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Morphological Changes in the Pancreas of Rats with Experimental Diabetes Chronically Exposed to Pesticides Over a 9-Month Period

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Abstract
The present study aims to investigate the dynamic morphological changes occurring in the pancreas of rats with experimentally induced diabetes mellitus under the influence of chronic pesticide exposure over different time periods, particularly within 6 months. During the initial 3-month period, the pancreas of rats with diabetes mellitus exposed to pesticides was examined after decapitation. The pancreatic response to pesticide exposure in diabetic conditions over a 3-month period was primarily manifested as acute injury. Morphologically, the pancreatic capsule appeared relatively thickened, the surface was irregular, and signs of vascular congestion were observed.

Keywords: Diabetes mellitus, morphology, pancreas, pesticides

Relevance of the Problem

Currently, diabetes mellitus ranks third among the most prevalent diseases worldwide and represents a major global medical and social problem affecting individuals of all age groups across all countries.

According to the World Health Organization, by 2030 approximately 18–20% of the world’s population will be affected by this disease, of which 80–90% will consist of patients with type 2 diabetes mellitus. In industrialized countries, the

prevalence of diabetes mellitus is about 5–6%, with a particularly high incidence and risk of progression among individuals over 40 years of age. By 2025, the WHO predicts a 41% increase in the number of patients with diabetes mellitus in developed countries.

In patients with diabetes mellitus, a decrease in quality of life, disability, and life-threatening complications are commonly observed, affecting nearly all organ systems. Despite significant advances in treatment, the majority of patients develop long-term complications leading to disability. Therefore, diabetes mellitus remains a serious medical and social issue.

Materials and Methods

In this study, an experimental model of diabetes mellitus was induced in 182 white laboratory rats (0.11 mg per 100 g of body weight). The animals were divided into three groups:

1. **Group 1** – Intact rats (control group)
2. **Group 2** – Experimental group consisting of 50 white laboratory rats with induced diabetes mellitus
3. **Group 3** – Rats with experimental diabetes mellitus subjected to chronic pesticide intoxication

Results and Discussion

The experiment was aimed at studying the dynamic morphological changes in rats subjected to oral administration of alcohol and pesticides under conditions of diabetes mellitus over 3-, 6-, and 9-month periods. During the initial 3-month period, the pancreas of rats with experimentally induced diabetes mellitus and alcohol intake was examined after decapitation.

From a morphological perspective, by the 9-month period, rats with diabetes mellitus chronically exposed to pesticides demonstrated more pronounced pancreatic alterations compared to the 3- and 6-month groups. These changes included a reduction in organ size, variability in the size of pancreatic lobules, and a macroscopically yellowish-pink appearance. In addition, an increased accumulation of adipose tissue was observed.

Furthermore, in the interlobular septa, a significant thickening due to excessive proliferation of dense fibrous connective tissue was identified, indicating progressive structural remodeling and chronic damage to the pancreas under the combined effects of diabetes mellitus and prolonged pesticide exposure.

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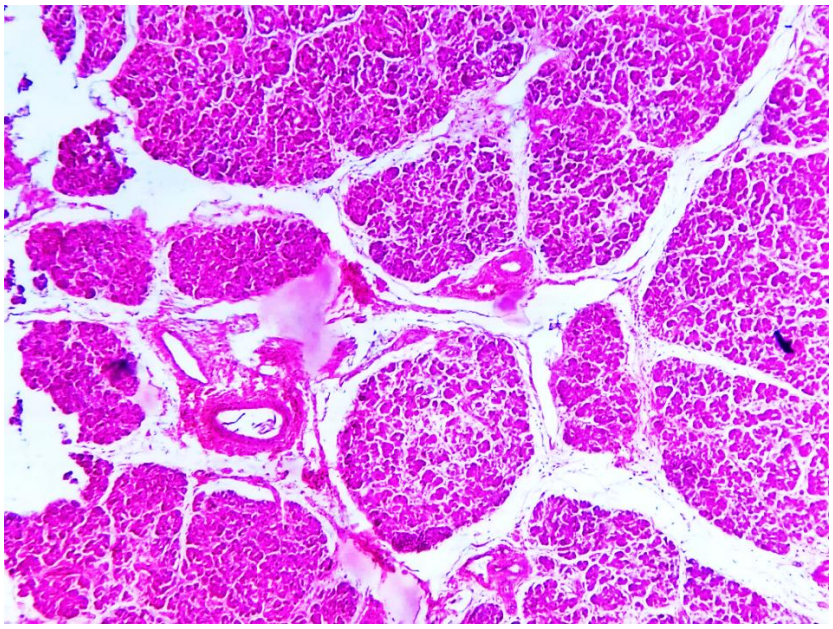

Figure 1. Pancreas of a rat at the 9th month under the influence of pesticides in experimental diabetes mellitus. Lobules of varying sizes are observed, with a marked increase in dense fibrous connective tissue between them. Staining: H&E (hematoxylin and eosin). Magnification: 4×10.

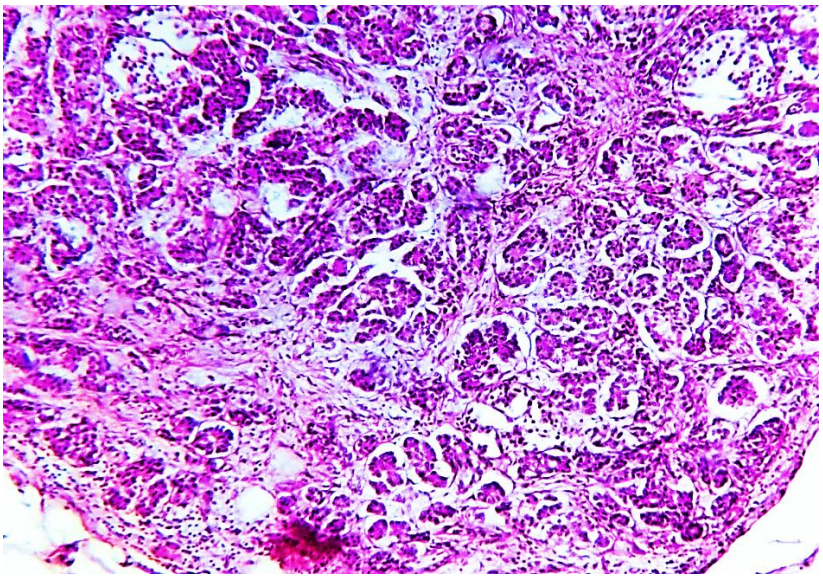

Figure 2. Pancreas of a rat at the 9th month under the influence of pesticides in experimental diabetes mellitus. Pancreatic acini show glandular epithelial cells stained with varying intensity and size. Interstitial edema is observed. Staining: H&E (hematoxylin and eosin). Magnification: 10×10.

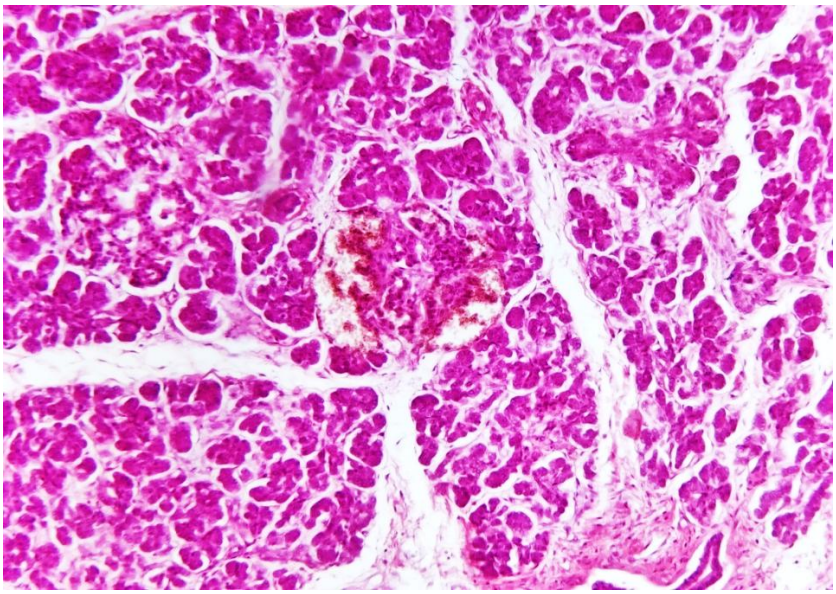

Figure 3. Pancreas of a rat at the 9th month under the influence of pesticides in experimental diabetes mellitus. Focal diapedetic hemorrhages are observed within the pancreatic acini, along with a reduction in the size of glandular acini. In the interlobular septa, focal thickening of connective tissue is noted. Staining: H&E (hematoxylin and eosin). Magnification: 4×10.

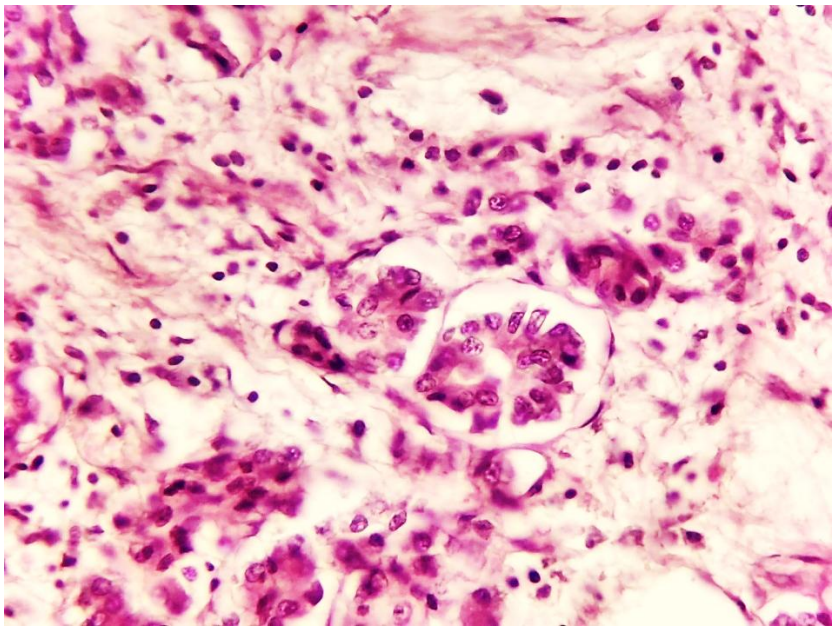

Figure 4. Pancreas of a rat at the 9th month after pesticide exposure in experimental diabetes mellitus. Segmental cell death is observed in the pancreatic acini, along with focal hemorrhages in the interstitial spaces.

Developing foci of lymphocytic infiltration are noted around the acini. Staining: H&E (hematoxylin and eosin). Magnification: 20×10.

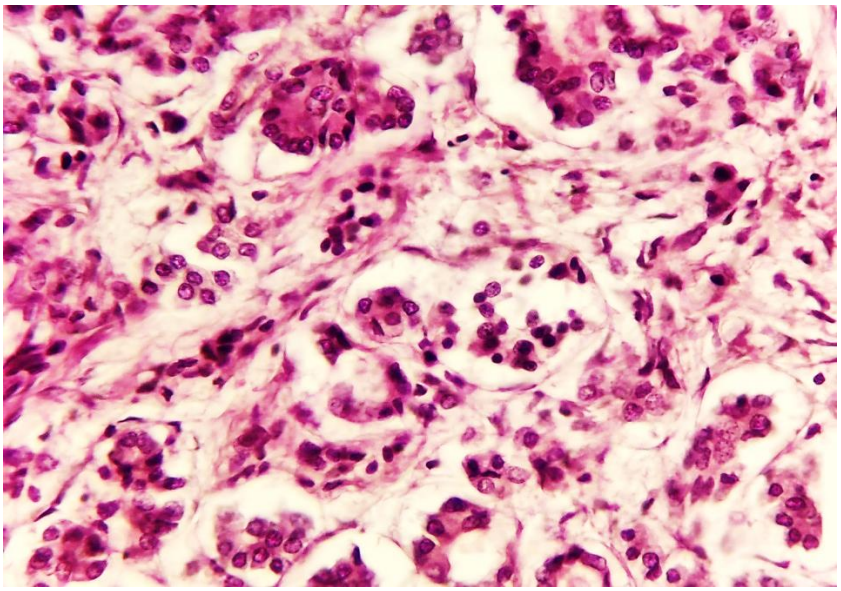

Figure 5. Pancreas of a rat at the 9th month under the influence of pesticides in experimental diabetes mellitus. Foci of lymphocytic infiltration are identified in the acini located near the main pancreatic duct, as well as in perivascular regions. Staining: H&E (hematoxylin and eosin). Magnification: 20×10.

Morphologically, the fibrous capsule of the pancreas is thickened and composed of dense collagen-rich connective tissue. Marked dilation of blood vessels is observed, along with proliferative foci of fibroblasts and an increased number of histiocytes. The presence of lymphohistiocytic infiltration in the interstitial spaces confirms the persistence of chronic inflammatory processes.

The pancreatic lobules vary in size, and excessive thickening of the interlobular connective tissue septa is noted, with persistent vascular congestion. The acinar glandular structures within the lobules appear reduced in size compared to the 3- and 6-month periods. Additionally, there is an increase in sparse and coarse fibrous connective tissue surrounding the acini.

Periacinar small-caliber blood vessels demonstrate congestion, while capillaries exhibit stasis and sludge phenomena. Within the acinar lumens, numerous pale eosinophilic inclusions are observed, along with the formation of interstitial edema.

At the cellular level, metabolic alterations are evident in the glandular epithelium, characterized by the accumulation of inclusions of various origins within the

cytoplasm. Nuclear polymorphism is also observed, with variations in staining intensity and size, reflecting ongoing degenerative and adaptive cellular changes.

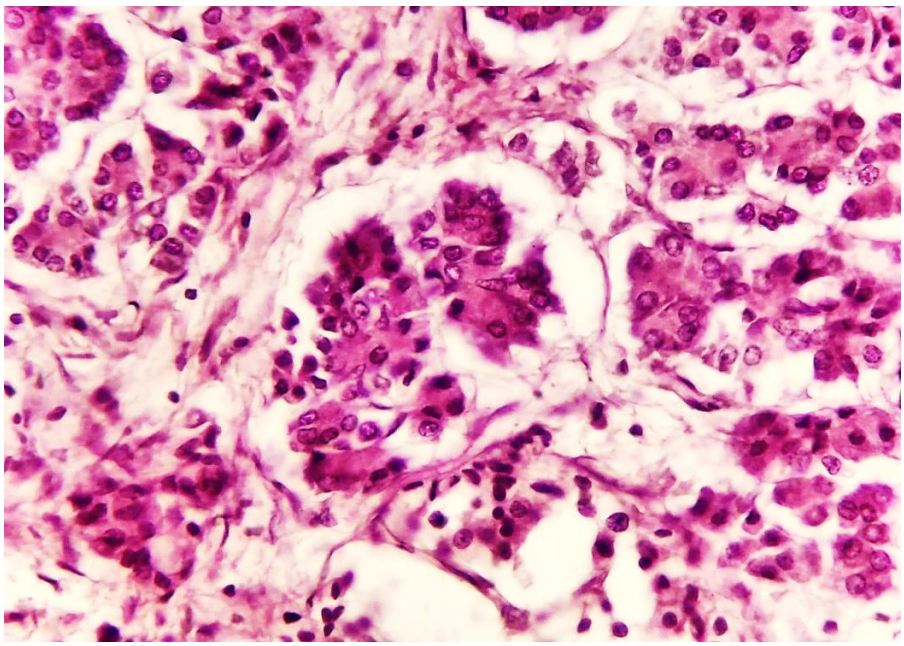

Figure 6. Pancreas of a rat at the 9th month under the influence of pesticides in experimental diabetes mellitus. A marked reduction in the cellular components of the islets of Langerhans is observed. Interstitial edema is present. Staining: H&E (hematoxylin and eosin). Magnification: 40×10.

In addition, the ingrowth of adipose tissue between the lobules is observed, which is associated with the replacement of pancreatic parenchyma by mesenchymal tissue. Compared to the 3- and 6-month periods, at the 9-month stage, mildly expressed foci of chronic inflammation are also detected within the interlobular septa, particularly in areas rich in adipose tissue and dense fibrous connective tissue.

As a result, a marked alteration in the histoarchitectonics of the acinar glands is observed. The glandular epithelial cells vary in size, and coarse cytoplasmic inclusions are present. Compared to earlier periods (3 and 6 months), there is a pronounced increase in dense fibrous structures between glandular cells, along with vascular congestion and proliferation of histiocytes and fibroblasts around the acini.

Lymphohistiocytic infiltration foci around the acini are more numerous compared to earlier stages, indicating the progression of chronic aseptic inflammation under the combined effects of diabetes mellitus and pesticide exposure. These findings suggest the continuous development of programmed cell death (apoptosis) in pancreatic epithelial cells. Consequently, dysregenerative processes occur, leading to reparative regeneration accompanied by excessive proliferation of connective tissue.

In the preserved acinar lumens, a decrease in homogeneous basophilic secretion is noted. The reduction in the size of glandular cells and variability in acinar size indicate a significant decline in morphofunctional activity. Glandular epithelial nuclei exhibit polymorphism in both size and staining characteristics, with mitotic figures observed at various stages.

The size of pancreatic lobules is also affected, reflecting morphofunctional changes in the acini. Chronic exposure leads to an increase in sparse and dense fibrous structures in periolobular areas, proliferation of fibroblasts and histiocytes, and the presence of macrophages and a small number of neutrophils surrounding apoptotic epithelial cells.

Small-caliber blood vessels and capillaries demonstrate congestion, focal hemorrhages, and thickening of the vascular wall muscular layer.

As a consequence, stagnation of secretions is observed in most acinar glands, extending into the main pancreatic ducts. This leads to retention of secretions within the ductal system, resulting in swelling of ductal epithelial cells and accumulation of eosinophilic inclusions in their cytoplasm.

Around dilated vessels, increased intercellular fluid is detected, and in the extracellular matrix, pale pink expanded areas are observed, indicative of edema. This contributes to compression of central acinar structures within lobules, leading to a reduction in epithelial cell volume.

In regions of prolonged vascular stasis, an increase in sparse and dense fibrous connective tissue is observed around blood vessels. As a result, the normal histoarchitectonics of the pancreas is progressively replaced by connective tissue expansion.

At the 9-month stage, in addition to the changes observed at 6 months, morphofunctionally active acinar epithelial cells demonstrate hypertrophy, alongside focal clusters of reduced cells. These changes show polarity, with enlarged cells predominantly located near vascular regions, and reduced cytoplasm observed in the apical portions. Within a ×200 field of view, 1–2

mitotic figures are detected, and many acini exhibit uniform polar structural changes.

The lobular capsule appears relatively thickened and contains areas of sparse and dense fibrous connective tissue. Persistent vascular congestion in small blood vessels and the presence of perivascular edema are also characteristic findings.

Conclusion

In rats with experimentally induced diabetes mellitus, chronic pesticide intoxication over a 6-month period leads to significant structural alterations in the pancreas. These changes are primarily characterized by an increase in dense fibrous connective tissue around the main excretory ducts, reduction in acinar size, thickening and stagnation of secretions, and uneven vascular congestion. Additionally, a decrease in the size of the islets of Langerhans, expansion of stromal spaces, and proliferation of connective tissue between lobules were observed.

These findings indicate that pesticide exposure in the context of diabetes mellitus severely disrupts pancreatic metabolism, promotes degeneration of acinar epithelial cells, and leads to a marked decline in morphofunctional activity of the pancreas.

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