

# Histology of Small Intestinal in Hypothyroid Model Rats

Sherly Usman<sup>1\*</sup>, Aisyah Luthfia Firdasari<sup>2</sup>, Zulkhah Noor<sup>3</sup>

<sup>1</sup>*Histology Departement, Faculty of Medicine, Universitas Muhammadiyah Yogyakarta*

<sup>2</sup>*Medical Doctor Program, Faculty of Medicine, Universitas Muhammadiyah Yogyakarta*

<sup>3</sup>*Fisiology Departement, faculty of Medicine, Universitas Muhammadiyah Yogyakarta*

\*Corresponding author. Email: sherlyusman@umy.ac.id

## ABSTRACT

More than 700,000 people were diagnosed with hypothyroidism, in Indonesia case is quite large. The study aims to see differences in the histological features of villi epithelium small intestine mucosa hypothyroid rats. The design was experimental post only group. This hypothyroidism is obtained by giving daily drinks that have been mixed with 0.025% Propylthiouracil (PTU). Ten of Subjects were divided into 2 groups: group 1 (control) and group 2 (hypothyroid), each group consisted of 5 mice. The PTU treatment was carried out for 8 weeks. Decapitation was carried out with chloroform and Intestinal organs were taken by opening the stomach. Intestinal organ then processed into histological preparations. The preparations are seen for changes in the histological picture through a microscope by scoring the damage to the intestinal mucosa. Data analysis used the Shapiro-Wilk and Independent T test. In control group showed bleeding was moderate. In hypothyroidism group showed heavy bleeding intestinal mucosa, while necrosis and erosion showed mild criteria. This research is be able to provide scientific support through data regarding histology of the mucosal lining of the small intestine in hypothyroid rat models. Conclusion: Histology of small intestinal in hypothyroid model rats showed damage mucosa with erosion, bleeding and necrosis.

**Keyword:** *Hypothyroidism; small Intestinal, mucosa;*

## INTRODUCTION

Hypothyroidism is a condition in which thyroid hormone levels in the body are lower than normal due to abnormal production<sup>1</sup>. Decreased levels of thyroid hormone in hypothyroid patients will result in increased levels of TSH in the blood. Normal TSH levels range from 0.5-4.5 mU/L. However, in thyroid patients, TSH levels will soar more than 5 mU/L<sup>2</sup>.

According to basic health research in 2013, as many as 0.4% of the Indonesian population aged 15 years or older admitted being diagnosed with hypothyroidism. although the percentage is small, the quantity is quite large because if in 2013 the population of Indonesia was 176,689,336 people, more than 700,000 people were diagnosed with hypothyroidism<sup>3</sup>.

Thyroid hormones have an impact on growth, development, and various cellular processes of the body. Thyroid hormone is an important hormone in brain growth, central nervous system development, metabolism, and autonomic nervous system function. Thyroid hormone plays an important role in basal metabolism throughout the body, especially in the intestines<sup>4,5</sup>.

When the body is deficient in iodine, the intake of iodide is disturbed. This will interfere with thyroid hormone secretion and cause disruption of cell function and the absorption of amino acids by the small intestine<sup>6</sup>. This situation has an impact on digestive problems, namely

constipation to weight gain<sup>3</sup>. Digestive problems that occur then affect the function of the epithelium and mucosa of the small intestine, namely cell damage such as bleeding, necrosis, and erosion<sup>7</sup>.

There have been many studies on the comparison of histology in hypothyroid model rat organs such as the thyroid gland, brain, testes, and so on that provide an influential picture. However, there have been no studies on the histology of the small intestine in hypothyroid rat models.

Therefore, in this study, the researchers wanted to know the comparison of histopathological features in the intestines of normal rats with hypothyroid rat models induced by 0.025% PTU. This research is be able to provide scientific support through data regarding histology of the mucosal lining of the small intestine in hypothyroid rat models.

## MATERIAL AND METHOD

This type of research is an experimental study with a post only group design approach to test animals. This research was conducted in the laboratory of the Faculty of Medicine and Health Sciences, University of Muhammadiyah Yogyakarta in the period from September to November 2020.

This study used Wistar rats with criteria; Weight are 200-250 grams and aged 3-4 month. The rats were then adapted in a rearing cage for one week with standard feeding and drinking.

The rats were then grouped into two, namely the

control group and the treatment group, each of which consisted of five rats. The grouping of rats was done by randomization system.

Hypothyroid rats as treatment group were made by induction of PTU 0.025% by mixing 25 mg of PTU into 100 ml of water and given to mice through daily drinking<sup>8</sup>. Rats that had been treated for eight weeks were necropsied and previously decapitated with chloroform. Intestinal organ taking by open the rat's abdomen and then processed into histological preparations.

The preparat have been made are seen for changes in the histological picture through a microscope. Intestinal mucosal damage was assessed based on bleeding, necrosis, and erosion using the intestinal mucosal damage score<sup>9</sup>. The research scoring is following the principles of Gibson-Corley et al (2013) (table.1).

**Table of 1. Intestinal Mucosal Damage Scoring**

Category	Definitons	Score
Bleeding	Normal	0
	Mild bleeding	1
	Moderate bleeding	2
	Severe bleeding	3
Necrosis	Normal	0
	Mild Necrosis	1
	Moderate Necrosis	2
	Severe Necrosis	3
Erosion	Normal	0
	Mild Erosion	1
	Moderate Erosion	2
	Severe Erosion	3

Normal: 0 or no bleeding, necrosis, or erosion  
 Mild: there are 0.1-2 bleeding, necrosis, and erosion in 1 field of view  
 Moderate: there are 3-5 bleeding, necrosis, and erosion in 1 field of view  
 severe: there are >5 bleeding, necrosis, and erosion in 1 field of view.

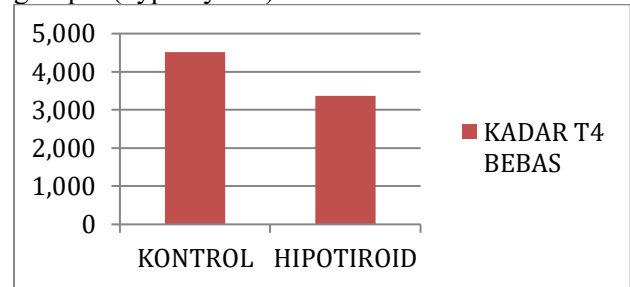
The data obtained were analyzed using SPSS version 15.0. The results tested for the normality of the data distribution using the Saphiro-Wilk test. After normal data results, the data was then tested with an independent sample T test.

**RESULT**

**Free T4 levels in the treatment group.**

The free T4 data in group 1 (control) and group 2 (hypothyroid) it was found that the average in group 1 (control) was 4,51 and in group 2 (hypothyroid) was 3,36, this indicates that there is a decrease in T4 levels in group 2 (hypothyroid) (Figure of 1).

Figure of 1. The free T4 data in group 1 (control) and group 2 (hypothyroid)



From the results of the independent sample t test, the t value of the free T4 level was 0,037. While the significance is 0,002. This shows that the free T4 levels in group 1 (control) and group 2 (hypothyroidism) have statistically significant differences.

**Scoring the intestinal damage mucosa small interstitial**

From the results of the scoring, the bleeding data in group 1 (control) obtained an average score of 2 in the entire visual field. This shows that bleeding in group 1 (control) is included in the moderate criteria.

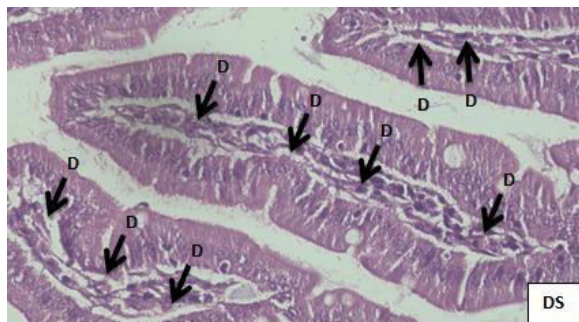


Figure of 2. bleeding (D) in the intestinal villi with moderate bleeding criteria (DS) in the control group.

The results of bleeding data in group 2 (hypothyroid) in the entire field of view obtained an average score of 3 which means that bleeding in group 2 (hypothyroid) is included in the severe criteria.

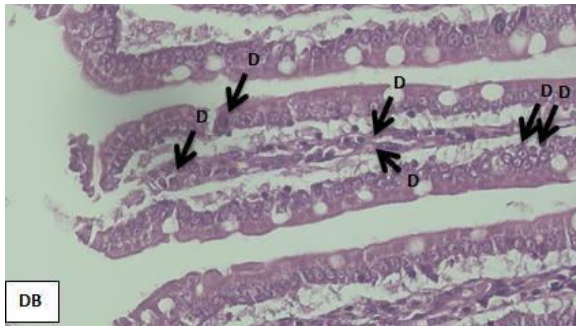


Figure of 3. bleeding (D) in the villi mucosae group 2 (hypothyroid). Included in the criteria for heavy bleeding (DB).

The average score for necrosis and erosion result in group 1 (control) and group 2 (hypothyroidism) for the entire visual field was 1. It showed that necrosis and erosion in group 1 (control) and group 2 (hypothyroid) are included in the mild criteria.

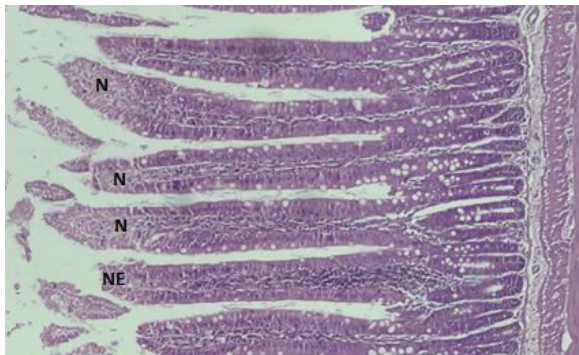


Figure of 4. intestinal villi in group 2 (hypothyroid) showed mild necrosis (N), the color looks paler and there is necrosis with slight erosions (NE).

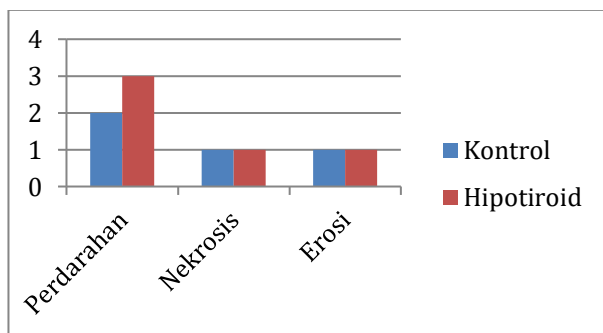


Figure of 5. The results of scoring observations of intestinal histopathological images of hypothyroid rat models.

The data from the scoring results were tested for normality using the *Saphiro-Wilk* test. Table 1 shows that all data distribution results are normal ( $p > 0.05$ ). the data was

further tested with the independent sample T test.

**Table of 2. Different test results Independent Sample T Test t-test for Equality of Means**

Independent Sample T Test		
	Sig.	Sig. (2-tailed)
bleeding	-9,099	0,000
Necrosis	-12,298	0,000
Erosion	-1,707	0,126

From the results of the independent sample T test, it was found that the t value for bleeding data was -9.009, necrosis data was -12.298, and erosion data was -1.707. In the bleeding data and necrosis data obtained a significance of 0.00. while the erosion data obtained a significance of 0.126. So that the bleeding and necrosis data have statistically significant differences.

## DISCUSSION

Hypothyroidism is a common condition of deficiency of thyroid hormone in the body which can be caused by radioactive iodine and surgical therapy for hyperthyroidism or thyroid cancer, inflammatory thyroid disease, iodine deficiency, and some medications that cause thyroid cancer interfere with the synthesis or availability of thyroid hormones<sup>10</sup>.

Thyroid hormone is a compound derived from the breakdown of protein into the amino acid tyrosine. In normal digestion, digested protein will be broken down into polypeptide forms and undergo further breakdown into shorter ones such as tripeptides, dipeptides, and amino acids. These amino acids will be absorbed by the intestinal walls so that the nutrients in the body are fulfilled<sup>11,12</sup>.

Hypothyroidism is generally defined as a deficiency in thyroid hormone production. The term primary hypothyroidism denotes a decrease in thyroid secretion of thyroid hormone by factors that affect the thyroid gland itself. The decrease in the serum concentration of thyroid hormone causes an increase in TSH secretion which results in an increase in the serum TSH concentration. Decreased thyroid secretion of thyroid hormones can also be caused by insufficient stimulation of the thyroid gland by TSH. Insufficient stimulation of this gland is caused by factors that directly interfere with pituitary TSH release (secondary hypothyroidism) or indirectly by reduced hypothalamic TRH release (hypothyroidism tertiary)<sup>13</sup>.

Hypothyroidism can cause decreased motor activity in the stomach, small intestine, and large intestine. The disorder involves the activity of the thyroid gland. The thyroid gland is one of the glands in the endocrine system. This gland is the largest gland in the endocrine system. The thyroid gland is important for normal body growth in infancy and childhood. This gland absorbs iodine from food and releases thyroid hormone in the form of iodine-containing compounds that help regulate the body's metabolic rate<sup>14</sup>.

In this study, wistar rats were used as hypothyroid

rats. To make hypothyroid rats, PTU 0.025% was induced. PTU is an antithyroid drug that works by blocking the production of new thyroid hormone. According to Gupta and Rehman (2020), this unproduced thyroid hormone triggers a detrimental effect in the rat's body, which causes the rat to experience hypothyroidism<sup>15</sup>. PTU works by inhibiting the conversion of T4 to T3. This then has an effect on thyroid hormones which are stored in the thyroid gland or circulated in the blood<sup>15</sup>.

In this study, it was found that there were significant differences in the histology of bleeding and necrosis intestinal mucosa between group 1 (control) and group 2 (hypothyroid). In group 2 (hypothyroid) more bleeding was found than in group 1 (control). This is evidenced by the histology of the intestinal mucosa found bleeding, necrosis, and erosion in some parts of the villi. This shows that there is an effect of changes in the intestinal mucosa in hypothyroid rats.

Bleeding occurs due to abnormalities of the blood vessel wall resulting in erythrocyte infiltration in the interstitial tissue or cells<sup>16</sup>. Necrosis is cell death due to loss of control of ionic balance, water uptake, swelling, and cellular lysis. lysis then releases many intracellular constituents, attracts immune cells and triggers an inflammatory response in the cells<sup>17</sup>. While erosion occurs when bleeding occurs causing problems in the blood circulation system causing edema<sup>18</sup>.

The occurrence of hypothyroidism will cause problems in the digestive system, namely constipation and weight loss<sup>19</sup>. Several studies have revealed that patients with constipation will experience disturbances in the composition and stability of the gut microbiota. Disruption of the composition and gut microbiota of the mucosa can affect the function of the epithelium and mucosa more than the fecal microbiota<sup>20</sup>.

The digestive system has a microbiota that helps the intestines in the breakdown of food products into absorbable nutrients, stimulates the immune system, prevents the growth of pathogenic bacteria, and produces various important compoundsbiologically, such as short chain fatty acids (SCFA) and neuro-modulating substances. Disorders that occur in the function of the epithelium and smooth mucosa can then be seen through bleeding, necrosis, or erosion<sup>20</sup>.

## CONCLUSION

Histology of small intestinal in hypothyroid model rats showed damage mucosa intestinal with erosion, bleeding and necrosis.

## Suggestion

It is necessary to conduct further research on the effect of hypothyroidism on the intestine by giving PTU using a randomized control trial design to determine the histology of the small intestine in hypothyroid rats more. Further research on PTU dosage variables should be more varied. Extend the research time and tiered

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