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EFFECTS OF CROWDING AND LONELINESS ON LIVER FUNCTIONS IN ADULT MALE ALBINO RATS

By

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ABSTRACT

Background: Crowding is one of the most popular stressors in experimental medicine since it could be regulated easily. Social isolation and lack of social support have deleterious effects on health. These are regarded as one of the most relevant causes of human diseases.

Objective: Evaluation of the possible effects of either crowding and loneliness on liver functions in adult male albino rats**.**

Material and methods: Fifty four adult local strain male albino rats were chosen as a model for the present work. They were divided into equal three groups; control group, crowded group and reduced space group. Animal behavior was observed, and blood samples were obtained for determination of blood glucose level, total cholesterol, triglycerides, low density lipoprotein (LDL), high density lipoprotein (HDL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total serum protein, serum albumin and globulin. Liver samples were obtained for histopathological study. **Results:** Crowding or loneliness led to different homeostatic changes including disturbed liver functions, glucose metabolism, lipid profile and altered behavior in addition to marked cellular changes on histopathological examination.

Conclusion: Housing conditions affected behavioral and biological responses of animals and could be considered risk factors for certain diseases as diabetes mellitus, dyslipidemia and liver injury. Further studies are required to demonstrate how chronic stress can exert a facilitative effect on inflammatory response and even increases the risk of developing pathological effects.

INTRODUCTION

Optimal population density is essential for all living organisms. It produces a significant impact upon behavior and physiology of individuals and social groups **(Saalu et al., 2011).** Abnormal population densities can affect functions of many organs in addition to behavioral disturbances. Differences in population densities are considered stress **(Cvijic and Dordevic, 2003).** Maintaining homeostasis is essential for life. The complex dynamic equilibrium is constantly challenged by intrinsic or extrinsic adverse, real or perceived forces and stressors **(Nagaraja and Jeganathan, 2003).**

Crowding is defined as "a state of stress that accompanies high population density", i.e. large number of people per unit space **(Maisa, 2012).** Crowding stress has many physical and psychological

effects. The physical effects include lower body weight, delayed maturation, increase adrenal weight, infertility and reduced resistance to infection (**Mostafa, 2010**). The psychological effects of crowding include heightened aggression, breakdown of normal social behavior and poor performance of tasks (**Kumar et al., 2009**).

Social isolation and lack of social support have deleterious effects on health. These are regarded as one of the most relevant causes of human diseases **(House, 2001).** It has been reported that in laboratory animals, group housing is advised to buffer the negative long term effects of a single defeat observed in isolated animals **(Isovich et al., 2001).**

The liver plays a critical roles in synthesizing molecules that are utilized elsewhere to support homeostasis, converting molecules of one type to another and regulating energy balances. So, the development of liver disease is accompanied by diverse manifestations of metabolic disorders **(Zakim and Boyer, 2003).**

The present study was planned to evaluate the possible effects of different population densities (crowding and loneliness) on liver functions in adult male albino rats.

MATERIALS AND METHODS

Fifty four adult male albino rats of local strain with average weight of 160 gm were chosen to be the model of the present study. They were left for two weeks in the laboratory area before any experimental interference for acclimatization with free axis to water and rat chow bellets. Rats were kept in suitable cages (20 × 30 × 20 cm for every 3 rats) at room temperature with the natural light dark cycle. Rats were divided into equal three groups:

Group I (Control group): Normal rats were kept in six cages (3 rats per cage) for four weeks.

Group II (Crowded group): Rats were kept in two cages (9 rats per cage) for four weeks.

Group III (Reduced space group): Rats were kept in eighteen cages where every rat was put alone in a cage (10 × 10 × 10 cm) for four weeks.

*** Induction of crowding:** Crowding was induced by multiplying the normal rat density by three, i.e. nine rats per cage **(Armario et al., 1987).**

*** Animal behavior** was observed during the experimental period for each group.

*** Blood samples:** At the end of the experimental period, rats were weighed, and blood samples were withdrawn from the retro-orbital plexus into test tubes. Serum was separated and stored frozen at -20^{o}C until assayed.

*** Biochemical assay:** The levels of the following parameters were detected:

Serum blood glucose **(Maughan, 1982),** serum ALT and AST **(Silverman et al., 1995),** total serum protein **(Doumas et al., 1981),** total serum albumin and globulin **(Alvarez and Radi, 2003),** total serum cholesterol **(Allain, 1974),** serum

triglycerides **(Fossati and Prencipe, 1982),** serum LDL **(Levy, 1981 and Steinberg, 1981)**, and serum HDL **(Lopez, 1977)**.

*** A/G ratio was calculated.**

*** Histopathological study:** Rats were killed, and abdominal cavities were opened to obtain livers for studying histopathological changes. Liver samples were kept in 10% formalin solution. Paraffin blocks were made and different sections at multiple levels were obtained. Slides were then stained by hematoxylin and eosin (H & E) and periodic acid Schiff (PAS), and examined using light microscope.

*** Statistical analysis:** Data input and analysis were done using SPSS computer program. All results were expressed as mean ± standard error. Mean values of the different groups were compared using a one-way analysis of variance (ANOVA). Least significant difference (LSD) post hoc analysis was used to identify significantly different mean values. P value < 0.05 was accepted to denote a significant difference.

RESULTS

Animal behavior: Continuous crowding was associated with heightened aggression manifested by increased incidence of causalities, increased psychomotor activities, (circus movement, jumping, standing on the hind limbs and nodding head movement) in the first two weeks of experiment followed by psychomotor depression. Isolation was initially associated with increased psychomotor activities (in the first week), then gradually declined with lapse of time, and rats fell quiet in one corner of their cages.

*** Changes in body weight and blood glucose (Table 1):**

There was significant increase in the mean body weight of the control rats from 162.11 ± 5.3 g to 211.5 ± 9 g (+ 30.46%) at the end of the experimental period. The overcrowded rats showed also significant increase in the mean body weight from 161.11 ± 4.2 g to 188 ± 9.5 g (+ 16.69%). Also, the isolated rats showed significant increase in the mean body weight from 161.95 ± 4.1 g to 182 ± 8.9 g (+ 12.38 %). The increased body weight was more evident in the control group.

At the end of the experimental period, there was significant changes between control, crowded and isolated rats, where the final weight of the control rats was 211.5 ± 9 g. The final weight of the crowded rats was 188 ± 9.5 g (- 10.68 %) and the final weight of the isolated rats was 182 ± 8.9 g (-13.94 %). It was noted that, differences in the final body weight was more evident in the isolated group.

Both crowding and isolation led to significant increase in the mean blood glucose level where it was 87.22 ± 2.22 mg% for the control rats, 105.78 ± 2.99 mg% (+ 24.71 %) for the crowded rats, and 104.00 ± 4.05 mg% (+ 19. 23 %) for the isolated rats.

Changes in liver functions (Table 2):

Induction of crowding led to significant increase in the AST level from 67.56 ±

3.16 U/L to 73.78 ± 0.94 U/L (+ 9.2 %) and ALT level from 29.33 ± 1.33 U/L to 33.78 ± 1.93 U/L (+ 15.17 %), significant decrease in the albumin level from 3.57 ± 0.07 g% to 3.33 ± 0.06 g% (- 6.72 %), insignificant decrease in the total protein level from 6.40 ± 0.08 g% to 6.14 ± 0.19 g% (- 4.06 %), globulin level from 2.83 ± 0.04 g% to 2.81 ± 0.03 g% (- 0.52 %) and A/G ratio from 1.26 ± 0.05 to 1.18 ± 0.04 (- 6.34 %).

On the other hand, isolation led to significant increase in AST level from 67.56 ± 3.16 U/L to 74.11 ± 0.92 U/L (+ 9.69 %), ALT level from 29.33 ± 1.33 U/L to 34.44 ± 1.30 U/L (+ 17.42 %), significant decrease in the albumin level from 3.57 ± 0.07 g% to 3.30 ± 0.06 g% (- 7.56 %), A/G ratio from 1.26 ± 0.05 to 1.1 ± 0.03 (- 12.69 %), insignificant decrease in the total protein level from 6.40 ± 0.08 g% to 6.18 ± 0.22 g% (- 3.43 %) and insignificant increase in the globulin level from 2.83 ± 0.04 g% to 2.88 ± 0.05 g% (+ 1.76 %).

It was noted that both crowding and isolation have a deteriorating effects on liver functions which were more evident in the isolated group.

Changes in lipid profile (Table 3):

Induction of crowding led to significant increase in the total cholesterol level from 132.00 ± 2.48 mg/dl to 139.56 ± 2.67 mg/dl (+ 5.72%), triglycerides level from 91.78 ± 3.76 mg/dl to 100.56 ± 2.64 mg/dl (+ 9.56%) and LDL level from 74.42 ± 2.52 mg/dl to 83.50 ± 3.81 mg/dl (+ 12.2%), while there was insignificant increase in the HDL level from 39.22 ± 1.20 mg/dl to 40.67 ± 1.97 mg/dl to (+ 3.69%).

Isolation also led to significant increase in the total cholesterol level from 132.00 ± 2.48 mg/dl to 140.0 ± 2.64 mg/dl (+ 6.06%), triglycerides level from 91.78 ± 3.76 mg/dl to 104.00 ± 4.82 mg/dl (+ 13.31%) and LDL level from 74.42 ± 2.52 mg/dl to 83.74 ± 2.60 mg/dl (+ 12.52%), while there was insignificant decrease in the HDL level from 39.22 ± 1.20 mg/dl to 37.22 ± 2.44 mg/dl (- 5.09%).

*** Histopathological results (figures 1-6):**

Histopathological study of the liver of the control group showed normal histological structure of the liver tissue in the from of radiated cords of hepatocytes in normal arrangement toward central vein and Kupffer cells (figure 1), and normal distribution of PAS materials within the hepatocytes (figure 2). Livers of rats exposed to crowding showed dilated congested portal vein and sinusoidal spaces associated with vaculated hepatocytes and pyknotic nuclei (figure 3), and decreased PAS materials within the central and portal areas (figure 4). Livers of rats exposed to isolation showed central vein congestion with hemolysed RBC, dilated congested portal vein, lymphocytic infiltration and destructed vaculated hepatocytes with pyknotic nuclei (figure 5), highly decreased PAS materials within the portal area associated with homogenous red color of hemolysed RBCs (figure 6).

Table (1): Changes in body weight and blood glucose in tested groups.

Groups / Parameters	Mean ± S.E		
	Group I	**Group II**	**Group III**
Initial weight (g)	162.11 ± 5.3	161.11 ± 4.2	161.95 ± 4.1
Final weight (g)	211.5 ± 9 *	188 ± 9.5 *	182 ± 8.9 *
% changes	+ 30.46 % ●	+ 16.69 % ●	+ 12.38 % ●
% changes		- 10.68 % ♦ *	- 13.94 % ♦ *
Blood glucose (mg%)	87.22 ± 2.22	105.78 ± 2.99 ♦	104.00 ± 4.05 ♦
% changes		+ 24.71 %	+ 19. 23 %

Group I: control. Group II: crowded. Group III: isolated.
● Compared to itself. ♦ Compared to group I. ***** Significant.

Table (2): Changes in liver functions in tested groups.

Groups / Parameters	Mean ± S.E		
	Group I	**Group II**	**Group III**
AST (U/L)	67.56 ± 3.16	73.78 ± 0.94*	74.11 ± 0.92*
% changes		+ 9.2 %	+ 9.69 %
ALT (U/L)	29.33 ± 1.33	33.78 ± 1.93*	34.44 ± 1.30*
% changes		+ 15.17 %	+ 17.42 %
Total Protein (g%)	6.40 ± 0.08	6.14 ± 0.19	6.18 ± 0.22
% changes		- 4.06 %	- 3.43 %
Albumin (g%)	3.57 ± 0.07	3.33 ± 0.06*	3.30 ± 0.06*
% changes		- 6.72 %	- 7.56 %
Globulin (g%)	2.83 ± 0.04	2.81 ± 0.03	2.88 ± 0.05
% changes		- 0.52 %	+ 1.76 %
A/G ratio	1.26 ± 0.05	1.18 ± 0.04	1.10 ± 0.03*
% changes		- 6.34 %	- 12.69 %

Group I: control. Group II: crowded. Group III: isolated.
***** Significant.

Table (3): Changes in lipid profile in tested groups.

Groups / Parameters	Mean ± S.E		
	Group I	**Group II**	**Group III**
Total Chol. (mg/dl)	132.00 ± 2.48	139.56 ± 2.67*	140.00 ± 2.64*
% changes		+ 5.72 %	+ 6.06 %
TGs. (mg/dl)	91.78 ± 3.76	100.56 ± 2.64*	104.00 ± 4.82*
% changes		+ 9.56 %	+ 13.31 %
HDL (mg/dl)	39.22 ± 1.20	40.67 ± 1.97	37.22 ± 2.44
% changes		+ 3.69 %	- 5.09%
LDL (mg/dl)	74.42 ± 2.52	83.50 ± 3.81*	83.74 ± 2.60*
% changes		+ 12.2 %	+ 12.52 %

Group I: control. Group II: crowded. Group III: isolated.
***** Significant.

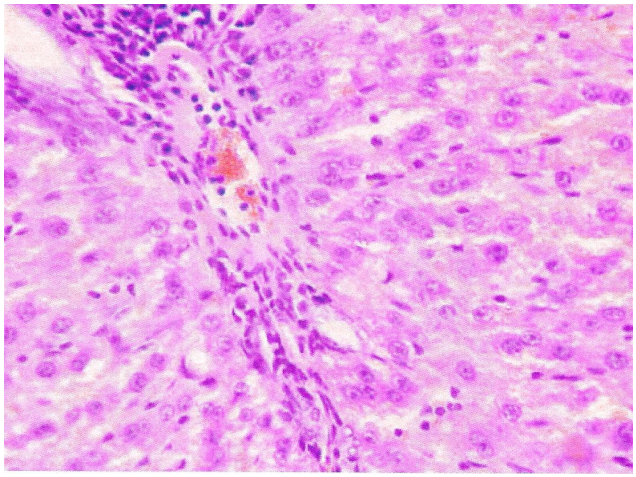

Figure (1): Normal liver structures of the control group (Hx & E X 400).

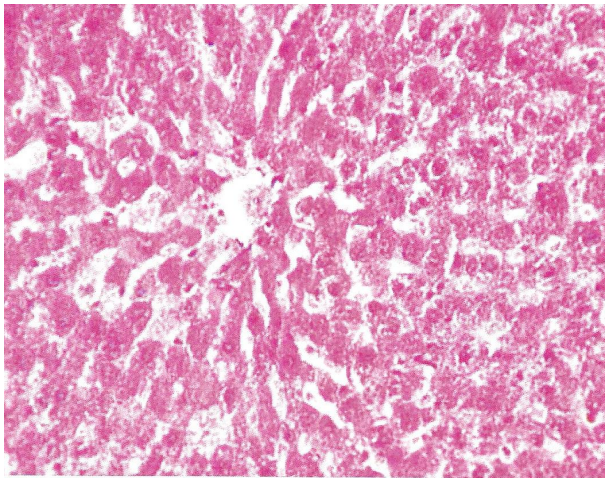

Figure (2): Normal distribution of PAS materials in the liver of the control group (PAS X 400).

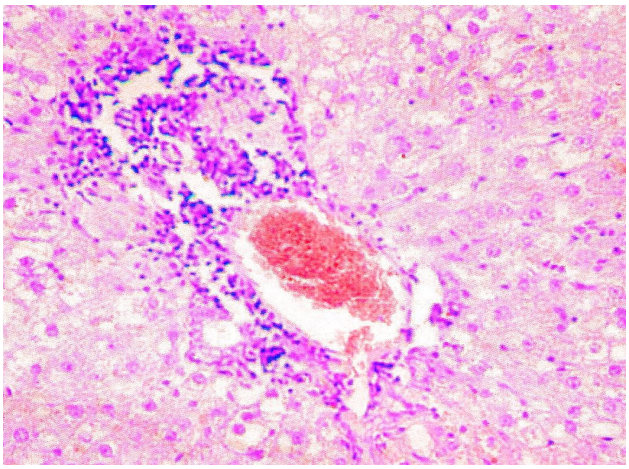

Figure (3): Dilated congested portal vein and vaculated hepatocytes of the crowded group (Hx & E X 400).

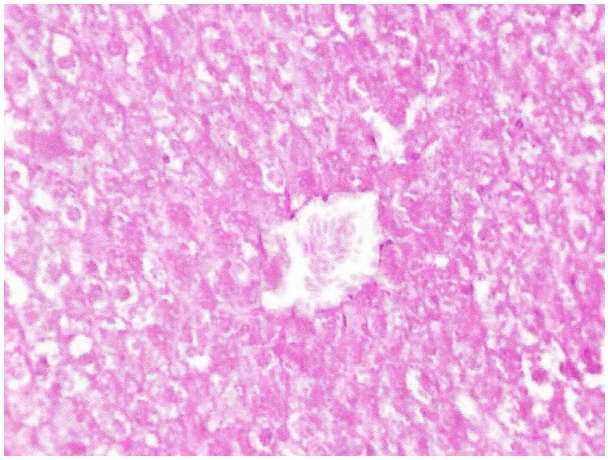

Figure (4): Decreased PAS materials within the central and portal areas of the crowded group (PAS X 400).

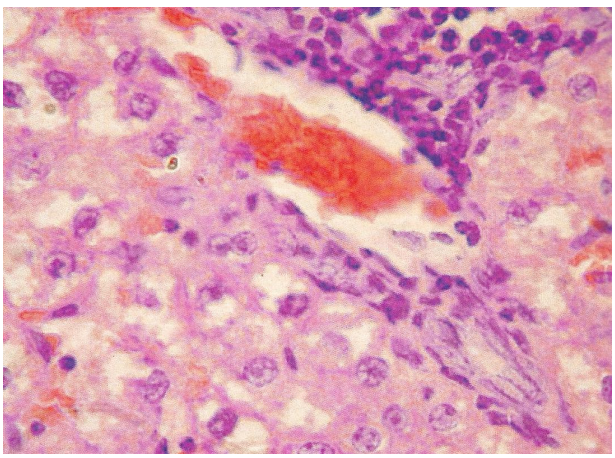

Figure (5): central vein congestion, hemolysed RBC and vaculated hepatocytes of the isolated group (Hx & E X 400).

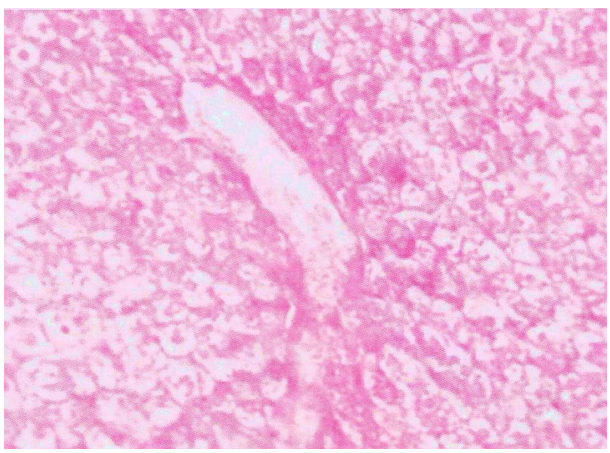

Figure (6): Highly decreased PAS materials within the portal area of the isolated group (PAS X 400).

DISCUSSION

Living organisms are continuously exposed to environmental stressors. In response to them, the organism develops more complex ways for stabilizing the internal environment to counter changes of the external circumstance **(Koolhaas, 2011).** The present work was designed to evaluate possible effects of either crowding and loneliness on liver functions in albino rats**.**

Results of the present work showed that either crowding or loneliness led to marked behavioral changes in the form of increased psychomotor activity and aggression followed by depression. These results were compatible with **Lepsch (2005)** who stated that crowding is associated with heightened aggressive behavior. The psychomotor activity initially increases then gradually declines, and the aggressive behavior is a constant finding in crowded situations. Also, **Brunton (2013)** has reported that rats exposed to social stress initially display increased anxiety-related behavior followed by increased depression-like behavior. The initial increase of psychomotor activity could be a mechanism through which the animal tries to escape from its situation then. Its activity gradually declines when the animal has accepted the new situation **(Lepsch, 2005).**

Results of the present work showed that either crowding or loneliness led to diminished weight gain after one month experiment. These results were in agreement with **Marcelo et al. (2007)** who mentioned that crowding causes reduced food intake and diminished body weight gain in rats. Also, the rate of growth and early nutrition cause continued weight loss. **Sadagurski et al. (2014)** demonstrated that limiting nutrient availability by increasing the number of pups in the crowded-litter model leads to significant diminished weight gain where the crowded mice are significantly leaner and consume more oxygen relative to control mice. Diminished weight gain might be attributed to decreased food intake induced by the high competition for food among crowded animals, catabolic effect of stress hormones or reduced secretion of anabolic hormones **(Dronjak et al., 2004).** In addition, **Karagiannides et al. (2014)** has studied the effects of single housing on rat feeding patterns and overall consumption. Daily feeding measurements reveal that feeding behavior became random irrespective of time of day, and the overall food consumption also reduced in stressed compared to control rats.

Both conditions of the present work showed elevated blood glucose level. These were in agreement with Nayanatra et al. (2009) **who** reported significant increase in the blood glucose level in rats exposed for chronic crowding. Also, **Karagiannides et al. (2014)** has reported that fasting glucose levels were higher in isolated rats compared to the control. In addition, it has been reported that negative emotions were associated with impaired blood glucose level and related to type II diabetes **(Choi et al., 2013).** Hyperglycemia reported in the present work could be due to excessive secretion of stress hormones in response to stressful situations where catecholamines rapidly stimulate glycogenolysis and the release of glucose into the circulation. **(Van-Cromphaut, 2009),** in addition to

decreased circulating insulin levels in stressed rats **(Karagiannides et al., 2014)**. Glucocorticoids and catecholamines may reduce insulin secretion from pancreatic beta cells in stressed rats and reduce the frequency of insulin release **(Van-Cromphaut, 2009).**

In the present work, there was disturbed liver functions as indicated by elevated liver enzymes and disturbed protein levels among either crowded or isolated rats. These results were in agreement with **Nayanatara et al. (2009)** who reported increased liver enzymes and disturbed functions in response to stress. The increased enzymes showed an intimate relation to the cell damage and necrosis and/ or increased the permeability of the cell membrane. It has been reported that a variety of stressors could increase liver enzymes **(Everds et al., 2013).** The observed increase activity of serum ALT and AST may be attributed to excessive release of such enzymes from the damaged liver cells into the blood circulation **(Maisa et al., 2012).**

Disturbed protein metabolism in the present work is a feature of disturbed liver functions. It has been reported that prolonged stress usually results in increasing breakdown of cellular and tissue proteins with mobilization of amino acids into the plasma **(Craig** et al., 2013). The reduction in blood albumin and decreased A/G ratio in rats exposed to either crowding or isolation may be due to deficiency of food intake (**Mueller, 2004**). **Inadequate** dietary protein intake has been reported to reduce albumin synthesis **(Fuhrman et al., 2004).** Decreased serum albumin concentration is the most characteristic finding in kwashiorkor disease due to chronic protein malnutrition (**Seres, 2005**). Stress hormones especially corticosteroids may play a role in the hypoalbuminemia through activation of inflammatory response and release of certain inflammatory mediators which usually decrease the rate of albumin synthesis **(Don and Kaysen, 2004).** The reduction in A/G ratio in stressed rats may be due to low level of albumin production associated with liver affection under chronic stress **(Blumenthal et al., 2000).**

The present work showed significant increase in total serum cholesterol, serum triglycerides and LDL levels with insignificant changes in HDL level in either crowding or loneliness rats. These results were in agreement with **Willis et al. (2009)** who mentioned that total plasma cholesterol increases in crowded animals maintained on standard laboratory diets. Also, **Ghulam et al.** (2009) has mentioned that stress induces an elevation in serum total cholesterol concentration which may persist through recovery period in addition to an increase in triglycerides, free fatty acid and LDL-C. In addition, **Nayanatara et al. (2009)** found significant increase in total serum cholesterol and serum triglycerides and LDL in rats exposed to chronic isolation. Alteration in plasma lipid during stress depends on the type and severity of stress as well as several individual characteristic such as heightened neuroendocrine or autonomic reactivity to stressors **(Chrousos, 2009).** It has been reported that hypercholesterolemia resulted during stress may be due to enhanced lipolysis secondary to increased circulating catecholamines levels while increased triglycerides may be attributed to increased hepatic triglyceride synthesis

(Willis et al., 2009 and Geerling et al., 2014).

It was noted that exposure to either crowding or isolation led to marked changes in the liver tissue including polymorphonuclear infiltration, Kupffer cell activation, dilated congested portal vein and sinusoidal spaces, vacuolated hepatocytes with pyknotic nuclei and hemolysed red blood cells. It was suggested that stress influences hepatic blood flow by inducing vasospasm and centrilobular hypoxia, leading to liver damage **(Chida et al., 2006)**. Also, **Steel et al. (2004)** stated that stress may account in part for rapid development of hepatocellular-carcinoma. Decreased polysaccharides in liver tissue post-exposure to stress may be due to failure of hepatocytes to synthesize or store glycogen and may be also a result of maculation and degeneration of hepatocytes **(Cogger et al., 2004).** It was noted that structural changes in isolated rats is more than crowded rats. Theses changes may be due to presence of many stressful conditions, i.e. reduction of space and lack of social interaction which may duplicate the stress response of the liver cells **(Vere et al., 2009).**

CONCLUSION

It could be concluded that housing conditions affect behavioral and biological responses of animals which may be considered as risk factors for certain diseases as diabetes mellitus, dyslipidemia and liver damage. In addition, the present work demonstrated how stress initiated or exacerbated liver diseases, and how chronic stress can exert a facilitative effects on the liver injury.

Quantitative studies are required to clarify more details about the mechanism (s) by which chronic stress facilitates the hepatic inflammatory response or increased risk of developing pathological effects.

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REFERENCES

1. **Allain, C. C. (1974):** Enzymatic determination of total serum cholesterol. Clin. Chem., 20:470-475.

2. **Alvarez, B. and Radi, R. (2003):** Peroxynitrite reactivity with amino acids and proteins. Amino Acids, 25:295–311.

3. **Armario, A., Garcia-Marquez, C. and Jolin, T. (1987):** Crowding-induced changes in basal and stress levels of thyrotropin and somatotropin in male rats. Behav. Neural Biol., 48 (3): 334-343.

4. **Blumenthal, M., Busse, W. R. and Goldberg, A. (2000):** The complete commission monographs. Therapeutic guide to Herbal Medicines. Boston, M.A. Integrative Medicines Communication, 80-81.

5. **Brunton, P. J. (2013):** Effects of maternal exposure to social stress during pregnancy: consequences for mother and offspring. Reproduction, 146: R175-R189.

6. **Chida, Y., Sudo, N. and Kubo, C. (2006):** Does stress exacerbate liver diseases? J Gastroenterol. Hepatol., 21: 202-208.

7. **Choi, S. E., Rush, E. B. and Henry, S. L. (2013):** Negative emotion and risk for type 2 diabetes among Korean immigrants. Diabetes, 39 (5): 679-688.

8. **Chrousos, G. P. (2009):** Stress and disorders of the stress system. Nat. Rev. Endocrinol., 5: 374-381.

9. Cogger, V. C., Muller, M., Fraser, R. and khan, J. (2004): The effect of oxidative stress on the liver sieve. J. Hepatology, 41: 370 - 376.

10. Craig, P., Hurren, N. M., Herndon, D. N. and B?rsheim, E. (2013): Whole body and skeletal muscle protein turnover in recovery from burns. Int. J. Burn Trauma, 3 (1): 9 - 17

11. Cvijic, G. and Dordevic, J. (2003): Hypo-thalamo-pituitary-adrenocortical and Sympatho-reno-medullary systems in stress response. J. Med. Biohem., 22: 3-10.

12. Don, B. R. and Kaysen, G. (2004): Serum albumin: Relationship to inflammation and nutrition. Semin. Dial., 17:432 - 437.

13. Doumas, B. T., Bayse, D. D., Carter, R. J., Peters, T. J. and Schaffer, R. (1981): A Candidate reference method for determination of total protein in serum. I. development and validation. Clin. Chem., 27 (10): 1642-1650.

14. Dronjak, S., Gavrilovic, L.J., Filipovic, D. and Radojcic, M. (2004): Immobilization and cold stress affect sympatho-adrenomedullary system and pituitary-adrenocortical axis of rats exposed to long-term isolation and crowding. Physiol. Behav., 81: 409 - 415.

15. Everds, N. S., Snyder, P. W., Bailey, K. L., Bolon, B., Creasy, D. M., Foley, G. L., Rosol, T. J. and Sellers, T. (2013): Interpreting stress response during routine toxicity studies. Toxicol. Pathol., 41 (4): 560 – 614.

16. Fossati, P and Prencipe, L. (1982): Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. Clinical Chemistry, 28 (10): 2077-2080.

17. Fuhrman, M. P., Charney, P. and Mueller, C. M. (2004): Hepatic proteins and nutrition assessment. J. Am. Diet Assoc., 104: 1258 - 1264.

18. Geerling, J. J., Boon, M. R., Kooijman, S., Parlevliet, E. T., Havekes, L. M., Romijn, J. A., Meurs, I. M. and Rensen, P. C. N. (2014): Sympathetic nervous system control of triglyceride metabolism: novel concepts derived from recent studies. The Journal of Lipid Research, 55: 180 - 189.

19. Ghulam, M. Q., Ghulam, M., Zardari, M. K., Zafar, A. P. and Siraj, A. A. (2009): Study of blood lipid, cortisol and hemodynamic variations under stress in male adult. J. Ayub. Med. Coll., 21(1): 256 - 264.

20. House, J. S. (2001): Social isolation kills, but how and why? Psychosom. Med., 63: 273 - 274.

21. Isovich, E., Engelmann, M., Landgraf, R. and Fuchs, E. (2001): Social isolation after a single defeat reduces striatal dopamine transporter binding in rats. Eur. J. Neurosci., 13: 1254 - 1256.

22. Karagiannides, I., Golovatscka, V., Bakirtzi, K., Sideri, A., Salas, M., Stavrakis, D., Polytarchou, C., Iliopoulos, D., Pothoulakis, C. and Bradesi, S. (2014): Chronic unpredictable stress regulates visceral adipocyte-mediated glucose metabolism and inflammatory circuits in male rats. Physiological Reports, 2: 284 - 294.

23. Koolhaas, J. (2011): Stress revisited: A critical evaluation of the stress concept. Neuroscience and Biobehavioral Reviews, 35: 1291 - 1301.

24. Kumar, R. S., Narayanan, S. N. and Nayak, S. (2009): Ascorbic acid protects against restraint stress-induced memory deficits in wistar rats. Clinics, 64 (12): 1211 - 1217.

25. Lepsch, L. B. (2005): Exposure to chronic stress increases the locomotor response to cocaine and the basal levels of corticosterone in adolescent rats. Addict. Biol., 10: 251 - 256.

26. Levy, R. I. (1981): Drug therapy of hyperlipoproteinemia. JAMA, 25 (11): 351-364.

27. Lopez, N. (1977): Cholesterol determination in high density lipoprotein separated by different three methods. Clin. Chem., 23: 882 - 885.

28. Maisa, M. (2012): Effects of overcrowding stress on fundus of stomach in adult male albino rats. J. of Biological Sciences, 4(4): 482 - 487.

29. Marcelo, T. M., Marin, F., Marecelo, T., Fabio, C. and Cleopatra, S. P. (2007): Chronic restraint or variable stress differently affects the behavior, corticosterone secretion and body weight in rats. Health Psychol., 90: 29-102.

30. Maughan, R. J. (1982): A simple, rapid method for the determination of glucose, lactate, pyruvate, alanine, 3-hydroxybutyrate

and acetoacetate on a single 20-mul blood sample. Clin. Chim. Acta, 122: 231-240.

31. Mostafa, H. K. K. (2010): Effect of the overcrowding on fundus of stomach in adult male albino rats with special reference to the protective role of Bran. J. Histol., Egypt, 33(3): 479 - 488.

32. Mueller, C. (2004): True or false: Serum hepatic proteins concentration measure nutritional status. Support Line, 26: 8 - 19.

33. Nagaraja, H. and Jeganathan, J. (2003): Effect of acute and chronic conditions of over-crowding on free choice ethanol intake in rats. Indian J. Physiol. Pharmacol., 47(3): 325 - 331.

34. Nayanatara, A. K., Nagaraja, H. S., Ramaswamy, C., Bhagyalakshmi, K., Ramesh, B.M., Damodara, G. K. M. and Venkappa, S. M. (2009): Effect of chronic unpredictable stressors on some selected lipids parameters and biochemical parameters in Wistar rats. J. Chinese Clin. Med., 4(2): 92 - 97.

35. Saalu, L. C., Jewo, P. I., Yama, O. E. and Oguntola, J. A. (2011): Evaluation of the histomorphometric evidences of hydroxyurea-induced testicular cytotoxicity in sprague-dawley rat. J. Pharmacol. Toxicol., 6: 409 - 417.

36. Sadagurski, M., Landeryou T., Blandino-Rosano, M., Cady, G., Elghazi, L., Meister, D., See, L., Bartke, A., Bernal-Mizrachi, E. and Miller, R. A. (2014): Long-lived crowded-litter mice exhibit lasting effects on insulin sensitivity and energy homeostasis. Am. J. Physiology - Endocrinology and Metabolism, 306 (11): E1305 - E1314.

37. Seres, D. S. (2005): Surrogate nutrition markers, malnutrition, and adequacy of nutrition support. Nutr. Clin. Pract., 20: 308 - 313.

38. Silverman, E. M., Sapala, J. A. and Appelman, H. D. (1995): Regression of hepatic steatosis in morbidly obese persons after gastric bypass. Am. J. Clin. Pathol., 104: 23-31.

39. Steel, J., Carney, M., Carr, B. I. and Baum, A. (2004): The role of psychosocial factors in the progression of hepatocellular carcinoma. Med. Hypotheses, 62: 86 - 94.

40. Steinberg, D. (1981): Antioxidants and atherosclerosis: A current assessment. Circulation, 320: 915 - 924.

41. Van-Cromphaut, S. J. (2009): Hyperglycaemia as part of the stress response: the underlying mechanisms. Best Practice and Research Clinical Anesthesiology, 23 (4): 375 – 386.

42. Vere, C. C., Streba, T. and Ionescu, G. (2009): Psychosocial stress and liver disease status. World Gastroenterol., 28: 2980 - 2986.

43. Wiilis, C., Armario, A. and Piganini, H. (2009): Cholesterol and triglyceride concentration in rat plasma after stress. Pharmacol. Biochem. Behav., 31(1): 75 - 79.

44. Zakim, A. and Boyer, M. (2003): Plasma endotoxin concentrations in patients with alcoholic and non-alcoholic liver disease: re-evaluation with an improved chromogenic assay. J. Hepatol., 12: 162 - 169.

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خلفية البحث: تعد الكثافة السكانية من الأولويات لكل الكائنات الحية لما لها من تأثيرات سلبية على صحة الفرد والمجموعة. ويعتبر الازدحام واحداً من أهم الضغوط فى التجارب الطبية. وعلى الجانب الآخر، تعتبر العزلة أو الوحدة وضعف الترابط الإجتماعى من المؤثرات السلبية على الصحة، وتعتبر واحدة من أهم المسببات المرضية للإنسان.

هدف البحث: التعرف على تأثير الإزدحام والعزلة على وظائف الكبد فى الفئران البيضاء.

مواد وطرق البحث: إستخدم في هذا البحث أربع و خمسون فأرا ذكرا بالغا من السلالات المحلية كنموذج للدراسة، وقد تم تقسيمهم إلى ثلاثة مجموعات متساوية: المجموعة الأولى ضابطة لم تتعرض لأى ضغوط، والمجموعة الثانية تعرضت للإزدحام المتواصل طوال اليوم داخل الأقفاص بمضاعفة عددها ثلاث مرات عن المجموعة الضابطة لمدة أربعة أسابيع، و المجموعة الثالثة تعرضت للعزلة بوضع كل فأر على حدة داخل قفص لا يسمح بغير حركته الشخصية ودورانه حول نفسه طوال اليوم لمدة أربعة أسابيع.

وقد تم ملاحظة السلوك لكل الفئران طوال فترة العمل. وفي نهاية العمل تم سحب عينات دم من كل فأر لقياس مستوى السكر و الكوليسترول والدهون الثلاثية والدهون منخفضة الكثافة والدهون عالية الكثافة مع قياس مستويات إنزيمات الكبد والبروتين الكلى والألبومين والجلوبيولين، وحساب نسبة ألبومين/جلوبيولين. كما تم إستئصال أكباد الفئران لدراستها ميكروسكوبيا.

النتائج: أظهرت نتائج البحث أن التعرض للإزدحام أو العزلة أدى إلى إضطرابات سلوكية و إضطرابات وظائف الكبد بالإضافة إلى إضطرابات الأيض للجلوكوز والدهون بالدم. وبالفحص الميكروسكوبى لوحظ وجود بعض التغيرات فى خلايا الكبد كزيادة الخلايا الليمفاوية والإحتقانات الكبدية.

الإستنتاج: التعرض للإزدحام أو العزلة يؤثر على السلوك ووظائف الكبد مما ينتج عنه بالضرورة التأثير على بعض قياسات الدم وكذلك عمليات الأيض، ومن الممكن إعتبارهما من العوامل المؤدية إلى بعض الأمراض مثل السكرى واضطرابات الدهون ووظائف الكبد. وعلى الرغم من نتائج هذا العمل، فمن الأهمية عمل دراسات تالية للتعرف على آليات تأثير كل من الإزدحام أو العزلة على إستجابات الجسم أو زيادة القابلية للمرض.