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Morphological Changes in the Lungs of 5-Month-Old Albino Rats Following Chronic Kidney Disease

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Abstract This scientific study investigates the histomorphological changes occurring in lung tissues under conditions of chronic kidney disease (CKD). The experiment involved 30 five-month-old albino rats. CKD was induced using a modified version of the Greven method by intramuscular injection of a 5% glycerol solution. Histological sections of the lung revealed pathological alterations such as thickening of the alveolar septa, interstitial fibrosis, alveolar collapse, and inflammatory infiltration. The obtained results demonstrated that severe morphological disturbances develop in lung tissue against the background of CKD.

Keywords Chronic kidney disease, Lung morphology, Histology, Rat, Glycerol, Greven method, Experimental model

1. Introduction

Chronic kidney disease (CKD) is a complex syndrome characterized by the progressive decline of renal function, which leads to pathological changes in various organ systems including the cardiovascular, endocrine, and respiratory systems. According to the World Health Organization, the global prevalence of CKD is steadily increasing, significantly affecting patients' quality of life and life expectancy [1].

Due to the close physiological relationship between the kidneys and lungs, impaired renal function can cause a range of respiratory system disorders. In CKD, hemodynamic changes, accumulation of nitrogenous waste products, hypoxemia, and disturbances in acid-base balance can lead to morphological alterations in lung tissues. Additionally, prolonged exposure to uremic toxins may damage alveolar barriers, capillaries, and bronchiolar structures [2,3,4].

While the impact of CKD on organs such as the heart, liver, and brain has been extensively studied, data on lung tissue changes remain limited. In particular, there is a lack of research focusing on young experimental animal models such as 5-month-old white outbred rats which highlights the relevance and urgency of this topic [5,8].

In this study, morphological changes in the lungs were histologically examined in rats with CKD induced using the Greven method. The aim was to identify and characterize structural alterations in lung tissues resulting from CKD and to evaluate age-related differences in these pathological changes [6,7,9,10].

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Chronic kidney disease (CKD) is a serious medical, social, and economic problem. It is characterized by the steady increase in the number of affected patients, the high cost of treatment, and poor work-related prognosis [12]. Chronic kidney disease is widespread globally, affecting more than 10% of the population, which corresponds to over 800 million individuals. This condition poses a significant public health burden, particularly in low- and middle-income countries, and is among the leading causes of death [13].

CKD and its consequences are among the few non-communicable diseases marked by a rising mortality rate over the past two decades [13]. The increasing prevalence of CKD is associated with longer life expectancy and reduced early mortality from complications of hypertension and diabetes. In addition, advancements in treatment such as the introduction of dialysis have dramatically changed the prognosis for CKD patients. However, there remains a growing need for more information about the condition of internal organs and systemic changes during prolonged uremia [14].

Chronic kidney disease leads to distinct structural changes in the interstitial tissues of the lungs. Microcirculatory disturbances occur along with redistribution of the intercellular matrix in the connective tissue [14,15]. In the bronchopulmonary system, mixed-type ventilatory impairments and reduced pulmonary diffusing capacity are observed [16]. One of these manifestations is pulmonary calcification, which contributes to decreased lung volume and impaired gas exchange [17]. Studies have shown that the lungs of uremic rats exhibit changes such as massive atelectasis, chronic edema, bronchiolitis, and pulmonary fibrosis. Lung damage during renal failure follows a progressive course [18].

Pulmonary hypertension is also a common pathological condition associated with CKD and end-stage renal disease

(ESRD). This condition not only leads to adverse clinical outcomes but also increases the risk of mortality. Although the relationship between pulmonary hypertension and mortality is not yet fully understood, observational studies support this association [19]. The interaction between the lungs and kidneys is clinically complex and may lead to fluid and acid-base imbalance, vascular tone changes, and hemodynamic disorders in the lungs. The kidneys influence overall physiology through sodium and water retention, as well as by disrupting perfusion and filtration processes [20].

Other systemic manifestations of CKD include malnutrition, muscle atrophy, anemia, osteoporosis, and cardiovascular diseases. These conditions highlight the crucial role of endothelial dysfunction in the early stages of CKD [11]. Moreover, increased venous pressure may disrupt the alveolar-capillary interface and lead to damage of capillary walls [12].

In this context, the main objective of the present study is to investigate morphological changes occurring in lung tissue under experimental chronic kidney disease (CKD) conditions, with a specific focus on the use of the Greven method. The findings of this research will contribute to a better understanding of lung tissue alterations associated with CKD and may serve as a foundation for developing future therapeutic strategies for pulmonary pathologies.

2. Materials and Methods

The study involved 30 healthy, 5-month-old outbred white rats weighing between 180–220 grams. To experimentally induce chronic kidney disease (CKD), a modified version of the Greven method was used. A 5% glycerol solution was administered intramuscularly (into the m. gluteus) at a dose of 8–10 ml/kg, twice, with a 24-hour interval between injections. Fourteen days after the experiment began, the animals were sacrificed under anesthesia, and their lung tissues were fixed in a 10% neutral buffered formalin solution for histological examination. The tissues were embedded in paraffin blocks, and sections of 5–7 µm thickness were prepared and stained with hematoxylin and eosin for analysis under a light microscope. Histomorphometric measurements were performed using a digital microscope system, such as the ToupView software.

3. Results and Discussion

Histological analysis of the lung samples revealed several significant morphological alterations in the CKD group. These included pronounced thickening of the alveolar septa, increased presence of fibroblasts and collagen fibers in the interstitial tissue, collapsed alveoli, and mononuclear inflammatory infiltration. These structural changes represent the pathological basis for impaired pulmonary gas exchange function.

The results of this study are consistent with several international sources. For instance, Faulkner et al. (2021) reported thickening of the alveolar walls and interstitial fibrosis in rats with CKD. Another study by Lee et al. (2020) highlighted that uremic toxins and oxidative stress in CKD can lead to apoptosis and inflammation in lung tissue.

The use of a 5% glycerol solution in this study enabled the development of a mild yet effective model of chronic kidney disease (CKD), characterized by minimal mortality among the animals and sufficiently distinct histological morphological alterations. This demonstrates the advantages of the experimental model.

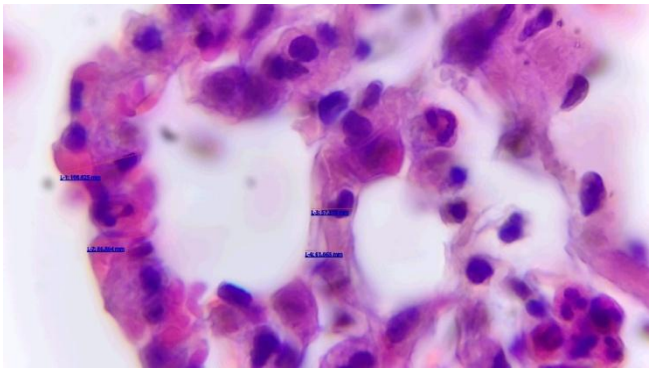

Figure 1. Histological Image of the Lung of a 5-Month-Old Albino Rat Stained with Hematoxylin and Eosin

Histological analysis of lung tissue from a rat model with experimentally induced chronic kidney disease (CKD) demonstrates irregularly shaped and variably sized alveolar spaces. The interalveolar septa are markedly thickened, likely due to proliferation of interstitial fibroblasts and increased deposition of collagen fibers. Perialveolar regions exhibit dense mononuclear inflammatory cell infiltration, predominantly composed of lymphocytes and macrophages. Occasional areas show alveolar collapse and deformation of alveolar walls. Histomorphometric measurements indicate alveolar wall thickness ranging from 57 to 108 µm, suggesting significant thickening compared to normal lungs. These structural alterations likely reflect secondary pulmonary injury driven by uremic toxins, oxidative stress, and systemic inflammation associated with chronic kidney disease.

Table 1. Inflammatory cells in the control group

Total number of detected cells	17
Leukocyte cells	9
Neutrophil Cells	5
Neutrophil Expression	57.3 %
General area	898456px^2

Table 2. Inflammatory cells in the experimental group

Total number of detected cells	55
Leukocyte cells	11
Neutrophil Cells	45
Neutrophil Expression	88.31 %
General area	884645px^2

Based on the histological examination of 5-month-old rats from both experimental and control groups, the following conclusions can be drawn:

In the chronic kidney disease (CKD) experimental group, a significant increase in neutrophilic infiltration, signs of inflammatory cell activity, and degenerative changes (such as nuclear pyknosis, karyorrhexis, cytoplasmic vacuolization) were clearly observed. The presence of extracellular nuclear fragments and cellular debris indicates a pronounced systemic inflammatory response syndrome (SIRS) triggered by CKD, which appears to affect not only the kidneys but also other tissues, including the lungs and peritoneal structures.

In contrast, the control group (healthy 5-month-old rats) demonstrated normal histological architecture, with no evidence of inflammation or cellular degeneration. The leukocyte count was low, and neutrophils retained normal morphology, indicating an absence of pathological immune activation.

These findings support the hypothesis that chronic kidney disease contributes to the development of systemic inflammation, characterized by heightened neutrophil activity and associated tissue damage in distant organs.

4. Conclusions

This experimental study was aimed at identifying the morphological changes occurring in lung tissue under conditions of chronic kidney disease (CKD). The results revealed that thickening of the interalveolar septa, inflammatory infiltration, alveolar deformations, and interstitial fibrosis are key histological features contributing to impaired pulmonary function in the context of CKD. These findings hold significant value for future pathogenesis research and the development of therapeutic strategies.

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