCGP, Consultant Diabetologist, Sevayan Diabetes Centre, Puri, Shree Hospitals, Bhubaneswar

Email ID: nullandzero@gmail.com

[2]Associate professor at the Department of Dravyaguna, Sri Sri College of Ayurvedic Sciences & Research Hospital, Sri Sri University, Cuttack, Odisha, India.

Email ID: drjaydeepsahu26@gmail.com

[3]Assistant professor, Department of science Krishna Vikash group of Institutions, Raipur.

Email ID: akankshasanadhya88@gmail.com

[4]Senior Medical officer (Ayush), All India Institute of Medical College, Bhopal

[5]Assistant Professor, Department of Physician Assistant, Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore.

[6]Research Fellow, Affiliation -King George's ,Medical University, Lucknow, Uttar Pradesh

Cite this paper as: Dr. Hariballav Mahapatra, Dr. Jaydeep Kumar Sahu, Dr. Akanksha Pandey, Danish Javed, Ramya.P, Dr. Dinesh Tripathi, (2025) A Short Of Review On Pancreatic β- Cell Function In Diabetes Mellitus Patients. *Journal of Neonatal Surgery*, 14 (23s), 292-296.

ABSTRACT

According to a study, IR & β-cell DF are involved in the onset and advancement of T2D. In addition to the harmful consequences of IR, IFM & OS have become significant characteristics that delineate β-cell DF. Key inflammatory markers, including CRP, TNF-α and IL-1β linked to β-cell DF in preclinical models. These effects demonstrate a PAT association between an aberrant IFM response and the production of OS in the advancement of T2D. Therefore, in this review we have discussed about the normal function and pathological aspect of β- cell.

Keywords: *T2D, β- cell DF , Inflammatory Response, CRP, TNF-α.*

1. INTRODUCTION

Authors have also estimated that DM affects approximately 10% of the population, with type 2 DM (T2D) accounting for over 90% of these cases.[1] The primary pathophysiological(PAT-PY) alterations observed in T2D include insulin resistance(IR) and dysfunction (DF) of the β-cells. According to past studies, T2D is commonly associated with IR, whereas, on the other hand, type 1 diabetes (T1D) may develop IR.[1,2] Moreover, IR according to study, refers to inability of insulin(ISN) to cause its intended effects, whereas β-cell DF denotes a reduction in insulin secretion(IS) capacity.[2] IR & β-cell DF play significant roles in the pathophysiology of T2D through a complex mechanism that leads to elevated blood glucose levels.[3] As the disease advances, there is a deterioration in β-cell function, which initially becomes evident during the prediabetic phase of DM progression.[4,5] Consequently, to alleviate challenges related to T2D, particularly those linked to inflammation and oxidative stress(OS), it is essential to delineate the PAT pathways responsible for β-cell DF. It has long been believed that inflammation is the primary component of DM.[6,7] Inflammatory substances released by fat cells and immune cells in fat tissue can make the harmful inflammation(IFM) caused by high blood sugar levels in T2D worse [9]. In T2D, according to past studies, OS, IR & β-cell DF exacerbate obesity or an excess of fat in the pancreas, among other significant factors.[8,9] It is possible to increase β-cell function and reduce oxidative stress by targeting intracellular antioxidant enhancement to fight diabetes-related problems.[10,11]

2. NORMAL B-CELL PHYSIOLOGY

Previous research has shown that RNA binding proteins found in the 5′ and 3′ untranslated regions (UTRs) often maintain the stability.[12,13] In contrast, studies on rodent islets demonstrate that proinsulin translation and processing enzymes

increases rapidly in response to glucose.[14,15] This observation suggests a posttranscriptional regulation mechanism governing INS expression.[14-16] Upon translation of preproinsulin and its subsequent insertion into the ER lumen, a signal peptide is cleaved. Study have shown that, protein disulfide isomerases had serve an integral role in the establishment of three intramolecular disulfide bonds.[17]

This mechanisms underlying the trafficking and organization of INS granules within cells remain poorly understood. In mature mouse islets, proinsulin is efficiently sorted to regulated secretory pathway with an efficacy of 99% upon its exit from the Golgi, where it subsequently undergoes folding.[17] The regulated secretory pathway efficiently directs IAPP to granules within mature islets, whereas the constitutive secretory pathway facilitates the release of approximately 50% of it in newborn islets.[17] Under baseline glucose conditions, the regulated secretory pathway primarily directed the trafficking of (pro) IAPP from human islets. In the context of an 8-day culture in high glucose conditions, the release of proIAPP via a constitutive pathway was observed.[18] Under appropriate testing conditions, the findings may suggest that immature or dysfunctional β cells could have modified the trafficking and release of secretory products. The conversion of proinsulin and proIAPP starts when prohormone convertase activity rises with increasing granule H+ and Ca2+ levels.[19] The C-terminus of both the intermediate and mature (MAT) peptides is further trimmed by carboxypeptidase E (CPE). This results in MAT-INS & C-peptide in the case of proinsulin. After CPE trims proIAPP, peptidylglycine α-amidating monooxygenase (PAM) adds an amidation to the C-terminus, resulting in mature IAPP.[19] Recently, there have been doubts about the role of β cells when processing proinsulin because it is hard to detect PC2 in these cells, even though some studies have shown that β cells do express it using transcriptomics and immunohistochemistry.[20] Following glucose stimulation, the association between stimulus and secretion leads to the swift release of INS in 2 distinct phases. The initial phase in humans commences with the initiation of glucose administration, generally concluding within a 10-minute timeframe, and signifies a pool of secretory granules that can be released rapidly. The subsequent phase is characterized by its duration, which is contingent upon the persistence of elevated glucose concentrations. This phase encompasses granules that contain newly synthesized insulin.[12] According to a study, IS is stimulated not only by glucose but also by fatty acids & amino acids(AA).[12] In the context of AA induced IS, mitochondrial glutamate dehydrogenase (GDH) serves as the primary enzyme responsible for anaplerosis, facilitating the deamination of glutamate to yield α-ketoglutarate.[12,21,22]To maintain euglycemia, insulin production is tightly regulated by various signals from many cell types inside the islet, including other endocrine cells, nerve fibers, endothelial cells, pericytes, and immune cells.[23]

3. PATHOPHYSIOLOGY OF B CELLS DF IN T2D

According to a study, pancreatic(PNC) β-cells play a crucial role in the production & secretion of INS, a hormone essential for metabolic regulation.[24] Studies have also concluded that, INS had a vital role in the metabolic regulation of essential energy substrates, including carbohydrates, lipids, and proteins to facilitate the uptake of glucose from the bloodstream into various targeted area of the body.[24] Thus, disturbances in INS signaling are said to be significant contributors for the development of IR.[24] Excessive expansion of adipose tissue results in increased circulating concentrations which ultimately contribute to the onset of IR [25] as shown in figure1.

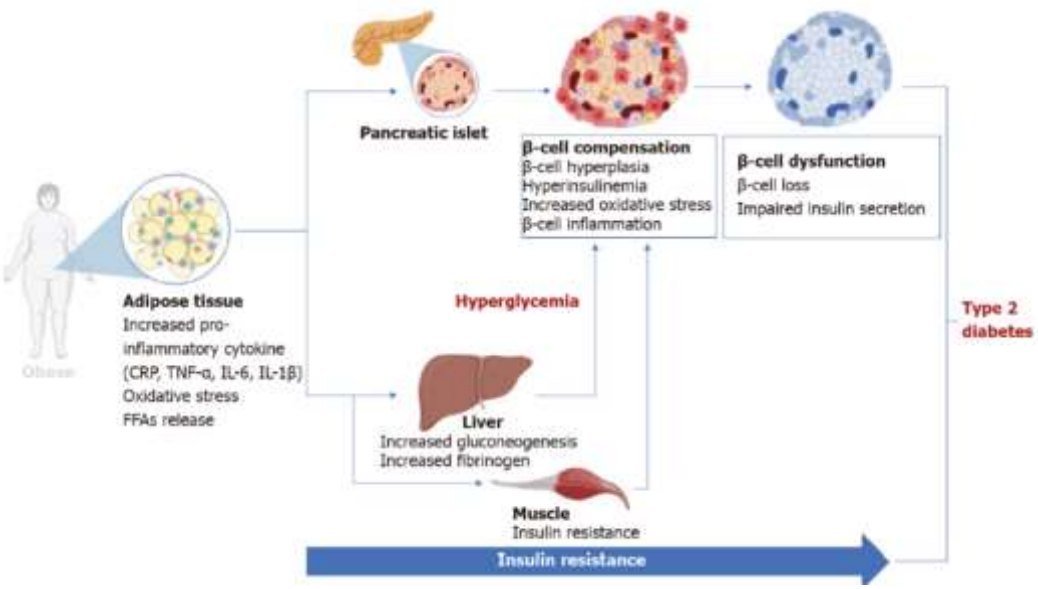

FIGURE 1: OVERVIEW OF PATHOLOGICAL IMPLICATIONS[1]

According to study, more blood flow, white blood cells moving in, and increased production of different chemicals show that inflammation is happening, which is usually a local reaction to damage in cells or tissues.[26] To hasten the elimination

of harmful substances and the repair of damaged tissue, this immunity response is essential.[26] Adipose tissue growth is recognized to play a significant part in DF process.[27]

CRP

Epidemiological studies have demonstrated a significant association between the progression of T2D and its complications, alongside increased levels of inflammatory biomarkers.[28] Obesity, frequently observed in individuals with T2D, is recognized as a primary contributor to the detrimental effects of IFM & triggered acute-phase proteins response.[29] Previous studies have shown that increased levels of high-sensitive CRP (hs-CRP) are associated with their advanced DF.[30-32] Studies have shown that CRP had various roles in inflammatory mechanisms, complement pathway, cell death, autophagy, modulation of nitric oxide, and the synthesis of cytokines, IL-6 and TNF- α. [33-36]

Fibrinogen [1]

Increased plasma levels of fibrinogen(FBN) have been linked to clinical problems of T2D for more than twenty years. Circulating fibrinogen levels indicate systemic IFM and tissue damage.[1] Enzymatic conversion to fibrin by thrombin is the primary mechanism by which this protein is secreted; its secretion is essential for coagulation, revascularization, and wound healing. Poor blood glucose control and an increased risk of CVS & are associated with elevated fibrinogen levels in T2D patients. In pancreatic stellate cells, fibrinogen increases profibrogenic and proinflammatory activities directly.

IL-6 and IL-1 β [1]

Increasing evidence links interleukin family proteins to innate immunity and numerous diseases, including inflammatory conditions. They had significant role in inflammatory response mechanisms, particularly during the development of metabolic disease as they induce CD4+ T cells. Here, IL-1, generated by activated macrophages. The 1β-processing platform, in contact with pattern recognition receptors, initiates signaling pathways that govern adaptive immunity and induce inflammatory responses. Abnormally regulated levels of them are linked to disruption of immune system.

TNF-α [1]

According to study they come from superfamily of type II transmembrane proteins and show significnat role in several physiological activities, including immune response and inflammation. A study done on mouse showed an increased levels of chemokines and pro-inflammatory cytokines in T2D patients.[21] Therapeutically it was also found that, TNF- α levels improved the insulin sensitivity in T2D patients and cause apoptotic cell death in pancreatic β-cells.

T-cells [1]

In addition to triggering inflammatory responses, the cytokines produced by innate immune cells have a direct and indirect impact on IS. Macrophages and neutrophils, might also help keep the immune response balanced, including the harmful activation of pancreatic immune cells. The adaptive immune response depends heavily on T cells. CD8+ "killer" T cells and CD4+ "helper" T cells are the two primary subtypes of T cells. Another subtype of T cells, regulatory T cells, are essential for tolerance, which allows immune cells to distinguish between parent and invading cells. As a matter of fact, the demise of PNC β-cells in diabetes has long been associated with activated helper (TH) 1 CD4+ T cells and CD8+ killing T cells. [24] Thus, vicious cycle including cytotoxic T cells, pancreatic islets, IL-12 and macrophages may activate CD4+ T cells. It is believed that TH1 promotes damage to β-cells by accelerating the process of cell death and its further worsening in DM patients as shown in figure 2.

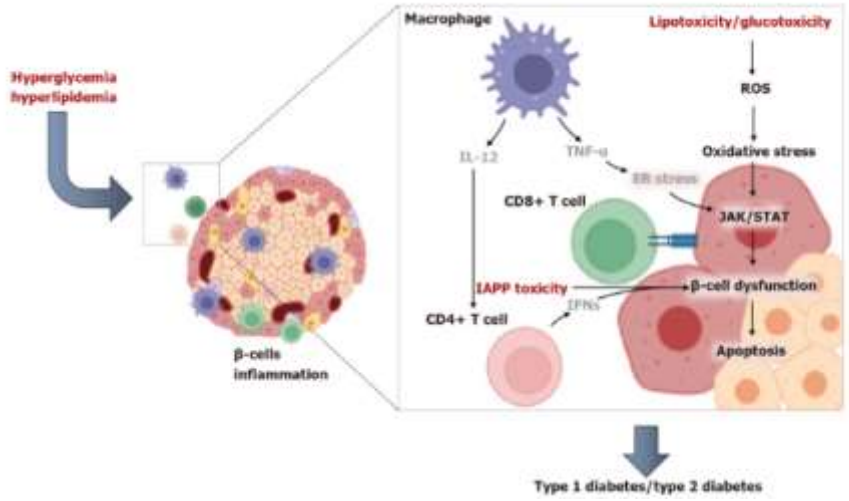

FIGURE 2 : OVERVIEW OF PATHOLOGICAL MECHANISM LINKED TO IMPAIR IMMUNE SYSTEM.[1]

4. CONCLUSION

Various PAT mechanisms are acknowledged as factors that contribute to the development and progression of T2D. Both types of DM are associated with β-cell DF; however, IR and obesity(OB) are the hallmark features of T2D. Thus, the effects correspond with a diminished immune response, potentially leading to heightened IR and increased blood glucose concentrations. OS occurs concurrently with inflammation and can interfere with various biochemical processes, ultimately leading to the death of PAN β-cells. Therefore, right now, there isn't much clinical evidence showing how well common diabetes treatments work to boost intracellular antioxidants that could protect against the problem. Thus, more longitudinal & cross sectional studies are encourged in future.

REFERENCES

[1] Dludla PV, Mabhida SE, Ziqubu K, Nkambule BB, Mazibuko-Mbeje SE, Hanser S, Basson AK, Pheiffer C, Kengne AP. Pancreatic β-cell dysfunction in type 2 diabetes: Implications of inflammation and oxidative stress. World journal of diabetes. 2023 Mar 15;14(3):130.

[2] Dludla PV, Mabhida SE, Ziqubu K, Nkambule BB, Mazibuko-Mbeje SE, Hanser S, Basson AK, Pheiffer C, Kengne AP. Pancreatic β-cell dysfunction in type 2 diabetes: Implications of inflammation and oxidative stress. World journal of diabetes. 2023 Mar 15;14(3):130.

[3] Cerf ME. Beta cell dysfunction and insulin resistance. Frontiers in endocrinology. 2013 Mar 27;4:37.

[4] Saisho Y. β-cell dysfunction: Its critical role in prevention and management of type 2 diabetes. World journal of diabetes. 2015 Feb 15;6(1):109.

[5] Do OH, Gunton JE, Gaisano HY, Thorn P. Changes in beta cell function occur in prediabetes and early disease in the Lepr db mouse model of diabetes. Diabetologia. 2016 Jun;59:1222-30.

[6] Pickup JC, Crook MA. Is type II diabetes mellitus a disease of the innate immune system?. Diabetologia. 1998 Sep;41:1241-8.

[7] Lontchi-Yimagou E, Sobngwi E, Matsha TE, Kengne AP. Diabetes mellitus and inflammation. Current diabetes reports. 2013 Jun;13(3):435-44.

[8] Rohm TV, Meier DT, Olefsky JM, Donath MY. Inflammation in obesity, diabetes, and related disorders. Immunity. 2022 Jan 11;55(1):31-55.

[9] Singh RG, Yoon HD, Wu LM, Lu J, Plank LD, Petrov MS. Ectopic fat accumulation in the pancreas and its clinical relevance: a systematic review, meta-analysis, and meta-regression. Metabolism. 2017 Apr 1;69:1-3.

[10] Lei XG, Vatamaniuk MZ. Two tales of antioxidant enzymes on β cells and diabetes. Antioxidants & redox signaling. 2011 Feb 1;14(3):489-503.

[11] Wang J, Wang H. Oxidative stress in pancreatic beta cell regeneration. Oxidative medicine and cellular longevity. 2017;2017(1):1930261.

[12] Kahn SE, Chen YC, Esser N, Taylor AJ, van Raalte DH, Zraika S, Verchere CB. The β cell in diabetes: integrating biomarkers with functional measures. Endocrine reviews. 2021 Oct 1;42(5):528-83.

[13] Itoh N, Okamoto H. Translational control of proinsulin synthesis by glucose. Nature. 1980 Jan 3;283(5742):100-2.

[14] Alarcon C, Verchere CB, Rhodes CJ. Translational control of glucose-induced islet amyloid polypeptide production in pancreatic islets. Endocrinology. 2012 May 1;153(5):2082-7.

[15] Martin SK, Carroll R, Benig M, Steiner DF. Regulation by glucose of the biosynthesis of PC2, PC3 and proinsulin in (ob/ob) mouse islets of Langerhans. FEBS letters. 1994 Dec 19;356(2-3):279-82.

[16] Greenman IC, Gomez E, Moore CE, Herbert TP. The selective recruitment of mRNA to the ER and an increase in initiation are important for glucose-stimulated proinsulin synthesis in pancreatic β-cells. Biochemical Journal. 2005 Oct 15;391(2):291-300.

[17] Verchere CB, D'Alessio DA, Prigeon RL, Hull RL, Kahn SE. The constitutive secretory pathway is a major route for islet amyloid polypeptide secretion in neonatal but not adult rat islet cells. Diabetes. 2000 Sep 1;49(9):1477-84.

[18] Gasa R, Gomis R, Casamitjana R, Novials A. High glucose concentration favors the selective secretion of islet amyloid polypeptide through a constitutive secretory pathway in human pancreatic islets. Pancreas. 2001 Apr 1;22(3):307-10.

[19] Chen YC, Mains RE, Eipper BA, Hoffman BG, Czyzyk TA, Pintar JE, Verchere CB. PAM haploinsufficiency does not accelerate the development of diet-and human IAPP-induced diabetes in mice. Diabetologia. 2020 Mar;63:561-76.

[20] Zhu X, Orci L, Carroll R, Norrbom C, Ravazzola M, Steiner DF. Severe block in processing of proinsulin to insulin accompanied by elevation of des-64, 65 proinsulin intermediates in islets of mice lacking prohormone convertase 1/3. Proceedings of the National Academy of Sciences. 2002 Aug 6;99(16):10299-304.

[21] Capozzi ME, Svendsen B, Encisco SE, Lewandowski SL, Martin MD, Lin H, Jaffe JL, Coch RW, Haldeman JM, MacDonald PE, Merrins MJ. β Cell tone is defined by proglucagon peptides through cAMP signaling. JCI insight. 2019 Mar 7;4(5):e126742.

[22] Khan R, Tomas A, Rutter GA. Effects on pancreatic Beta and other Islet cells of the glucose-dependent insulinotropic polypeptide. Peptides. 2020 Mar 1;125:170201.

[23] Van Der Meulen T, Donaldson CJ, Cáceres E, Hunter AE, Cowing-Zitron C, Pound LD, Adams MW, Zembrzycki A, Grove KL, Huising MO. Urocortin3 mediates somatostatin-dependent negative feedback control of insulin secretion. Nature medicine. 2015 Jul;21(7):769-76.

[24] Wondmkun YT. Obesity, insulin resistance, and type 2 diabetes: associations and therapeutic implications. Diabetes, Metabolic Syndrome and Obesity. 2020 Oct 9:3611-6.

[25] Dludla PV, Nkambule BB, Jack B, Mkandla Z, Mutize T, Silvestri S, Orlando P, Tiano L, Louw J, Mazibuko-Mbeje SE. Inflammation and oxidative stress in an obese state and the protective effects of gallic acid. Nutrients. 2018 Dec 21;11(1):23.

[26] Böni-Schnetzler M, Meier DT. Islet inflammation in type 2 diabetes. InSeminars in immunopathology 2019 Jul 1 (Vol. 41, pp. 501-513). Springer Berlin Heidelberg.

[27] Cerf ME. Beta cell physiological dynamics and dysfunctional transitions in response to islet inflammation in obesity and diabetes. Metabolites. 2020 Nov 10;10(11):452.

[28] Tsalamandris S, Antonopoulos AS, Oikonomou E, Papamikroulis GA, Vogiatzi G, Papaioannou S, Deftereos S, Tousoulis D. The role of inflammation in diabetes: current concepts and future perspectives. European cardiology review. 2019 Apr;14(1):50.

[29] Pfützner A, Standl E, Strotmann HJ, Schulze J, Hohberg C, Lübben G, Pahler S, Schöndorf T, Forst T. Association of high-sensitive C-reactive protein with advanced stage β-cell dysfunction and insulin resistance in patients with type 2 diabetes mellitus. Clinical Chemistry and Laboratory Medicine (CCLM). 2006 May 1;44(5):556-60.

[30] PrayGod G, Filteau S, Range N, Kitilya B, Kavishe BB, Ramaiya K, Jeremiah K, Rehman AM, Changalucha J, Olsen MF, Andersen AB. β-cell dysfunction and insulin resistance in relation to pre-diabetes and diabetes among adults in north-western Tanzania: a cross-sectional study. Tropical Medicine & International Health. 2021 Apr;26(4):435-43.

[31] Ndevahoma F, Nkambule BB, Dludla PV, Mukesi M, Natanael KN, Nyambuya TM. The effect of underlying inflammation on iron metabolism, cardiovascular risk and renal function in patients with type 2 diabetes. EJHaem. 2021 Aug;2(3):357-65.

[32] Daousi C, Casson IF, Gill GV, MacFarlane IA, Wilding JP, Pinkney JH. Prevalence of obesity in type 2 diabetes in secondary care: association with cardiovascular risk factors. Postgraduate medical journal. 2006 Apr;82(966):280-4.

[33] Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. Frontiers in immunology. 2018 Apr 13;9:754.

[34] Kaneko N, Kurata M, Yamamoto T, Morikawa S, Masumoto J. The role of interleukin-1 in general pathology. Inflammation and regeneration. 2019 Dec;39:1-6.

[35] Sun W, Wu Y, Gao M, Tian Y, Qi P, Shen Y, Huang L, Shi L, Wang Y, Liu X. C-reactive protein promotes inflammation through TLR4/NF-κB/TGF-β pathway in HL-1 cells. Bioscience reports. 2019 Aug;39(8):BSR20190888.

[36] Zhang L, Shen ZY, Wang K, Li W, Shi JM, Osoro EK, Ullah N, Zhou Y, Ji SR. C-reactive protein exacerbates epithelial-mesenchymal transition through Wnt/β-catenin and ERK signaling in streptozocin-induced diabetic nephropathy. The FASEB Journal. 2019 May;33(5):6551-63.