



**THE RELATIONSHIP BETWEEN METABOLIC EFFECTS AND THE HORMONE CORTISOL ON ANXIETY DISORDER PATIENTS TREATING AT MADANI HOSPITAL MEDAN**

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## ABSTRACT

*Introduction: Anxiety disorder is a condition that is often found in society in general. Long-term anxiety disorders can cause an increase in the hormone adrenaline resulting in an increase in free fatty acids and blood glucose levels, and also cause the release of the hormone cortisol, which is a glucocorticoid hormone synthesized from cholesterol in the adrenal cortex, which can have a negative impact on cardiovascular, metabolic and respiratory effects. Cortisol is commonly known as the "stress hormone", which is only released during stressful conditions. Research method: This research is a numerical analytic study with a cross sectional method, the sampling method is non-probability sampling with consecutive sampling type, with a total sample of 25 people. Results: There was a significant difference between anxiety disorders and an increase in blood sugar ( $p=0.001$ ,  $r=0,625$ ) and cholesterol levels ( $p<0.001$ ,  $r=0,717$ ). There was no significant difference between anxiety disorders and an increase in cortisone hormone with  $P=0.366$ ,  $r=0,189$ . Conclusion: There was a significant difference between anxiety disorders and an increase in blood sugar and cholesterol levels, there was no significant difference between anxiety disorders and an increase in the hormone cortisol.*

*Key words: Anxiety disorders, KGD, cholesterol, cortisol hormone*

## ABSTRAK

*Pendahuluan: Gangguan ansietas merupakan suatu kondisi yang sering dijumpai pada masyarakat secara umum. Gangguan ansietas jangka panjang dapat menyebabkan peningkatan hormon adrenalin sehingga terjadi peningkatan asam lemak bebas dan kadar glukosa darah, dan juga menyebabkan pelepasan hormon kortisol, yaitu hormon glukokortikoid yang disintesis dari kolesterol di korteks adrenal, yang dapat memberikan dampak negative terhadap efek kardiovaskular, metabolisme dan pernapasan. Kortisol umumnya dikenal sebagai "hormon stres", yang hanya dilepaskan selama kondisi stres. Tujuan: tujuan penelitian ini untuk melihat hubungan antara efek metabolik terhadap peningkatan hormon kortisol pada pasien yang mengalami gangguan ansietas. Metode: penelitian merupakan penelitian analitik numerik dengan cara cross sectional, cara pengambilan sampel dengan cara non probability sampling jenis consecutive sampling, dengan jumlah sampel sebanyak 25 orang. Hasil: Terdapat perbedaan bermakna antara gangguan ansietas terhadap peningkatan kadar gula darah ( $p=0.001$ ,  $r=0,625$ ) dan kadar kolesterol ( $p<0.001$ ,  $r=0,717$ ). Tidak Terdapat perbedaan yang bermakna antara gangguan ansietas terhadap peningkatan hormon kortisol dengan nilai  $P=0.366$ ,  $r=0,189$ . Kesimpulan: Dijumpai perbedaan bermakna antara gangguan ansietas terhadap peningkatan kadar gula darah dan kolesterol, tidak dijumpai perbedaan yang bermakna antara gangguan ansietas terhadap peningkatan hormon kortisol.*

*Kata kunci: Gangguan Ansietas, KGD, kolesterol, hormon kortisol*

## INTRODUCTION

Anxiety disorders are the most common mental disorders and get global attention because there are negative impacts such as a decrease in one's performance. Developed countries also experience the negative impact of anxiety which has an impact on the quality of physical strength<sup>1</sup>. There are some that are part of the anxiety symptoms, namely Generalized Anxiety Disorder (GAD), Obsessive-Compulsive Disorder (OCD), Post-Traumatic Stress Disorder (PTSD), panic disorder,

social phobia, agoraphobia.<sup>2</sup> Research by Caliskan H in 2019 stated that the prevalence of anxiety disorders in the global population is 3.6%<sup>3</sup>, and a study by Puspitasari IM in 2018 stated that the prevalence of anxiety disorders in Indonesia reached 9.8%.<sup>1</sup> According to research conducted by Goiato MC in 2019 an increase in the hormone cortisol in people with anxiety disorders affect the increase in blood sugar levels<sup>4</sup>, the Dehesh T study in 2020 stated that anxiety disorders can increase blood sugar levels, the Chaturvedi SK study in 2019 had a significant value ( $p < 0.002$ ) that anxiety disorders could increase blood sugar levels.<sup>2</sup> Total population who experience anxiety disorders is 3.6% in the world,<sup>5</sup> while the national data for basic health research (Ris Kesda) 2018 the prevalence of anxiety disorders in the Indonesian population aged over 15 years reached 9.8%, and anxiety disorder patients in North Sumatra province were around 12%.<sup>6</sup>

Anxiety disorder is an emotional condition that arises such as feeling uncomfortable in a person such as worrying about the object and the reasons for being uncertain and discomfort caused by something that is not yet clear.<sup>4</sup> The indirect effect of anxiety disorders is an increase in cholesterol, research conducted by Papakostas GI et al in 2004, explained that total cholesterol was found to be higher in anxiety disorders.<sup>7</sup>

Anxiety disorder is an emotional condition that encompasses a range of uncomfortable feelings such as inexplicable worries about something that is not clear or even nothing in particular. Anxiety disorders cause high cortisol and adrenaline release, where high cortisol release affects blood glucose levels that can stimulate gluconeogenesis in the liver and the result can be released into the bloodstream and some of it is stored as glycogen. Adrenaline and noradrenaline catecholamines have important roles as neurotransmitters and hormones that produce cardiovascular, metabolic, and respiratory effects, adrenaline and noradrenaline increase two to ten times during times of anxiety and affect increased myocardial contraction and blood flow<sup>4,8</sup>. Research conducted by Nasrallah AH in 2018, explained that total cholesterol was found to be higher than in patients without anxiety disorders in Taiwan.<sup>9</sup> Research conducted by Assadi SN in 2017, explained that total cholesterol had increased in patients with anxiety disorders with a value of which means ( $P < 0.05$ ).<sup>10</sup> High levels of cholesterol in the blood are a risk factor for various diseases such as heart disease, stroke, and diabetes mellitus. Based on studies that have been carried out the risk of atherosclerosis which is the cause of coronary heart disease will increase if total cholesterol levels in the blood exceed normal limits<sup>11</sup>. This study focuses in seeing the relationship between metabolic effects and the hormone cortisol on patients with anxiety disorders who seek treatment at the psychiatry ambulatory unit at Madani Hospital Medan.

## **METHOD**

This study is a numerical analytic study with the cross-sectional method to see the relationship between metabolic effects and the hormone cortisol on patients with anxiety disorders who seek treatment at the psychiatry ambulatory unit at Madani Hospital Medan. The samples were taken consecutively. This study involved patients with anxiety disorders who received outpatient treatment at the psychiatry policlinic at Madani Hospital as many as 25 people, with the following inclusion criteria: patients diagnosed with anxiety disorders based on the diagnostic criteria for PPDGJ III or DSM 5, patients aged 20-60 years, willing to participate in the study and signed informed consent. The exclusion criteria were patients who had a severe physical illness (such as stroke, kidney failure, etc.) or incomplete examination. The data that has been collected will be

checked for completeness of the data, then coding, data tabulation, and data entry into the computer will be carried out.

The results were then analyzed descriptively using a frequency distribution table and was processed by the Spearman statistical test.

## RESULTS AND DISCUSSION

In this study, there were 25 patients with anxiety disorders, then blood sugar, cholesterol, and cortisol levels were checked in these patients.

**Table 1.**  
**Distribution of Research Sample Demographic Data**

Demographic Data	N	%
Gender		
Men	11	44.0
Women	14	56.0
Age		
30-40 years old	8	32.0
41-50 years old	10	40.0
>51 tahun	7	28.0
Glucosa Ad Random		
<200	7	28.0
>200	18	72.0
Cholesterol		
<200	5	20.0
>200	20	80.0
Cortisol Hormone		
<19	25	100.0
>19	0	0.0
Anxiety		
Mild	4	16.0
Moderate	13	52.0
Heavy	8	32.0
Total	25	100.0

In the table above, based on the demographic characteristics of sex, the most commonly found are women with the count of 14 people (56.0%) and 11 (44.0%) for men. Based on age, 10 people was around 41-50 years (40.0%), 8 people in the range of 30-40 years (32.0%), and age above 51 years

as many as 7 people (28.0%). Blood sugar levels above 200mg/dl were found in 18 people (72.0%), and blood sugar levels below 200mg/dl were found in 7 people (28.0%). Cholesterol levels above 200 were found in 20 people (80.0%), and cholesterol levels under 200 were found in 5 people (20.0%). Cortisol hormone under 19 were found in 25 people (100.0%). Patients with anxiety disorders were most commonly categorized at moderate level, which is 13 people (52.0%), and 8 people were categorized as severe (32.0%), and there are four people the mild level category (16.0%).

**Table 2.**  
**The Correlation of Metabolic Effects and Cortisol Hormones on Patients with Anxiety Disorders Treated at the Madani Hospital Medan**

	Patient with Anxiety disorders			P value	r
	Mild	Moderete	Severe		
<b>Metabolic Effects</b>					
Glucosa (mean ± SD; 0.001*¥ 0,625 ; median (min-max)	132.50±10.85; 132.50 (120-145)	250.15 ± 83.67; 276.00 (110-380)	302.00 ± (51.898) 285.00 (230-370)		
Cholesterol (mean ± SD; 0.001*¥ 0,717 median (min-max)	153.50 ± 19.29; 149.50 (135-180)	279.62 ± 70.40; 285.00 (133-380)	350.88 ± 64.839 377.50 (230-405)		
<b>Cortisol Hormone</b>					
(mean ± SD; 0.366*¥ 0,189 median (min-max)	3.20 ± 0.34; 3.05 (3.0-3.7)	4.385 ± 1.89; 3.80 (2.3-9.1)	4.400 ± 2.065 3.850 (2.3-9.1)		

Based on the table above, the average blood glucose in patients with mild anxiety was  $132.50 \pm 10.85$ , the average blood glucose in patients with moderate anxiety was  $250.15 \pm 83,664$ , and the average blood sugar in patients with severe anxiety was  $302.00 \pm 51,898$ . There was a statistically significant relationship between blood glucose values and the level of anxiety disorders in patients ( $p = 0.001$ ,  $r = 0.625$ ). In patients with mild anxiety, the average cholesterol level was  $153.50 \pm 19.29$ , the average cholesterol level in patients with a moderate anxiety disorder was  $279.62 \pm 70.40$ , and the average cholesterol level in patients with a severe anxiety disorder was  $350.88 \pm 64.84$ . There was a statistically significant relationship between cholesterol levels and the patient's level of an anxiety disorder ( $p < 0.001$ ,  $r = 0.717$ ). The mean cortisol hormone value for patients with mild anxiety is  $33.05 (3.0-3.7)$ , the mean cortisol hormone value for patients with moderate anxiety is  $3.80 (2.3-9.1)$ , and the mean cortisol hormone value for patients with severe anxiety is  $3.85 (2.3-9.1)$ . There was no significant relationship between cortisol hormone levels and the patient's level of an anxiety disorder ( $p=0.366$ ).

In this study, it was found that as many as 25 patients with anxiety disorders experienced an increase in blood sugar levels ( $p = 0.001$ ,  $r = 0.625$ ) and cholesterol levels ( $p < 0.001$ ,  $r = 0.717$ ). The results of this study are in line with a study conducted by Ludhiana in 2017, and a study conducted by Wijayanto in 2019 in Lampung, which found a significant increase in blood sugar levels in patients with anxiety disorders, and also a similarity in results showed by a study conducted Elviani et al and Thirsty et al were found an increase in cholesterol levels in patients with anxiety disorders.<sup>12,13,14,15</sup> The hormones adrenaline and noradrenaline in severe anxiety disorders increase two to ten times during the patient experiencing anxiety disorders.<sup>4,16</sup> Adrenaline hormone causes an increase in free fatty acids and glucose levels. Blood and adrenal hormones also increase gluconeogenesis in the liver so that it can release most of the glucose into the bloodstream, therefore excess gluconeogenesis and glycogenolysis cause blood sugar levels to increase<sup>17</sup>. Activation of the HPA-axis by anxiety disorders also causes an increase in the release of a stimulatory hormone, namely the Corticotropin-releasing hormone (CRH), which stimulates the synthesis and secretion of glucocorticoids from the hypothalamus. CRH helps release Adrenocorticotrophic hormone (ACTH) which stimulates the secretion of glucocorticoids which activates gluconeogenesis in the liver. Increased production of glucocorticoids stimulated by the hormone adrenaline, the release of adrenaline causes the process of glycogen in the liver to increase, where previously glycogen has been obtained from glycogenolysis which is then converted into glucose, the result of this glucose entering the bloodstream causing blood glucose levels to increase<sup>12</sup>. In this study, the examination of cortisol hormone levels did not find a relationship between anxiety disorders and an increase in the hormone cortisol ( $p=0.366$ ,  $r=0.189$ ). This study is not in accordance with a study conducted by Goiato and colleagues in 2019 in Brazil where an increase in the hormone cortisol was found in patients with anxiety disorders. This may be due to the number of samples and the different ways of sampling in these studies<sup>4</sup>.

Anxiety disorders are one of the causes of an increase in glucocorticoid hormones (cortisol), and catecholamines (epinephrine). The physiological responses involved in anxiety disorders can affect the action of the pituitary hypothalamus which has an impact on endocrine functions such as increased cortisol levels which have an impact on insulin excretory function and can stimulate gluconeogenesis and inhibit glucose absorption so that it triggers an increase in glucose and cholesterol levels in the blood<sup>12</sup>.

The specific stress response is the release of adrenocorticotrophic hormone and cortisol into the bloodstream as a result of activation of the hypothalamic-pituitary-adrenal axis. Cortisol is a glucocorticoid hormone synthesized from cholesterol in the adrenal cortex. Cortisol is commonly known as the “stress hormone”, which is only released during stressful conditions<sup>18</sup>. Central neuropeptides, in particular, CRH induce a response to stress by triggering neuro endocrinological pathways, such as the HPA-axis, the sympathetic nervous system, and angiotensin, resulting in the release of stress hormones (i.e. corticosteroids, catecholamines, glucagon, growth hormone, and renin). This process together with stress-induced cytokines causes the Acute Phase Response and activation of acute phase proteins, which are important inflammatory mediators. Norepinephrine in the central nervous system can also cause an Acute Phase Response by activating macrophages and releasing cytokines. The brain can activate the inflammatory process or inhibit it. In addition, stress and inflammation are mediated by the same neuropeptide (ie, CRH). Cytokines evoked by the inflammatory or stress response can pass similarly, passing through somatosensory pathways

to signal the brain. Repeated episodes of acute or chronic psychogenic stress can cause chronic inflammatory changes in the brain and other organs<sup>19</sup>.

Some studies showed that psychological stress increases the risk of acute upper respiratory tract infections. They also found that due to repeated stressful events, immune cells fail to control the inflammatory response thereby increasing susceptibility to disease. That studies demonstrated that prolonged stress alters the efficacy of cortisol to modulate immune responses due to reduced tissue sensitivity to cortisol. A meta-analysis showed that the experience of chronic stress can alter the immune system's response, which may increase the susceptibility to disease<sup>19</sup>. The importance of maintaining mental health (anxiety, and depression) because it not only affects the body's metabolism and hormone regulation but can also have an impact on a person's activity and performance. This is in accordance with a study conducted by Nopa et al., stress or anxiety disorders can affect a person's performance, and stress at work can reduce performance on the job<sup>20</sup>.

### **LIMITATION OF THE STUDY**

In this study, blood sampling was carried out by checking blood sugar levels ad random and only assessing total cholesterol levels, which should also be checked for fasting blood sugar levels, triglycerides, LDL and HDL. The patient's activity, exercise and diet were also not assessed so they could also be confounding factors in blood sugar and total cholesterol levels.

### **CONCLUSION AND SUGGESTIONS**

In this study, a significant difference was found between anxiety disorders and increased blood sugar and cholesterol levels, but there was no significant difference between anxiety disorders and increased levels of the hormone cortisol.

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