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Effect of Turmeric Rhizome Extract (*Curcuma longa* L.) on Kidney Histology of Preeclampsia Rats (*Rattus norvegicus* L.)

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Abstract. Preeclampsia (PE) is second death in pregnancy in Indonesia. This study aims to determine the effect of turmeric extract (*Curcuma longa* L.) on renal necrosis, narrowing of the proximal tubulus, renal weight and changed of renal color of rats. This study used a type of analytic study with an experimental quasi design in pregnant female rats (*Rattus norvegicus*) consisting of four treatments with six replications each. The study consisted of a negative control group (K-) with only feed given *ad libitum*, positive control (K +) in injection of LPS *intervena* with a dose of 0.2 / kgBW, and 2 group giving turmeric extract (*Curcuma longa* L.) with doses of 400 mg / kgBW (P1) and 600 mg / kgBW (P2). Rats (*Rattus norvegicus*) are dissected to take the kidneys. Kidneys are made into a preservative preparation with the paraffin method and staining Hematoxylin-Eosin (HE). The results of renal morphology observations showed a change in color in the treatment group P2. The histological features of the kidneys in the proximal tubulus showed a decrease in P1 compared to the P2 group and the percentage of renal necrosis in P2 had a significant change compared to the positive control group (K+). Extract of Turmeric rhizome (*Curcuma longa* L.) is proven to be able to maintain and improve the structure of cells of the kidneys in the Rats preeclampsia model.

1. Introduction

Pregnancy was defined as a fertilization of spermatozoa and ovum and followed with nidation or implantation. Intra-uterine fetal growth and development starts from conception and ended until the beginning of labor [1,2]. Preeclampsia is one of the main causes of morbidity and mortality do perinatal in Indonesia. Until now the preeclampsia disease is still a problem that can not be solved thoroughly [2-4]. Preeclampsia was the second leading cause of maternal death in the world after bleeding [3,5]. According to the Indonesian Demographic and Health Survey in 2007, PE contributed to 24% of maternal deaths in Indonesia, this makes PE the second leading cause of maternal mortality in Indonesia at high risk [5].

The kidney have a role in the excretion process of a compound, then if there is impaired kidney function, it will result in a change in the pharmacodynamic compounds that are caused by changes in the levels of compounds in the blood, especially the compound are mostly excreted through the kidney [6]. PE can cause diseases of the liver [7,8] and kidneys that are at risk for the sufferer. These diseases may not be initiated by pregnancy, but are very disturbing to pregnancy. The correct diagnosis therefore has high clinical relevance [9].

Turmeric, *Curcuma longa* L. (Zingiberaceae) is a tropical plant widely found in the Asian continent extensively used as a food coloring, *bis*-demethoxy curcumin. While the essential oil consisting of sesquiterpen ketones, turmeron, tumeon, zingiberen, felandren, sabinen, borneol, and sineil. The other



content of turmeric include fat, carbohydrates, protein, starch, vitamin C, carotene, mineral salts (iron, phosphorus, calcium) [10].

2. Materials and Methods

This research is an experimental study conducted at Laboratory in the Biology Laboratory University of Sumatera Utara, Indonesia. The material that used is turmeric extract (*Curcuma longa* L.) [11-14]. This research is using the analytic study type with an experimental quasi design in pregnant female rats (*Rattus norvegicus*). The rats used are 10 weeks aged rats with the average weight around 150-250 g as many as 24 tails consisting of 4 treatments with 6 replications on each treatment.

The method of grouping is with filled up 4 groups of rat that are divided into 4 treatments, where the group 1 is for negative (normal) control, the pregnant rats not given any treatment, group 2 is for positive control of the pregnant rat by the LPS injection (lipopolysaccharide) to became preeclampsia rat, the group 3 is for the rats that were pregnant by the LPS injection (lipopolysaccharide) and given turmeric rhizome extract (*Curcuma longa* L.) with a dose of 400 mg/kgBW in twice a day, the group 4 is for pregnant rats by the LPS injection (lipopolysaccharide) and turmeric rhizome extract (*Curcuma longa* L.) with a dose of 600 mg/kgBW in twice a day. This treatment is in accordance with Fereder's formula, that:

$$(t-1)(n-1) \geq 15$$

Information :

t = Number of treatment groups

n = Number of replications

The rats were given feed and drink in *ad libitum*, then rats were injected with the LPS through intervena on the tail in order to became a rat model for preeclampsia. After that, a proteurinaria check is done every day (8-10 a.m.) and rat's systolic blood pressure is monitored every three days. LPS injected rats then were given turmeric extract (*Curcuma longa* L.) orally with a dose of 400 mg / kgBW and 600 mg / kgBW and given in twice a day. Giving extract done orally using gavage needles and 1 ml syringe [1,15-18].

Pregnant rats were dissected on the 17th day of pregnancy by anesthetizing using chloroform, then dislocated neck after surgery in the anesthetic condition performed on the abdomen. After the abdominal cavity is opened, the kidneys are taken and inserted into the sample bottle which contains 10% Formalin Neutral Buffer. And histological preparations with paraffin method and Hematoxylin Eosin (HE) staining to observe necrosis and narrowing of the tubulus in the kidneys. Data was processed using the SPSS 22 program with the Kruskal Wallis test.

3. Result And Discussion

3.1. Color of Kidney

Based on Figure 1, it can be seen that there is no difference color between the rats (*Rattus norvegicus*) control group (-), and the treatment group of preeclampsia rats given turmeric rhizome extract (*Curcuma longa* L.) with a dose of 400 mg/kg and 600 mg doses/kgBW. The control kidney shows a dark red color. Dark red color in the kidney means that the kidney was in a good condition and has a high blood flow. The kidney has the role of receiving 22% of the blood flow from all the volume of blood pumped by the heart. The blood supply received by the kidneys is the same as other organs containing nutrients, besides the kidneys produce metabolic waste in the form of keratin, urea and other substances that are excreted in the urine [3].

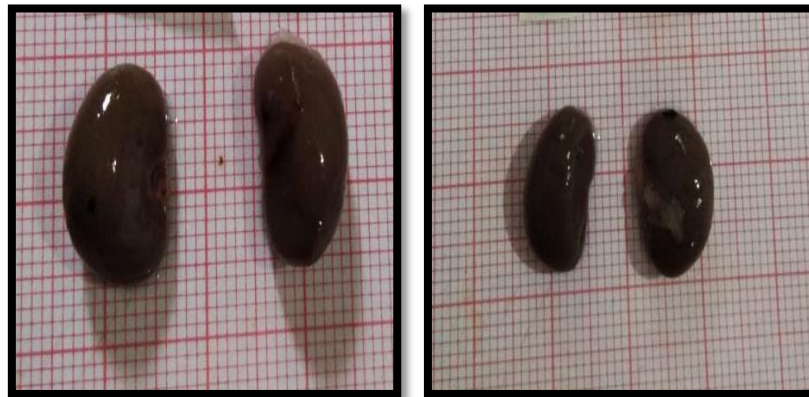


Figure 1. Right and left kidneys of female rats (*Rattus norvegicus*) in Control group (Left) and the Treatment group (Right).

3.2. Weight of Kidney

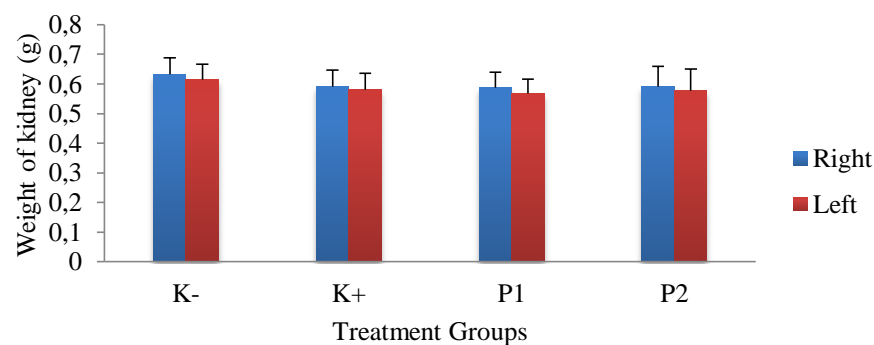


Figure 2. Average weight of right kidney and left of female rats (*Rattus norvegicus*) in the control group (-), control group (+), group P1: those given turmeric rhizome extract (*Curcuma longa* L.) with a dose of 400 mg/kgBW, P2 group was given turmeric rhizome extract (*Curcuma longa* L.) with a dose of 600 mg/kgBW.

Based on Figure 2, the average weight of the right kidney and the weight of the female rat (*Rattus norvegicus*) left kidney between the control group (-), the control group (+) of preeclampsia mice, group P1 of preeclampsia rats were given turmeric extract (*Curcuma longa* L.) with a dose of 400 mg/kgBW and P2 preeclampsia rats given turmeric extract (*Curcuma longa* L.) with a dose of 600 mg/kgBW did not increase and statistically also did not experience a significant difference ($p > 0.05$), it is proven that (*Curcuma longa* L.) is not toxic so it does not affect the kidney's weight in each treatment. The shape of the kidney affects the size and weight of the kidney. Enlarged kidney size is usually related with widening the system of pelvicalices due to obstruction in the distal area causing hydronephrosis which forces the renal cortex and causes cortex thinning. shrinking kidney size usually occurs due to chronic processes, including prerenal disorders [3].

3.3. Percentage Of Proximal Tubulus

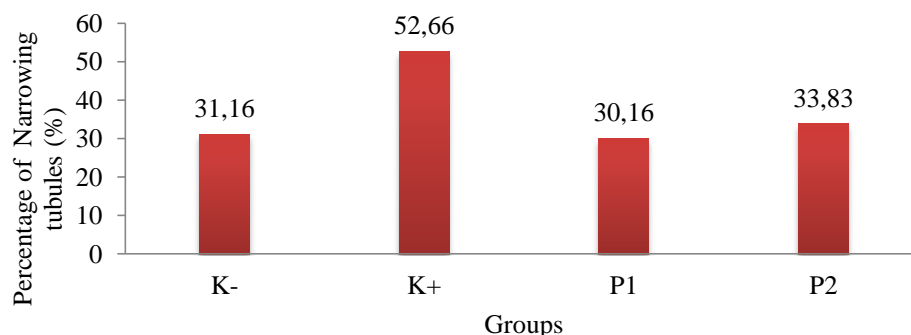


Figure 3. The percentage of narrowing renal tubulus rats (*Rattus norvegicus*) in the control group (-), control group (+), group P1: those given turmeric extract (*Curcuma longa* L.) with a dose of 400 mg/kgBW, P2 group is given turmeric extract (*Curcuma longa* L.) with a dose of 600 mg / kgBW

Based on Figure 3, it can be seen the percentage of female rats (*Rattus norvegicus*) narrowing renal tubules between the control group (-), the control group (+) preeclampsia rats, group P1 preeclampsia rats that given turmeric rhizome extract (*Curcuma longa* L.) with a dose of 400 mg / kgBW and P2 preeclampsia rats is given turmeric extract (*Curcuma longa* L.) with a dose of 600 mg / kgBW statistically had a significant difference ($p < 0.05$), where in the P1 preeclampsia rats were given turmeric rhizome extract (*Curcuma longa* L.) with a dose of 400 mg/kgBW decreased tubules constriction of 30.16%, this indicates that with a dose of 400 mg/kgBW turmeric extract (*Curcuma longa* L.) is able to repair narrowed tubulus. Initial damage to the kidneys causes swelling of the cells, resulting in loss of tubular cell polarity. This results in redistribution of membrane proteins from the basolateral surface to the lateral surface of the tubular cells so that the distribution of protein to the distal tubule increases causing vasoconstriction. In addition to the tubules, it can also be found that cell injury is accompanied by vacuolization and dense inflammatory cell groups in response to the presence of necrotic cells [3]. The pathway of cell death can also occur through apoptosis [19,20].

3.4. The Percentage of Necrosis Kidney

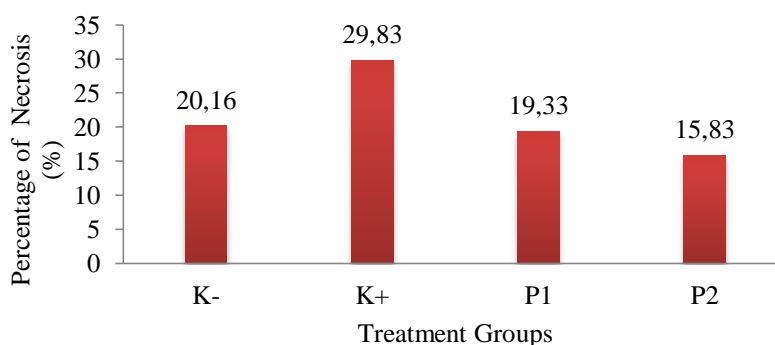


Figure 4. The percentage of kidney necrosis in female rats (*Rattus norvegicus*) in the control group (-), control group (+), group P1: those given turmeric rhizome extract (*Curcuma longa* L.) with a dose of 400 mg/kgBW, P2 group extracted turmeric rhizome (*Curcuma longa* L.) with a dose of 600 mg/kgBW

Based on Figure 3.4 can be seen that the percentage of necrosis narrowing in female rats kidney (*Rattus norvegicus*) between the control group (-), control group (+) preeclampsia rats, group P1 preeclampsia rats is given turmeric extract (*Curcuma longa* L.) with a dose of 400 mg/kgBW and P2 preeclampsia rats is given turmeric extract (*Curcuma longa* L.) with a dose of 600 mg/kgBW statistically experienced a significant difference ($p < 0.05$), where in P2 preeclampsia rats is given turmeric extract (*Curcuma longa* L.) with a dose of 600 mg/kgBW decreased the necrosis percentage which is 15.83%, this indicates that with a dose of 600 mg/kgBW turmeric extract (*Curcuma longa* L.) is able to improve kidney necrosis [31,33-37]. The causes of cell damage include lack of oxygen, infection, immune reactions, genetic defects, nutritional imbalances, drugs and chemicals [2,4].

3.5. Histology of Kidneys

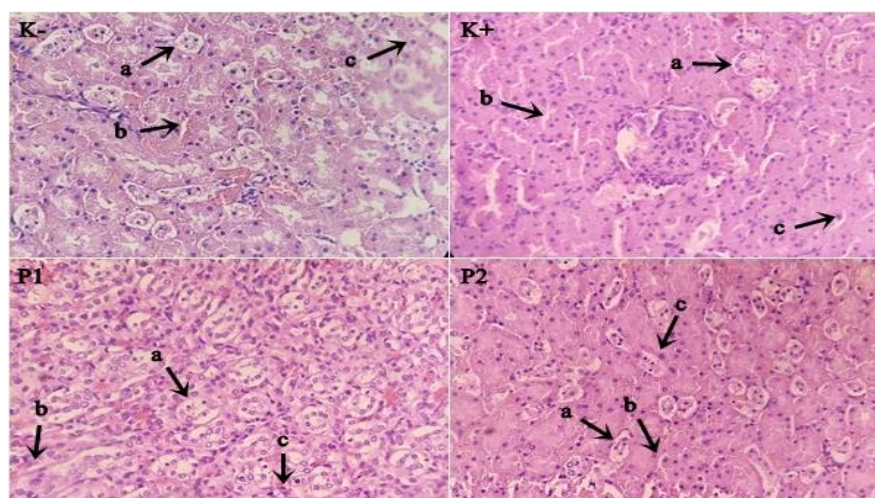


Figure 3.5 Histology of kidneys. K(-): Control; K(+): Preeclampsia; P1: Turmeric extract (*Curcuma longa* L.) with a dose of 400 mg/kgBW P2: Turmeric extract (*Curcuma longa* L.) with a dose of 600 mg/KgBW. a) Normal Tubulus b) Narrowing tubulus. c) Necrosis

Based on histological observations of the kidneys, the proximal tubule narrowing is found in K+, but the given of turmeric rhizome extract at a dose of 400g/kgBW on P1 can repair damage from the tubulus. While a dose of 600g/KgBW in P2 can reduce kidney necrosis. Kidney damage in PE can cause proximal tubular epithelial cells to swell with the granular cytoplasm. Swelling that occurs causes the proximal tubular lumen to narrow to close. The proximal tubular epithelial cells are sensitive to anoxia, and are easily destroyed by poisoning, due to contact with substances that are excreted through the kidneys, which can cause the pale cortex, enlarged kidney and edema, pyramidal congestion, vacuolated cytoplasm of epithelial cells in proximal tubulus [3]. Acute kidney injury (AKI) is a serious problem during pregnancy and understanding the physiological kidney adaptation during pregnancy is essential for early detection, diagnosis, and appropriate management to prevent obstetric complications [26] Kidney disease is one disease that in PE women has a high risk of pregnancy abnormalities, although until now there have been no reports of maternal deaths, premature birth or neonatal death [29,31,32].

4. Conclusions

Turmeric extract (*Curcuma longa* L.) with a dose of 400 mg/kgBW can improve the narrowing of kidney proximal tubules in preeclampsia rats but unable to improve kidney necrosis. Unlike the turmeric extract (*Curcuma longa* L.) with a dose of 600 mg/KgBW which is able to improve kidney's necrosis. Therefore from the turmeric extract (*Curcuma longa* L.) it is safe to consume for preeclampsia.

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