Summary:

The present study was designed to demonstrate the effect of a Hyaluronic acid dermal filler type, Neuramis Volume Lidocaine (NVL), at a subcutaneous on male and female laboratory rats (*Rattus norvegicus*), aged (١٢-١٦) weeks, over a period of (٢،٤،٩،١٠،١٣) weeks, respectively, this study was conducted in the animal house of the College of Education for Pure Sciences/University of Thi-Qar., The results of the present study showed a set of behavioral and phenotypic changes in the treated groups, represented by pain, swelling, redness, and bruising a few days after injection, while the animals suffered from the hardening and migration of the filler in the last weeks of the experiment.

In this study of male and female laboratory rats, statistical analysis showed that the group treated for two weeks had a non-significant decrease in the body weight compared to the control group treated for the same amount of time and the groups treated for (٩, 10, ١٣) weeks .There was no significant difference compared to the group treated for four weeks. However, there was a non-significant decrease in the group treated for four weeks compared to the control group treated for the same period of time and the groups treated for different periods of time (٩, 10, ١٣ weeks),There was no significant difference during the periods of time (4, 9, 10, 13 weeks, respectively) when compared with each other and with the control for the same periods of time for each of them at a probability level ($p < 0.05$).

The results showed a significant decrease in the rate of red blood cells, hemoglobin, and platelets for both males and females in the treatment group after two weeks compared to the control group during the same time period and compared to treated groups (٩, 10, ١٣ weeks) at a probability level ($p < 0.05$), There was insignificant rise compared to the treated group for four

weeks. The treated group for four weeks showed a significant decrease when compared with the control group and the treated groups for nine, 10, and 13 weeks. There was a significant decrease in the treated group for nine weeks when compared with the control of the same period, while no significant difference appeared when compared with the two groups (10, 13). However, comparing the groups (10, 13) weeks with the control groups for the same period revealed no significant difference.

The statistical analysis of showed a significant increase in the number of white blood cells , The neutrophils was significantly higher ($p < 0.05$) in the group that was treated for two weeks compared to the control group for the same period and to the groups that were treated for nine, ten, and thirteen weeks, respectively. The group that received treatment for four weeks showed no significant difference. This group showed a significant increase when compared with the control for the same period and with the groups treated for the periods (9,10,13)weeks, respectively, while no significant difference appeared between the groups treated for the periods (9,10,13) weeks, and a non-significant decrease was found in the rate of lymphocytes and monocytes when comparing the treated group for two weeks with the control group and the treated group for four weeks, and there was no significant difference in the rate of lymphocytes when comparing the treated group for two weeks with the other groups for different time periods (9,10,13) weeks, and a non-significant decrease in the rate of lymphocytes was observed in the group The group that received treatment for four weeks showed a significant increase when compared to the control group for the same period of time. However, there was no significant difference when compared to the groups that received treatment for periods of nine, ten, and thirteen weeks. Furthermore, the final treatment groups did not show any significant difference when compared to each other or the control group for the same period .

The results of the light microscope examination of the skin tissue showed a significant ($p<0.05$) gradual increase in the thickness of the epidermis, dermis and subcutaneous layer using the Ocular micrometer when compared with the control group and the groups treated with dermal fillers for (2, 4, 9, 10, 13 weeks).

The histological study of the skin in rats treated with dermal filler Hyaluronic acid who examined at different magnification powers showed histological changes after two weeks of injection. These changes included areas suffering from collagen loss in the reticular and papillary layer, infiltration of macrophages, and the presence of a thin network of branched collagen fibers. Additionally, a few small blood vessels and atrophied muscle fibers were present in the subcutaneous tissue. The group treated for four weeks displayed a thin layer of epidermis, a layer of keratin, a branched network of collagen, and abundant adipose tissue, while the group treated for nine weeks displayed mild hyperplasia in the stratum basale. The dermis exhibited a dense network of collagen, featuring few voids in the papillary layer, small blood vessels, and thick elastic tissue in the muscle fiber layer. The group treated for ten weeks showed clear hyperplasia in the stratum corneum and the presence of collagen fibers, Thick and regular with the presence of wide blood vessels, the histological examination of the skin in the treatment group for (١٣) weeks indicated the presence of a thick network of collagen fibers in the papillary layer with the presence of hair follicles and blood vessels and hypertrophy of fibers in the smooth muscle fibers and proliferation in the elastic connective tissue with a little adipose tissue.

The results of the scanning electron microscopy (SEM) and the transmission electron microscopy (TEM) also revealed that the presence of histological changes in the skin, These changes included invaginations and holes on the rough dermal surface, along with fine and long hairs, and a

smooth collagen surface with dermal papillae, Immature fibroblasts and euchromatic nucleus with peripheral heterochromatin represent the cellular changes in the two week-treated group. Many expanded cisterns of the endoplasmic reticulum, multiple vesicles, a few collagen fibers are present in the cytoplasm, along with inflammatory cell nuclei and a small number of mitochondria. The group that received treatment for four weeks displayed an active fibroblast with a central folded nucleus, inflammatory cells in the cytoplasm, and a rough endoplasmic reticulum surrounded by a few collagen fibers. While the group treated for (9) weeks showed active fibroblasts with a hyperchromatic nucleus and numerous mitochondria with a rough endoplasmic reticulum and two centrioles in addition to multiple vesicles, and in the group treated for(10)weeks there were active fibroblasts, a rough endoplasmic reticulum, multiple vesicles, and thick elastic tissue, and thick bands of collagen fibers were observed, while the group treated for (13)weeks showed thick bands of collagen fibers with the presence of active fibroblasts with a flat nucleus and numerous mitochondria surrounded by collagen fibers.

We conclude from the results of our study that changes occur in blood parameters in the early periods after injection of hyaluronic acid dermal filler and that tissue and epithelial changes occur at the cellular level after injection in the later periods of time.