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DIABETES IS NOT A DISEASE

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ABSTRACT

Background: Since the centenary of the insulin discovery, our ability to manage diabetic conditions has remained low. What we do is only control blood sugar levels, preventing fatal complications. There has never been a cure for the condition. **Methods:** This stems from a misinterpretation of Banting et al's insulin discovery It is insulin that treats hyperglycemia. So this condition was thought to be due to the absence or deficiency of insulin. In fact, the cause is the massive release of glucagon. **Results:** The massive release of glucagon is the body's response to an extensive inflammatory reaction. An inflammatory response that causes discomfort. A response that triggers activation of autophagy mechanism by glucagon. Glucagon not only activates autophagy but also gluconeogenesis. A process that results in the condition of hyperglycemia, diabetes. **Conclusion:** That is the reason why diabetes does not deserve to be called a disease. Diabetes is a compensatory mechanism that is very likely to be present in every disease and is bound to end. Attempts to inhibit or ignore this process will only lead to new compensations, called complications..

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INTRODUCTION

Diabetes mellitus is a disease that has been known for a long time. In the Ebers papyrus dating back to 1550 BC, the disease has been mentioned since the time of the Ancient Egyptian Kingdom. Meanwhile, the papyrus dates back to the New Egyptian Empire. This means that diabetes mellitus has been recognized for more than 3000 years BC (Lee, 2002;Ahmaed, 2002). Even so, our knowledge still cannot find the perfect solution to this condition. All curren t treatments are aimed at controlling blood sugar levels (Grozer et al, 2002; Lee et al, 2021;ADA, 2011, Niswender 2022).

Uncontrolled blood sugar levels lead to various complications. These complications are divided into two, namely macroangiopathy and microangiopathy (Grozzer et.al, 2002;.Lee & Sajan, 2021; Haas & Donnel, 2017; Lawall et al, 2020; Avogaro & Fadini, 2019;Lawall, 2020) This condition is thought to be caused by insulin deficiency or increased cellular resistance to insulin (Lee et al, 2021). It is true that diabetes is caused by insulin deficiency or decreased sensitivity of cells to insulin. So the solution to the condition of diabetes is the administration of insulin or drugs that stimulate the release of insulin (ADA, 2011). Is it true that the problem with diabetes is due to increased blood glucose levels? So that complications arise in the form of microangiopathy and macroangiopathy?

This paper is a review of various scientific papers on autophagy, diabetes, and other related topics. It seeks to point out various discrepancies in various studies. It will show the fallacies that are more than a hundred years old. By looking at the relationship between various literatures, this paper proves that diabetes is not a disease. Diabetes is a condition that is not permanent and will resolve naturally. This study aims to explain whether diabetes is not a disease.

METHODS

This study is a narrative review study that explains Diabetes, using several related literature taken from Google Scholar, EBSCO and other digital sources. Furthermore, this study will prove and explain whether diabetes is not a disease.

RESULTS

The results of several collected articles consist of:

1. Diabetes Not Due to Insulin Deficiency
2. Diabetes is the Other Side of Autophagy
3. Blood Sugar Check
4. Regulation of Body Fluid Balance
5. Role of Insulin Use
6. Impact on Disease Concept

Next, we will discuss each of these items, based on related literature.

DISCUSSION

1. Diabetes Not Due to Insulin Deficiency

It has been agreed that diabetes is a disease. Even this disease can cause various severe complications. So it gets the title Mother of All Diseases. This assumption became stronger when Banting and Best discovered insulin in 1921. Banting and Best demonstrated the successful treatment of Leonard Thompson. A 14-year-old child, who showed symptoms of severe glucosuri, 5 liters per day and hyperglycemia, more than 500 mg/dl. Even though this child had restricted food intake (Lee & Yoon, 2021;Lewis & Brubaker, 2021).

After previous trials on dogs. Leonard Thompson was the first human to receive insulin injections. The insulin administration gave encouraging results. The various complaints that the boy suffered from slowly diminished. Described as fitter and stronger (Lee & Yoon, 2021;Lewis & Brubaker, 2021).

The success of insulin administration led many to make quick conclusions. Insulin deficiency is thought to be the cause of diabetes. Moreover, animal tests have previously been carried out in the form of removing the pancreas. This trial resulted in the animal developing diabetes. It is known that insulin is produced by the pancreas (Lee & Yoon, 2021;Lewis & Brubaker, 2021).

The suspicion that diabetes is related to the pancreas has long been raised before. Joseph von Mering and Oskar Winskowsky were the first to state this in 1889. However, it was not yet known what substances the pancreas produced at that time (Lee & Yoon, 2021;Lewis & Brubaker, 2021). [14'15]

Clues began to emerge when Paul Langerhans discovered an island-like pattern in the pancreas (Langerhans, 1869;Sakula, 1988). [22'24] In 1909, Belgian physician Jean de Mayer hypothesized the islands' connection to carbohydrate metabolism. Meyer also used the term insulin which comes from the word insula which means island (Lee &

Yoon, 2021;Lewis & Brubaker, 2021;Michael, 2007).

Until finally F. Banting, C. Best, J. J. R. MacLeod and J. Collip discovered insulin in 1921-1922. The findings were so phenomenal and gave euphoria to the treatment of diabetes. Since then, research on insulin as a diabetes therapy has expanded (Lee & Yoon, 2021;Lewis & Brubaker, 2021;Hegele & Maltman, 2020; Rosenfeld, 2022).

Meanwhile not long ago, 1922-1923 Kimball and Murlin also discovered glucagon in the pancreas.[17][28] Unfortunately, the findings at that time did not have too much impact. So the understanding of diabetes as a result of insulin deficiency remained (ADA, 2011). [7] The name glucagon comes from the term glucose agonist Muller et al, 2016;Kimball 1923). It means that it gives the same effect as glucose. So it is considered to have no effect on the cure of diabetes.

It wasn't until 1947 that glucagon's better function came to light. This was discovered accidentally when Christian de Duve was asked to research insulin products from the Eli Lily company. The insulin produced resulted in an increase in blood sugar. It was revealed that the insulin product was contaminated with glucagon. This caused the recipient's blood glucose to rise (Bouckaert & de Duve, 1947.

In the 1950s, researchers at the Eli Lily company succeeded in isolating it in crystal form. [30] In 1959, researchers led by Roger Unger succeeded in describing it with radioimmunoassay techniques (Muller et al, 2016).

Glucagon plays a major role in glucose metabolism. Even the role of glucagon in the occurrence of diabetic conditions is quite visible. Hyperglycemic conditions are caused by the release of glucagon (Harp et al., 2016;Muller et. Al., 1970;Unger et al., 1970). Even some studies refer to diabetes mellitus as a hyperglucagonemic condition (Janah et al., 2019).

Glucagon plays a role in the processes of gluconeogenesis and glycogenolysis. Both of these processes are compensatory due to hypoglycemic conditions (Kulina & Rayfield, 2016). However, recent studies have shown that it is not only hypoglycemic conditions that trigger the release of glucagon (gromada et., al. 2007; Thorens, 2011).

Many things can trigger the release of glucagon. Most of them are related to stressful conditions (Ashcroft, 2013). Either physical stress or psychological stress. This condition is the most common cause of diabetes (Bloom et al., 1973).

There are many studies that prove the relationship between physical stress and diabetes. One of them is inflammation (Lu & Weng, 2022). Evidence of inflammation, with the discovery of cytokines in the pancreas of diabetics. Cytokines will affect the release of somatostatin from pancreatic delta cells (Li et al, 2020).

Somatostatin will then affect alpha cells and beta cells. As a result neither glucagon nor insulin is released. This condition results in an increase in blood glucose levels. Because glucose cannot enter the cells (Bloom & Polak, 1987;Janeca et al., 2001). As a result, the cell is in a state of starvation. Lack of energy for intra-cellular metabolic processes. Unfortunately, this condition does not immediately trigger the activity of lysosomes and peroxisomes. Lysosomes and peroxisomes will be triggered when the brain starts releasing catecholamines. Especially epinephrine and norepinephrine influence the alpha cells to release glucagon (Verberne et al., 2016).

Catecholamine release occurs due to increased nerve activity. Nerve cells are the only cells that do not require insulin in glucose transport (Dienel, 2019). Nerve cell activity is also affected by the release of various mediators of inflammation (Cheng et al., 2020).

The discovery of cytokines certainly indicates the release of other mediators of inflammation (Cheng et al., 2020;Calle &Fernandez, 2012). These mediators of inflammation are released to treat the injury that caused the inflammation. [48][49] The effects of these various mediators often cause discomfort. [50][51]For example, histamine and prostaglandin cause smooth muscle relaxation. As a result, the capillaries dilate until swelling occurs. [50][51][52] The effect of capillary dilation is to give way to immune cells that respond to cytokine signals. If the cause of the injury is an infection, it can be treated immediately (Cheng et al., 2020;Calle &Fernandez, 2012).

In the airway, the effect is hypersecretion of snot and narrowing of the airway. The body does this to prevent more germs from entering.

The next task is done by stress hormones. This is mainly done by epinephrine and norepinephrine (Dienel, 2019). These hormones naturally function to limit the effects of mediators of inflammation (Russell et al., 2021). Until the unpleasant effects of inflammation do not occur continuously. One example is in capillaries, resulting in vasoconstriction (Russell et al., 2021). While in the airway, it causes relaxation. So that the airway returns to normal.

Epinephrine and norepinephrine affect the release of glucagon in pancreatic alpha cells . (Russell et al., 2021). Glucagon will activate the function of peroxisomes and lysosomes. [54]Peroxisomes and lysosomes will digest the remaining germs that managed to enter the cell (Kim et al., 2019).

Peroxisomes also perform the process of gluconeogenesis. With this process, the blood glucose level increases again. [31][39] This condition can again trigger an increase in brain activity (Dienel, 2019). Two things trigger brain activity due to increased blood glucose levels. The first is the increased intake of glucose into the nerve cells (Dienel, 2019). The second is the presence of the nucleus supraopticus, which responds to an increase in osmotic pressure. This nucleus will give a message to the hypophysis gland to release vasopressin (Buijs et al., 2021).

Osmotic pressure increases due to increased blood glucose levels. This will affect the fluid balance. This will also result in the transfer of fluid from tissue to intravascular (Fayfman, 2017) [56]Intravascular hydrostatic pressure will increase. As a result, the rate of blood flow to the kidney increases. Urine formation also increases. If it occurs repeatedly, this condition is called polyuria (Cipriani et al., 2012;Ziegler, 2018;Hill, 2014).

Vasopressin released will cause constriction of arteries and arterioles (Pelletier et al., 2014; Te Riet et al., 2015). So that fluid loss due to polyuria does not occur continuously. The rate of blood flow to the kidneys also activates the renin angiotensin system. As a result, aldosterone is released which will cause vasoconstriction in the capillaries (Te Riet et al., 2015).

In glomerular capillaries, vasoconstriction will increase sodium restriction and reabsorption (Hill, 2014). So that the sodium level in the blood is maintained. However, aldosterone does not only work in glomerular capillaries (Te Riet et al., 2015). Also in other capillaries. In peripheral nerve tissue this results in impaired transport of nutrients, especially oxygen. This is why in diabetes, peripheral neuropathy is an early complaint (Feldman et al., 2019;Byrd et al., 2018). This complaint belongs to the complications of microangiopathy.

Vasopressin acts on arteries and arterioles. In some arteries, continuous narrowing may result in impairment. In general, narrowing of arteries and arterioles will result in increased intravascular hydrostatic pressure. This will lead to an increase in blood flow rate (Pelletier, 2014).

This condition will also increase the workload of the heart. The heart will be forced to pump more strongly. Over time, this will lead to hypertrophy of the heart muscle. This condition is further exacerbated if the coronary arteries are also narrowed due to the influence of vasopressin (Pelletier, 2014). The heart will experience a lack of nutrients, especially oxygen.

The hypoxic condition will worsen if the burden on heart also increases. Severe result is infarction, damage to the heart muscle. [65] Hypoxia due to the effect of vasopressin is felt as chest pain (Pelletier, 2014). In an experiment, pain increased as amount of vasopressin in the blood increased. Cardiac complaints and hypertension are complications of macroangiopathy. Macroangiopathic disorders are caused by release of vasopressin. While microangiopathic disorders are caused by aldosterone. These antidiuretic hormones act when the fluid balance disorder is not resolved.

The visible result of excessive gluconeogenesis is an increase in blood glucose levels. Increased blood glucose levels increase blood osmotic pressure. [66] Increased osmotic pressure results in the transfer of fluid from tissue to intravascular. The increase in fluid increases hydrostatic pressure of blood fluid. The increase in hydrostatic pressure results in compensatory mechanisms by antidiuretic hormones.

Therefore, it can be concluded that the problem arising from hypergluconeogenesis is disturbance of fluid balance. It is not solely due to increased blood glucose levels. This means that the most important thing in diabetes is to manage fluid balance.

Here, it is hardly seen that the absence of insulin affects increase in blood glucose levels. Except at onset of inflammation. Everything shows the role of glucagon in process of hypergluconeogenesis (Liu et al., 2017). This is also in line with the story of Leonard Thompson's treatment. Where restriction of food intake did not reduce the occurrence of hyperglycemia and glucosuri (Schertzer & Lam, 2020; Rehfeld, 2018).

The role of glucagon in diabetic conditions became clear when the discovery of incretin in 1934 by La Barre from Belgium. Incretins are hormonal compounds produced by gastrointestinal tract. Incretins, specifically GIP and GLT-1 play a role in release of insulin and cessation of glucagon release. Incretin release itself is strongly influenced by food intake (Schertzer & Lam, 2020; Rehfeld, 2018).

Several studies have shown that direct glucose administration through blood vessels does not affect insulin release. Whereas peroral glucose administration affects incretin release. Incretins then trigger release of insulin by the pancreas. [19,20] This finding also shows that if blood glucose increase levels due to process of gluconeogenesis, does not affect release of insulin. Fasting conditions actually increase process of gluconeogenesis. [45] This shows strong role of glucagon in occurrence of diabetes.

Although there is a decrease in blood glucose levels after insulin administration. This does not mean that the cause is lack or absence of insulin. Diabetes is a condition of hypergluconeogenesis and hyperglycogenolysis. The causes are diverse, but what causes condition to be excessive is inflammatory process. Massive inflammation that triggers various compensatory mechanisms of the body.

2. Diabetes is the Other Side of Autophagy

In 1955 and 1965, Christian de Duve discovered the organelles lysosomes and peroxisomes. This finding was quite phenomenal, because it was accompanied by the introduction of the term autophagy. The term corrected previous term autolysis. [68,71,72]

The term autolysis was proposed because it considered it a cytoplasmic activity. De Duve found that it is not done by cytoplasm, but a type of organelle. The organelle was later named lysosome by de Duve. Ten years later, peroxisomes were discovered, which have almost same function. The difference is in type of enzyme produced.

Lysosomes produce hydrolase enzymes. It digests macromolecules that can be dissolved in water. While peroxisomes use peroxide. Furthermore, peroxide will be broken down by the enzyme catalase into water and oxygen. The discovery of peroxisomes, which was previously based on discovery of lysosomes, in its development became separate. As if they were two different fields of study. There was even one researcher who examined the peroxisomes in detail. However, he did not mention lysosomes at all (Islinger et al., 2018).

This separation has led to many erroneous conclusions. Especially with regard to the concept of diabetes and autophagy. In fact, the interest in studying autophagy is quite high. Moreover, the study of autophagy is often associated with the process of cell regeneration. [70]Lysosomes work under influence of the same hormones as peroxisomes, they even work at the same time (de Duve, 2005). This is what often makes researchers who work in a partialistic way make mistakes in making conclusions. Although many genes that affect lysosomes work were known. But integrating them with research on peroxisomes has never been done (Matoba & Noda, 2021).

There is a study that highlights the role of autophagy mechanism in type 2 diabetes mellitus. In conclusion, diabetes mellitus is considered to be the result of impaired autophagy mechanism? [74,75] In fact, many researchers have mentioned the role of autophagy in maintaining homeostasis. Unfortunately, they see diabetes and autophagy as something different. Even autophagy to manage diabetes (Li, 2019).

The fallacy also arises when understanding autophagy as a method of fasting (Mizusima, 2011). This assumption refers to Ohsumi's description of the autophagy process in yeast cells. So that research on autophagy is always related to fasting methods. As a result, it is concluded that autophagy is contra-indicated for people with diabetes mellitus. Because there is an increase in blood glucose levels after autophagy diet.

To understand relationship between diabetes mellitus and autophagy, we should go back to story of lysosomes and peroxisomes discovery by Christian de Duve. Lysosomes and peroxisomes are considered the same organelle. The reason is because their activity is triggered by glucagon at the same time. The difference is in type of enzyme produced.

Lysosomes produce hydrolase enzymes. This will affect what molecules are digested by lysosome. Whether part or all of macro molecule (Xu & ren, 2015). While peroxisomes produce various oxidase enzymes. This also affects type of molecules digested and the result of oxidation process (Schrader et al., 2019). Lipid molecules are unlikely to be digested by lysosomes. Lipids cannot dissolve in water. On the other hand, carbohydrates can be digested by lysosomes. That is why various sugar-laden gene pieces are always the target organelles of lysosomes.

At the same time lipids can be digested by peroxisomes. The process of fat oxidation produces glucose needed by the cell. Furthermore, the oxygen produced from the peroxidase breakdown process is used for the oxidation process of glucose into pyruvate. Pyruvate will be the source of energy for the cell (Bouce, 2004). Meanwhile, water will help dissolve the molecules digested by lysosomes. Unfortunately in people with obesity, the amount of glucose produced is far more than the oxidation ability of the cell. As a

result, it will be released into the plasma fluid. This is what we call blood glucose level. Excess gluconeogenesis products that cannot be used by cells.

So it is very ambiguous if the HbA1C examination method is now developed. Because the relevance of excess glucose levels that are not used is not seen. Diabetes is not a disorder of the autophagy mechanism. The condition of diabetes occurs because amount of glucose produced from gluconeogenesis process is more than that used by cells.

The same is true for heart disorders. It is not the autophagy mechanism that is associated with coronary heart disease incidence. Narrowing of coronary arteries is an effect of vasopressin. Vasopressin release occurs due to increased intravascular osmotic pressure. Osmotic pressure increases because there is blood glucose increase levels due to gluconeogenesis process. Gluconeogenesis occurs along with autophagy process. Of course vasopressin release can be prevented, if we understand diabetic condition that will occur when triggering autophagy mechanism. Maintaining fluid balance during autophagy prevents vasopressin release. So that triggering autophagy mechanism to overcome the disease can still be done. The condition is to maintain fluid balance, so that hyperosmotic conditions do not occur for too long.

3. Blood Sugar Check

Diagnosing diabetes is done by checking blood sugar levels. Generally, it is done by checking blood sugar during, fasting blood sugar and 2 hours after eating. This method is done with the assumption that diabetes occurs due to insulin deficiency (Park et al., 2021). Unfortunately, this examination does not pay attention to the role of glucagon in the occurrence of diabetes. Likewise, the function of insulin is not well described.

Many studies have shown that the working period of insulin is between 30 to 100 minutes after it is released. The figure of 100 minutes indicates not cessation of insulin release. But number at which insulin is still found in blood. (Park et al., 2021).

This means that insulin stops being released by pancreas before the 100-minute period. This is greatly influenced by glucose level in the blood. Also by incretin stimulation of the gastrointestinal tract. However, if what happens is due to a drop in blood glucose levels. Then after 100 minutes is the body's attempt to rebalance by releasing glucagon (Park et al., 2021). This condition will certainly increase blood glucose levels again. Fasting conditions also trigger the release of glucagon. This will also lead to a potential increase in blood glucose levels. It is necessary to rethink how to measure blood sugar levels. This is important, to get a picture of the real situation.

The ideal time to check blood glucose levels is when gluconeogenesis process has been completed. This is characterized by considerable urination after fasting. The mechanism of profuse urination is due to fluid balance compensation. In the previous section, it has also been mentioned.

A high increase in osmotic pressure, in addition to causing fluid displacement, also triggers the release of somatostatin. The release of somatostatin results in the cessation of glucagon and insulin release. Therefore, this is the most optimal time to measure blood sugar levels (Nelson, 2021). After that, a post-prandial check is carried out. Ideally no more than one hour. This will see how much incretin affects insulin release. No wonder the results obtained are within normal range. Even lower than when measuring after urination. It is possible for blood sugar to be higher after eating. This really illustrates the true condition of hypoinsulinemia. Other conditions such as gastrointestinal disorders should be considered. This may cause impaired incretin release (Campbell, 2013).

4. Regulation of Body Fluid Balance

Problems that occur in diabetes conditions are mainly due to fluid balance disorders. This actually causes various complaints in diabetic conditions. Complaints caused by body's efforts to compensate for the balance. Increased blood glucose levels result in increased blood osmotic pressure. This condition results in fluid transfer from tissue to intravascular. This displacement results in an increase in intravascular hydrostatic pressure (Fayfman, 2017).

An increase in hydrostatic pressure will result increase in rate of blood flow to the kidneys. The filtration rate in glomerulus will also increase. As a result, a lot of urine will be formed. [58'159]The formation of urine along with its release results in a condition called polyuria. Not only does it excrete excess glucose but also some smaller water soluble molecules. These include electrolytes, such as sodium, potassium and bicarbonate ((Hill, 2014).

This will trigger renin angiotensin release. Which in turn affects aldosterone release. Aldosterone increases sodium reabsorption in glomerulus. Aldosterone will also cause glomerular vasoconstriction resulting in reduced water secretion (Te Riet, 2015).

At the same time, decreased blood volume and increased osmotic pressure stimulate vasopressin release. The main effect of vasopressin is arteries and arterioles vasoconstriction. In addition, as a neurotransmitter, it also has other effects according to its receptors. [60,61]

Currently, various vasopressin receptors have been identified. Some of these receptors act in the gastrointestinal tract. This increases rate of emptying of small intestine. The mechanism affects daily defecation function. This also affects complaints in diabetic conditions. [61]Aldosterone release not only affects glomerular capillary vasoconstriction. Aldosterone also affects vasoconstriction of other capillaries. One of them that bleeds peripheral nerve (Te Riet, 2016). [62]

The narrowing of capillaries not only results in a paler skin color but also reduced nutrient transport. Nutrients, especially oxygen, are reduced, resulting in damage to myelin sheath. It is felt as a tingling sensation in the extremities. This is commonly referred to as a complication of neuropathy (Feldman 2019; Byrd et al, 2018).

Both constriction by aldosterone and vasopressin will result in an increase in hydrostatic pressure. This will increase blood pressure. Heart will pump more forcefully to keep the blood flowing. If this condition lasts long enough, it will lead to cardiac hypertrophy (Feldman 2019; Byrd et al, 2018). This condition will become more severe when the coronary arteries are also narrowed. Heart muscle experiences hypoxia, ischemia. This condition can progress to infarction. As a result, heart rhythm disturbances occur. Because part of heart does not contract completely (Byrd et al, 2018).

Conditions related to capillary disorders are called microangiopathies. Those associated with arteries and arterioles are called macroangiopathies. Both types of abnormalities can be found not only due to osmolarity disturbance by hyperglycemia but also by other causes. It can be concluded that result of diabetes is a disturbance of fluid balance. This can be referred to as a side effect of autophagy process and diabetes. This side effect should be the focus of diabetes treatment.

5. Role of Insulin Use

Although insulin can resolve hyperglycemic conditions, it does not mean that cause is absence or deficiency of insulin. It functions much more than glucose transport. Insulin actually acts as an anabolic hormone. This role must be restored in insulin use (Heise, 2021).

Many studies show glucose utilization by cells increases in absence of insulin. This mainly follows increased intracellular oxidation process. [85] Oxidation of glucose will produce pyruvate. Pyruvate plays a role in the process of phosphorylating adenosine into ATP, the actual energy reserve (Alberts, 2002).

Insulin does more than just transport glucose. Insulin affects the transcription process in ribosomes. This means that regeneration process will be complete when insulin is released in transcription process. This role is forgotten by those who believe diabetes is a disease. Or those who believe in autophagy as a therapeutic approach (Heise, 2021;Thevis et al., 2010).

As a result, insulin use becomes haphazard. Not on time administration. This has led to misconception that absence of insulin is cause of diabetes. Also the fallacy that insulin is an inhibitor of autophagy process. Insulin should be given following autophagy process. Complete the process of gluconeogenesis. Increase intracellular oxidation process. After that, then administer insulin.

The process that supports each other will give optimal results for autophagy process, diabetic condition. Neglecting timing of administration results in process never being completed. Instead, it becomes a catastrophic condition.

6. Impact on Disease Concept

Understanding diabetes not as a disease has an impact on concept of disease. Not only condition of diabetes, but also other conditions. The basis of disease comes from inflammatory process (Chen et al., 2017). Whatever we call diseases are various inflammatory responses. This is particularly evident in diabetes. A lot of various inflammation mediators are found. This information indicates cell damage. Regardless of thecause (Karam et al., 2017).

Diabetic condition and autophagy process are responses to damage of cells. When inflammatory mechanisms are unable to cope with massive damage conditions. Involving the function of various organs. The autophagy-diabetic condition can be applied to understanding of various diseases. [48] Cellular damage that occurs in diabetes is extensive. Resulting in discovery of various mediators of inflammation in various organs. Most common in infectious diseases (Lontchi, 2013).

Thankfully, there is currently a covid-19 pandemic. Due to ignorance of this disease, anything is checked. Some patients showed elevated blood glucose levels. Even though they did not have a history of diabetes mellitus before

(Abu-Rumaileh, 2021). Similar conditions also occur in gestational diabetes. There is a discovery of various mediators of inflammation. Especially cytokines in the pancreas (Graves et al.,2019).

Previously, it was known that cytokines affect somastatin release in hypophysis gland. Somastatin was also found in pancreatic delta cells. This hormone causes cessation of glucagon and insulin release. This is one of basic information that diabetes mellitus is not a disease.

Whatever symptoms appear in covid-19 are related to inflammation ptocess and autophagy. Regarding various organs of body. Not only the respiratory tract. [4]Another example is cardiovascular disease. Cardiovascular disease is the most common complication of diabetes (Haas & Donnell, 2018). However, cardiovascular disease often occurs without hyperglycemia. Therefore, they are considered unrelated.

In fact, hyperglycemic conditions can occur not always for a long time. It is possible to have a biphasic condition. Increased blood sugar occurs at certain times. In accordance with circadian patterns. Increased blood sugar results in increased osmotic pressure. Osmotic pressure will affect fluid balance. Disturbance of fluid balance is basis of various compensatory mechanisms. Compensation that initially aims to maintain integrity of organism (Fayfman, 2017). Various diseases that result in impaired blood osmolarity have same effect. Resulting in compensatory reactions by anti-diuretic hormones (Forrest, 2001;Pelleter et al., 2014). So autophagy-diabetes process approach can be applied. In pandemic period, As not specifically, I have applied it. It gave encouraging results in just 1-2 days. I have also applied it to hepatitis B patients. It only took 1 month to achieve negative HbS Ag.

It is necessary to conduct separate research on various diseases in applying the autophagy-diabetes process. Until we can apply a standard treatment based on the autophagy mechanism.

CONCLUSION

Diabetes mellitus is not a disease. Diabetes mellitus is a condition in which body regenerates massively. Diabetes mellitus goes hand in hand with autophagy mechanism. Although insulin can overcome hyperglycemic complaints, that is not its function. Insulin also plays a role in cell regeneration process. Haphazard administration eliminates that function. A side effect of autophagy-diabetes process is fluid balance disturbance. Not just an increase in blood glucose levels.

Fluid disturbances trigger compensatory reactions. Commonly called macroangiopathy and microangiopathy compensation Further research is needed to look at autophagy process and diabetes mellitus together. Interrelated in a massive regeneration process.

CONFLICT OF INTEREST

The author declare that no conflict of interests in this work.

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