

Abstract

Heart failure is a leading cause of mortality worldwide. Specified diagnostic approach for heart failure remains a serious dilemma for scientist and physicians. It's the need of time to develop the cost effective specified diagnostic strategies that may predict the heart damage at pre and post ischemic stage. Therefore, the current study aimed to develop assay based on Endothelin-1 as the diagnostic marker for periodic heart failure. Endothelin-1 is a potent neurohormone is involved in the vasoconstriction after binding to respective G-coupled receptor and mediated cardiac signaling. In preliminary studies, we have worked on elucidating the role of Endothelin-1 in different experimental models of cardiac disorders. Diabetes induced cardiac hypertrophy model and cardiac ischemia models were established and confirmed by assessing morphological parameters, heart weight/body weight, heart weight/tibia length, cell surface area, histopathological examination and molecular cardiac biomarkers. Lipid peroxidation, oxidative and antioxidative profile analysis were also performed to delineate the pathways involved in cardiovascular signaling. The expression of endothelin-1 was assessed in *invitro* and *invivo* models both at transcriptional and translational level. This diagnostic model may serve as potential molecular indicator of heart health.

Background

Diabetic cardiomyopathies are cardiovascular complication of diabetes. It is described as the presence of abnormalities in cardiac structure, adverse cardiomyocytes remodeling and operating in the absence of other risk factors including hypertension, damage to heart valve and coronary arteries diseases (Jia et al., 2018). The structural indication of diabetic heart are left ventricular hypertrophy and increased in vascular and interstitial thickness (Tate et al., 2017). Diabetes plays role in the progression of heart failure through various mechanism activated by metabolic disturbance, hyperglycemia, change in insulin level and oxidative stress (Jia et al., 2016).

Endothelial cells produced a powerful vasoconstrictor peptide known as Endothelin-1 (Nishiyama et al., 2017). Et-1 causes vascular injuries in cardiac diseases and also causes abnormalities in endothelial function in diabetic patients (Schneider et al., 2002). Et-1 is expressed in various organs including heart and kidney, whereas the main source of Et-1 is vascular endothelial cells. Et-1 is frequently produced in blood vessels, where it help to regulate blood pressure and vascular tone of blood vessels (Sandoo et al., 2010). Et-1 involves in the production of vascular superoxide and also enhances cell proliferation by inducing ROS activation (L. Li et al., 2003). Et-1 is involved in the production of ROS in the vascular cells, so have role in insulin resistance and abnormal endothelial function. Particularly, this happen due to activation of protein expression of NADPH oxidase (Wedgwood, McMullan, et al., 2001; L. Li et al., 2003; Romero et al., 2009).

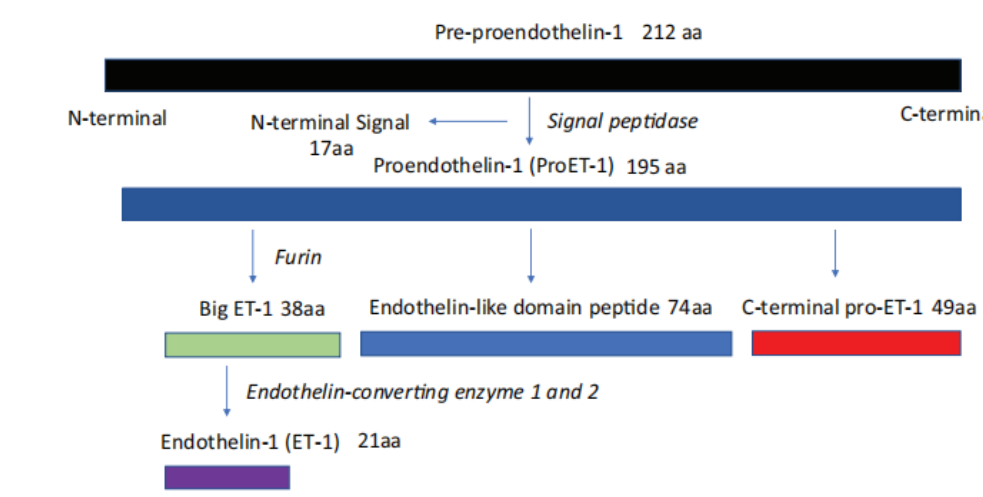


Figure 1: Processing of Endothelin-1 (Jankowich & Choudhary, 2020)

Objective

- To Investigate the current study aimed to develop an assay based on Endothelin-1 as the diagnostic marker for periodic heart failure

Materials & Methods

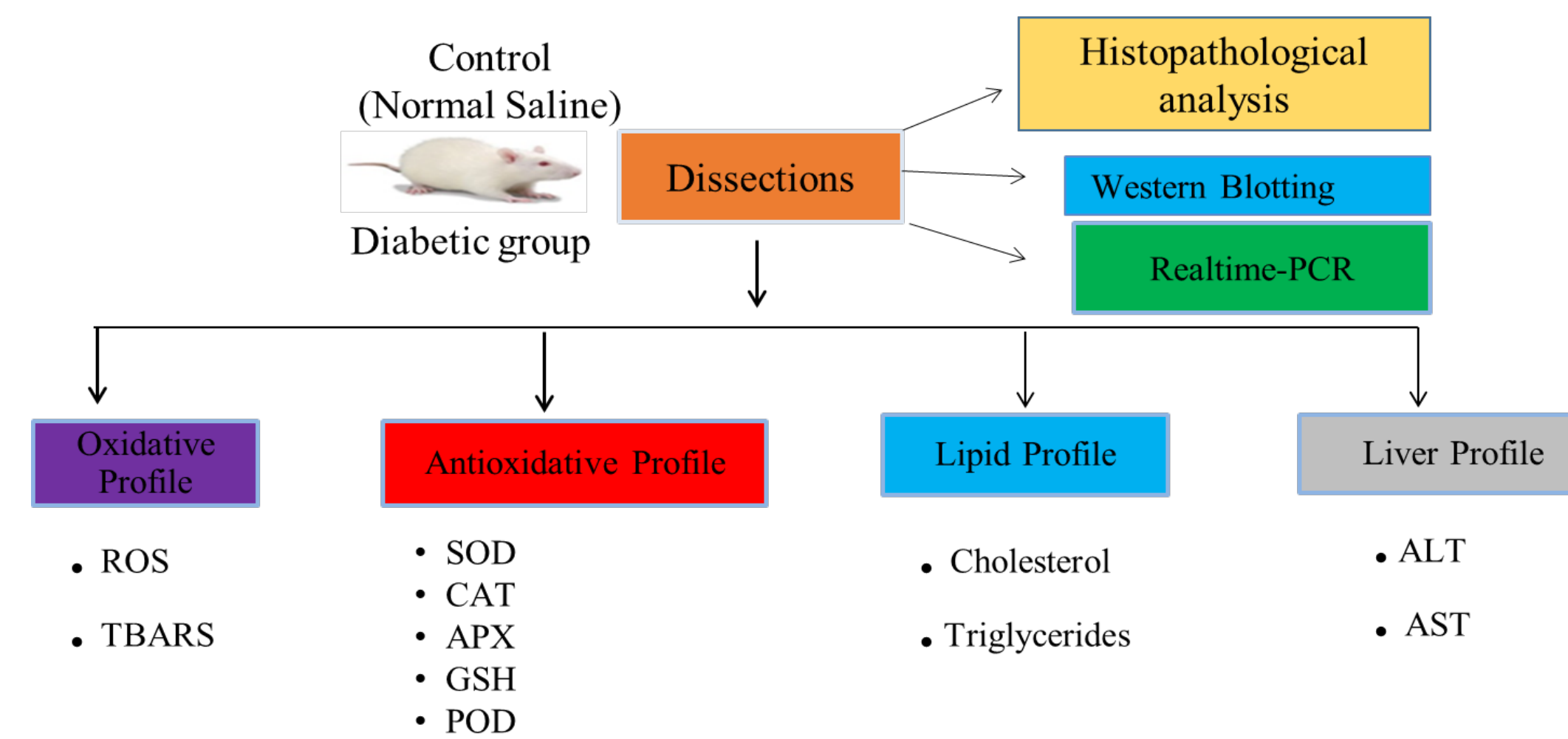


Figure 2: Study design in diabetes-induced cardiac failure model

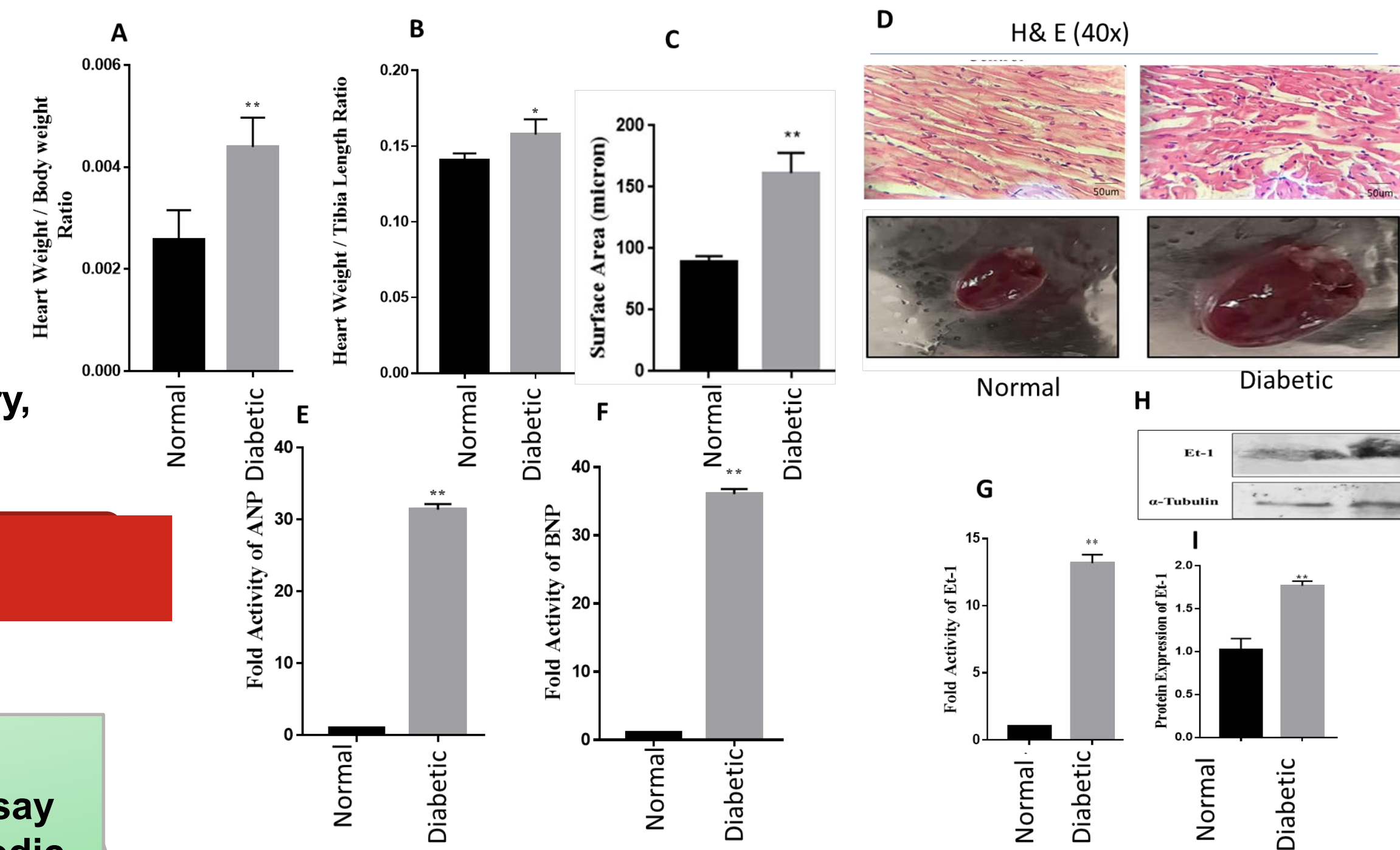


Figure 3: Morphological, Baseline, Histopathology, mRNA and protein levels in diabetes induced cardiac failure model. (A) HW/BW ratio (B) HB/TL ratio (C) Cell surface area (D) Histopathological and morphological images (E) ANP mRNA levels (F) BNP mRNA levels (G) Endothelin-1 mRNA levels (H) Endothelin-1 western blots (I) Densitometry of Endothelin-1 protein

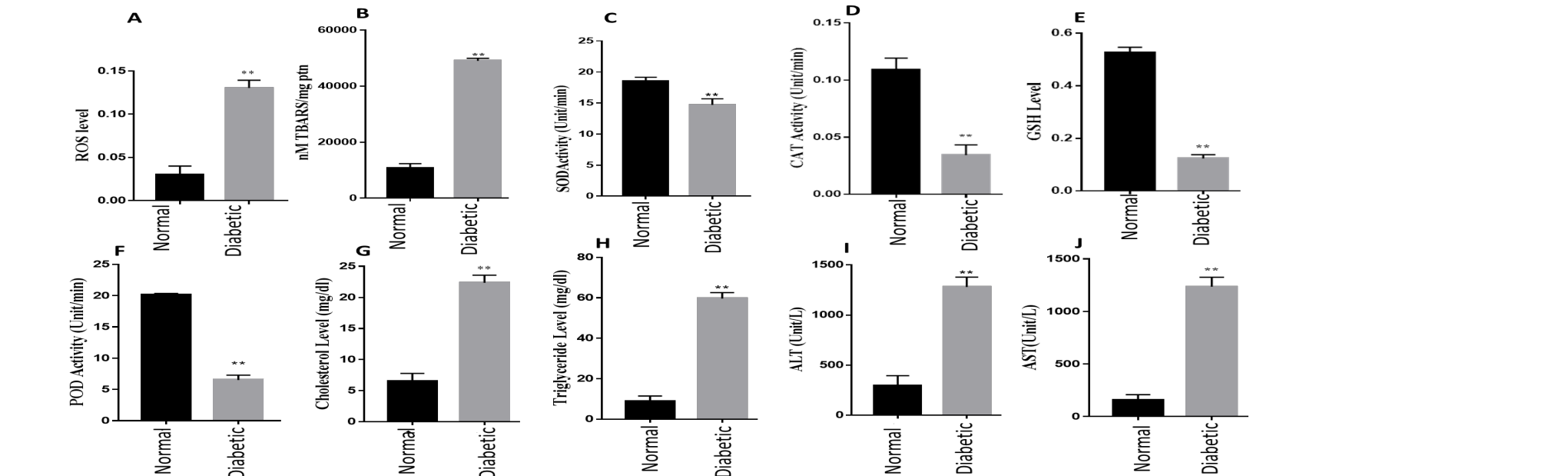


Figure 3: Oxidative, Antioxidative, Lipid and Liver profiling in diabetes-induced cardiac failure model. (A) Reactive oxygen species levels (B) Thiobarbituric acid reactive substances levels (C) Superoxide dismutase (SOD) levels (D) catalase levels (E) Glutathione levels (F) Peroxidase levels (G) Cholesterol levels (H) Triglyceride levels (I) ALT levels (J) AST levels

Discussion

Cardiovascular diseases are the major contributor of mortality and morbidity in diabetic patients worldwide (Ghantous et al., 2020) (Miller et al., 2019; Paneni et al., 2013). In case of DCM, changes in heart function and morphology is observed mainly in left ventricle (Jia et al., 2018). Current study will provide a platform to develop a detection method and therapeutic against diabetes induced cardiac pathologies.

References

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