

## Abstract

Obesity has been recognized as a global health problem and linked with chronic diseases such as diabetes mellitus, cardiovascular syndromes, musculoskeletal disorders and some cancers. Children exposed to high carbohydrate, high fat, energy dense food, are vulnerable to developing chronic health conditions. On long term exposure to low nutrient quality food, childhood obesity is associated with a higher chance of obesity in adulthood (Puhl, 2012). As the prevalence of obesity increases, it is imperative to develop animal models to understand the pre-existing metabolic milestones leading up to an obesogenic condition. It is with this goal that our team has developed a juvenile animal model replicating childhood exposure to a high carbohydrate, high fat diet. To develop our juvenile animal model, three week old male Sprague-Dawley rats were weaned and exposed to cafeteria diet for 10 weeks. Our findings show that body weight increased gradually with the treated group (CAF) becoming obese and reaching statistically significant weight gain. Furthermore, the lipid profile and plasma glucose levels of the CAF group showed increases in comparison to their standard chow fed counter parts. In conclusion, an exposure to a caloric overload induces obesogenic effects indicated by changes in body morphology, by increased abdominal adiposity, blood glucose levels and lipid profile.

## Introduction

Obesity is defined as the abnormal or excessive accumulation of total body fat that is a global health concern in developed and developing countries among adults as well as children (Karnik & Kanekar, 2012). Childhood related obesity has been highlighted over the past decade due to its increasing incidence.

In 2014, the World Health Organization (WHO) reported that 41 million children under the age of 5 years were classified as overweight or obese (World Health Organization, 2016). Additionally, it has been reported that 48% of obese and overweight children lived in Asia. As obesity reaches epidemic proportions, the prevalence of childhood related obesity has proportionately increased in the Gulf countries ranging from 5-14 % among males and 3-18% in females (Al Nohair, 2014). The Qatar World Health Survey (WHS) reported that 16% of Qatari children were obese and about 28% below the age of 5 years were overweight (Mandeya & Kridli, 2015). In 2014, Qatar ranked as the 16th country with the most obese adult population in the world (Central Intelligence Agency, 2014).

The genesis of obesity is complex that is a result due to the chronic imbalance in the energy intake and energy expenditure. However, the influence of the western diet, socioeconomic and demographic factors, sedentary lifestyle and urbanization has been attributed to the rising prevalence of obesity in the region. Obesity is known to be associated with metabolic co-morbidities like type 2 diabetes, cardiovascular disease (CVD), infertility and cancer (Kanasaki & Koya, 2011). Obesity is an important predictor of CVD, which begins when several risk factors, including lipid abnormalities, high blood pressure, impaired glucose tolerance, proinflammatory and pro-thrombotic states co-exist in obese individuals. As the prevalence of obesity continues to increase at the national and international level, it became imperative to develop animal models to replicate the co-morbidities associated with obesity and understand the pathogenesis of obesity and develop preventions and treatments (Lutz & Woods, 2013). Animal models are important towards understanding the basic parameters that regulate the physiological and genetic components of metabolism. Hence, to understand the mechanisms behind childhood obesity in Qatar, we developed an animal model relevant to Qatar's childhood obesity problem.

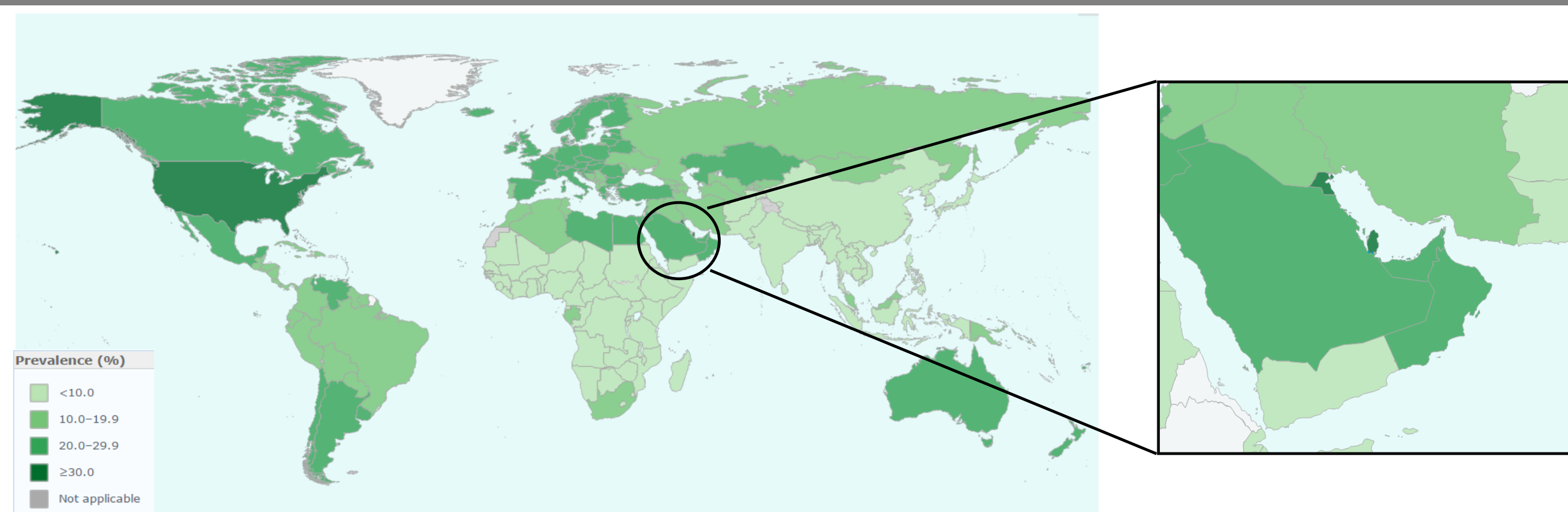


Fig. 1a: Prevalence of obesity in the world and in the Gulf region. (WHO, 2016)

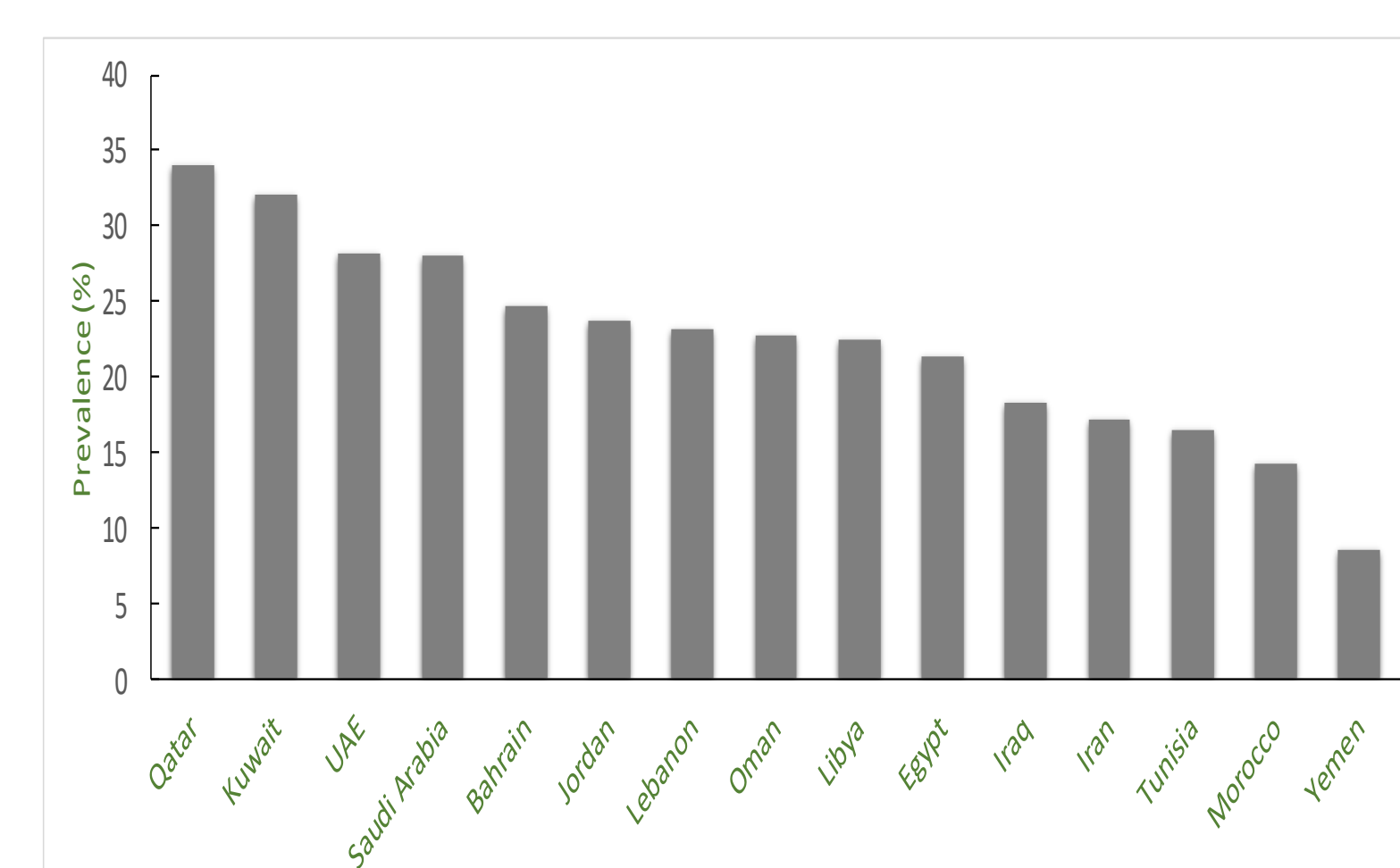


Fig. 1 b: Prevalence of obesity in the Gulf region. (WHO, 2016)

## Methodology

Weaned three-week old Sprague-Dawley male rats were housed in Qatar University's Laboratory Animal Research Center (LARC) under standard conditions (12h light/dark cycle, RH: 65-70% and room temperature :  $28 \pm 2$  °C) and subjected to hypercaloric diet for 10 weeks with free access to standard chow and water. The rats were randomly divided to control and treated groups wherein the treated group received the hypercaloric diet. Their weekly body weight gain, daily food consumption and water consumption were monitored. On reaching an obesogenic body weight, the rats were euthanized and blood samples were collected for further analysis. The collected blood was analyzed for the serum lipid profile and plasma glucose levels. Statistical analysis of the findings were done by one-way ANOVA using Excel. This study was approved by the Institutional Animal Care and Use Committee (IACUC) of Qatar University under the protocol number QUUG-CAS-BES-13/14-18.

## Results and Discussion

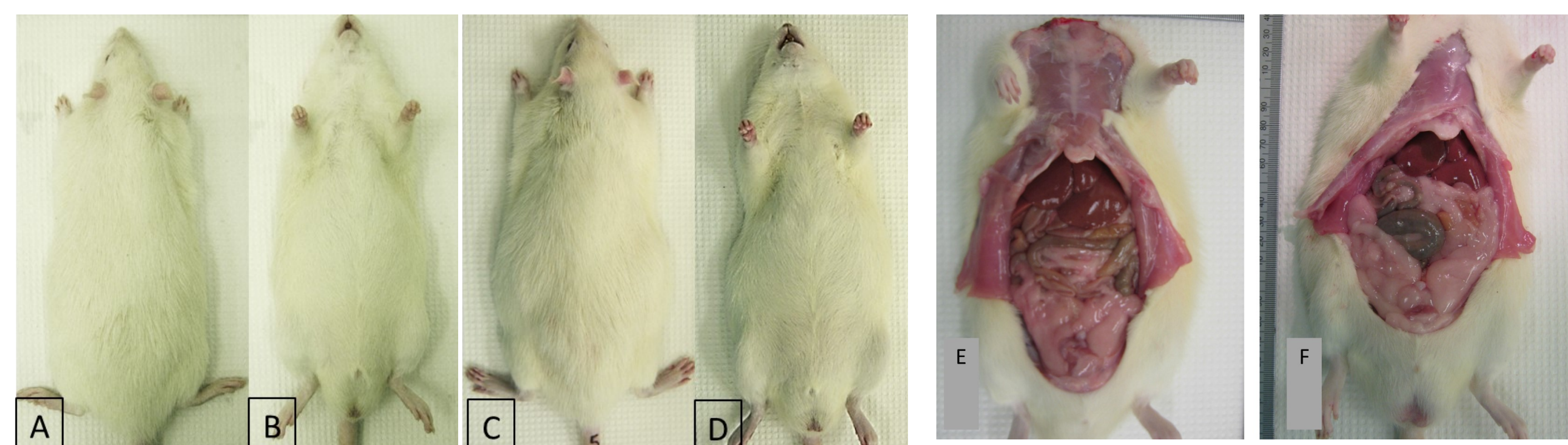


Fig. 2: Morphology of Juvenile Male SD Rats. (A & B) Overall body appearance of chow-fed rats shows lean morphology. (C & D) Overall body appearance of CAF-fed rats shows the abdominal adiposity by the rounding of the abdominal area due to the increase in adiposity. (E & F) Deposition of adipose tissue in abdominal area.

Fig. 3: Growth Curve of Juvenile Male SD Rats. CAF-fed rats exhibited highly significant weight gain over the period of the study compared to the control group with P-value  $\leq 0.001$ .

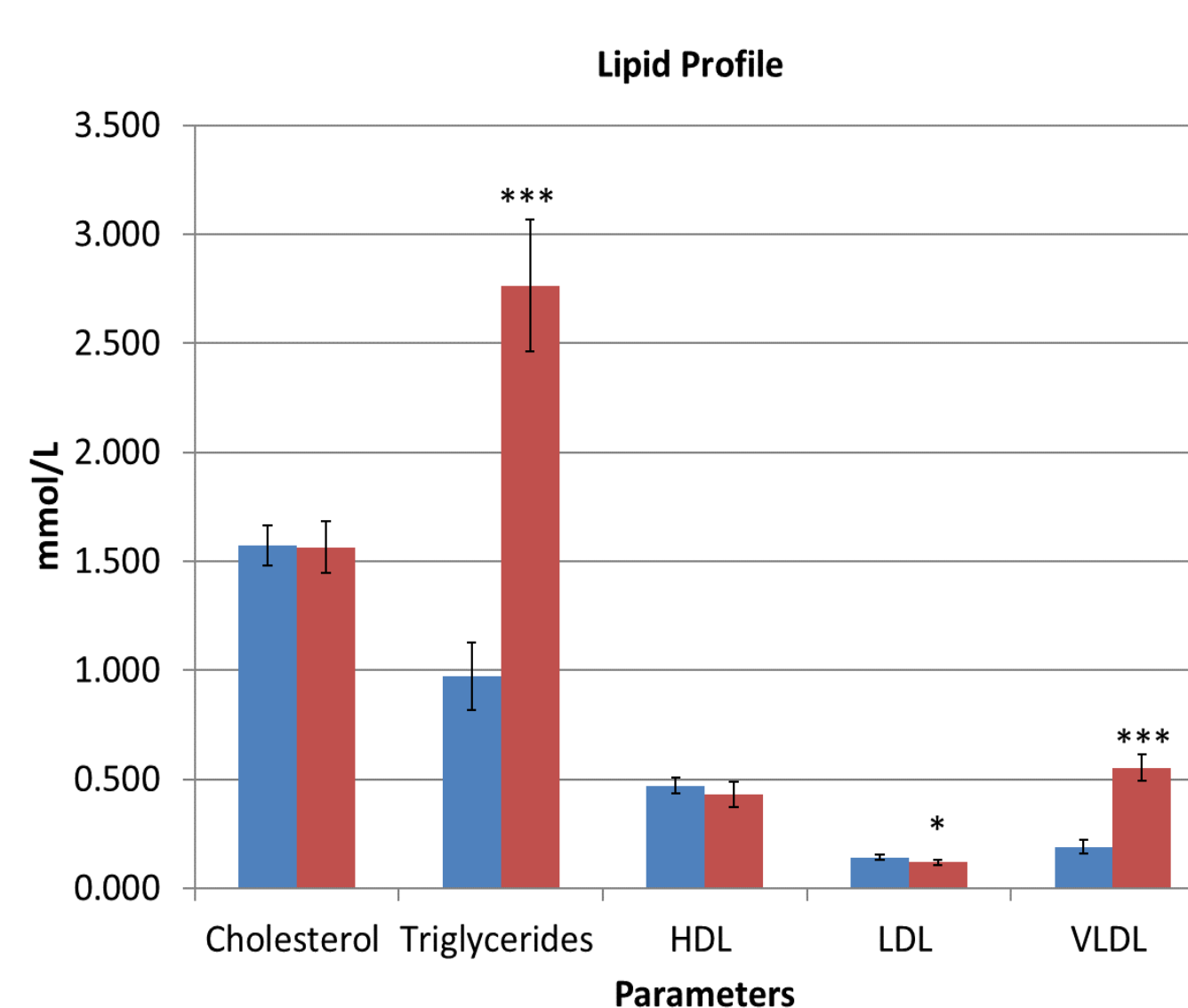
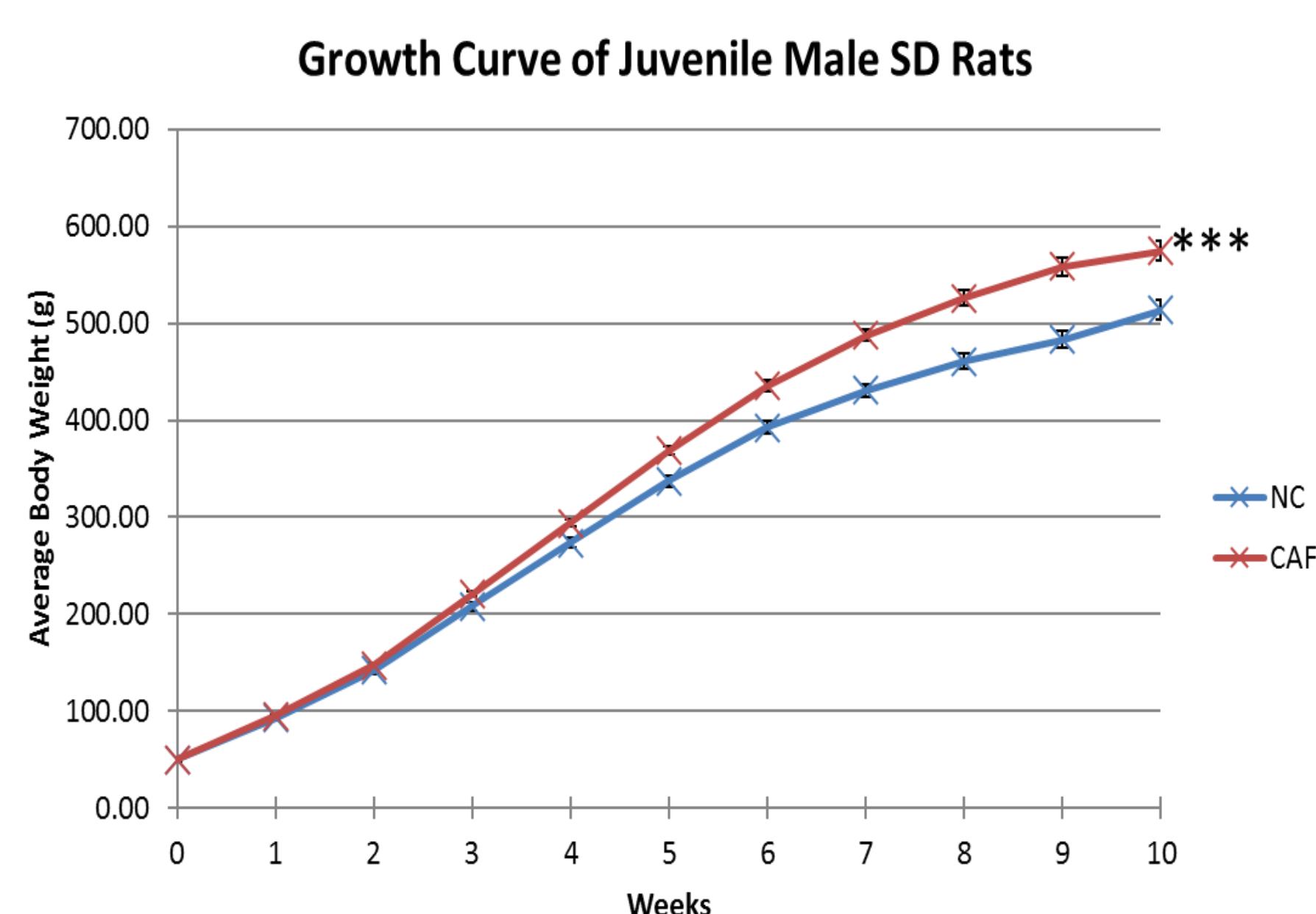


Fig. 4: Lipid Profile of Juvenile Male SD Rats. The lipid profile comprised of the evaluation in the levels of cholesterol, triglycerides, HDL, LDL and VLDL. A highly significant difference was noted in the level of triglycerides and VLDL of the CAF-fed group (P-value  $\leq 0.01$ ) compared to the control group.

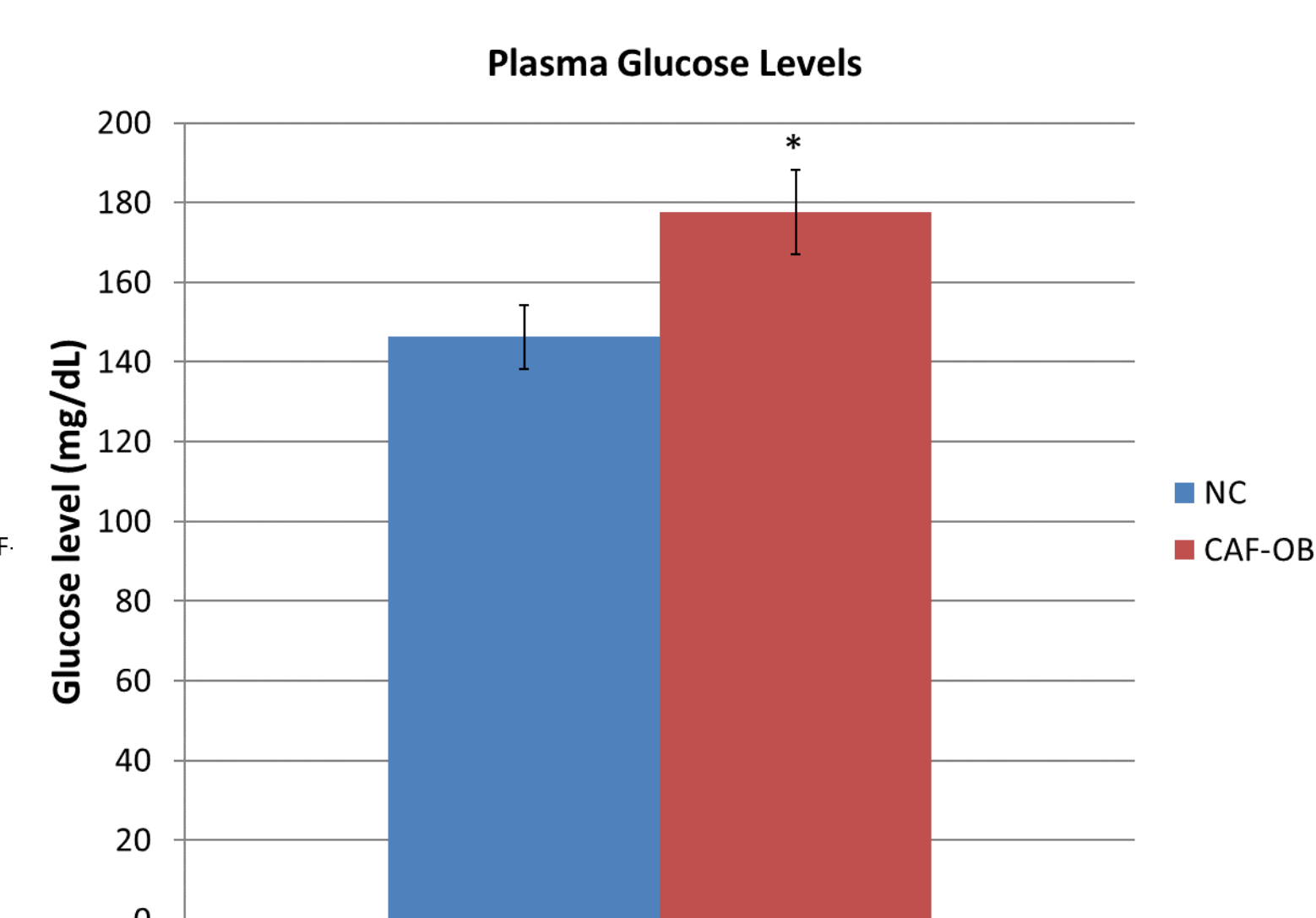


Fig. 5: Plasma Glucose Levels of Juvenile Male SD Rats. A statistically significant increase in the plasma glucose levels of the CAF-fed obese group was found (P-value  $\leq 0.05$ ).

## Conclusion

This study demonstrated that a hyper-caloric overload of CAF diet resulted in high weight gain and diet induced obesity resembling the patterns of human obesity specifically childhood obesity relevant to Qatari children. This pattern of obesity was associated with significant increase in blood glucose levels and lipid profile. This rodent animal model can be used to further investigate the pathophysiology of high-energy consumption under obese and non-obese conditions.

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