

Chronic unpredictable environmental stress is harmful to humans

Stress refers to the mental and emotional change of state from normal homeostasis. In another words we can say that stress happens when we are worried for something and feeling uncomfortable. Chronic unpredictable environmental stress (CUES) refers to long-lasting stress that occur due to harsh dynamic environmental factors like limited food, limited space to live (crowding), heat, cold, light and dark etc. These dynamic environmental factors if prolonged may cause harmful changes in the blood circulation, hormonal secretion and release, glucose metabolism along with other changes in behaviors of an organism. This harmful effect of CUES on human health is contributed by two most important hormones namely catecholamines and corticosteroids that releases from the adrenal medulla and adrenal cortex respectively. However, release of some adrenocorticotropin from anterior pituitary also responsible for this imbalance of health in CUES. Chronic stress leads to the onset of diabetes mellitus due to uncontrolled hyperglycemia and impaired insulin release. Similarly, CUES also contribute to the damage to DNA and other organs like skeletal muscles, liver, pancreas and kidney. Moreover, CUES poses threat to the enzymes involved in glucose metabolism such as hexokinase, fructose 1, 6 bis phosphatase and glucose-6- phosphatase. CUES also lead to the generation of free radicals that further causes decrease in efficiency of antioxidant defence of the biological system.

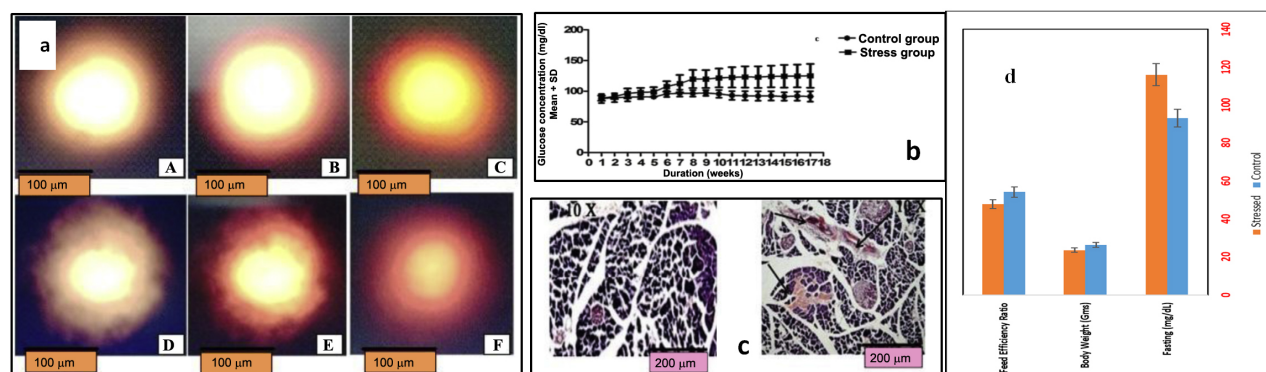


Fig. 1. (a): Effect of chronic unpredictable environmental stress on average comet tail length of tissues (A) liver (control group) (B) kidney (control group) (C) pancreas (control group) (D) liver (stressed group) (E) kidney (stressed group) (F) pancreas (stressed group). The images of ethidium bromide stained slides were captured with fluorescent microscope. The comet tail length was measured with Komet 5.5 imaging system to acquire images. (b): Evaluation of chronic unpredictable environmental stress on weekly plasma fasting glucose (mg/dL). Stressed mice were showing significant increase in fasting plasma blood glucose compared to control. Data are presented as mean+SD. A p value less than 0.05 were considered as significant (n = 20 in each group) (c): Haemotoxylin and Eosin stained sections of tissues under bright field microscope with 10X pancreas (control group) showing normal pancreatic acini, islets cells and blood vessels arrangement while pancreas of stressed group showing lymphocytic infiltration in islets cells &

moderate congestion of blood capillaries; shown by thick solid black arrow. (d) Fasting glucose (mg/dL); feed efficiency ratio and body weight (gms) of control and CUES received animals.

In our study, we demonstrated harmful effect of CUES on organs, antioxidant defence system, enzymes involved in glucose metabolism and DNA. The hypothesis of the present study was tested on Swiss Albino mice model. We applied CUES in the form of starving, forced swim, changing in lights cycle, restraining, crowding, cold force swimming and wet bedding for a period of 16 weeks for 5 days in a week using different stressors. Feed consumption of animals, their body weight along with other parameters like fasting glucose were recorded weekly to know whether CUES have any impact of these parameters. Levels of HbA1c, cortisol, epinephrine, insulin, lipids along with activity of enzymes like catalase (CAT), superoxide dismutase (SOD), GSH (Glutathione, Glutathione-S-transferase (GST), Glutathione peroxidase (Gpx) Hexokinase (HK), Fructose, 1-6 bis phosphatase and Glucose-6-phosphatase were measured. Plasma corticosterone, plasma epinephrine, HOMA-IR were also found significantly higher compared to healthy animals. Moreover, CUES also caused damage to DNA integrity (Fig. 1a) and activities of enzymes involved in carbohydrate metabolism and antioxidant. Consistent CUES to animals significantly increased their blood fasting glucose (Fig. 1b) and HbA1c compared to the animals of control groups who did not received any type of stress. Severe damage to pancreas was observed in animals receiving CUES compared to healthy (Fig. 1c). Similarly, body weight and feed efficiency were also found to be increased due to CUES (Fig. 1d).

In conclusion, the present study showed that CUES leads to the adverse changes in the body and initiate impairment in the homeostasis. It induced hyperglycemia that further exacerbated free radicals scavenging ability of body and malfunctioning of carbohydrate metabolizing enzymes. DNA comet assay and histopathological examinations of tissues like pancreas showed adverse irreversible changes that probably contribute in the predisposition towards onset of diabetes mellitus.

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