Background and Objectives:
The World Health Organization states that cardiovascular disease is the leading cause of death worldwide. The increasing prevalence of obesity and diabetes indicate that cardiovascular disease will remain a major health concern for decades to come. The Gulf States including Qatar, the Middle East and the North African (MENA) region as whole, but also elsewhere in the world, face a pandemic of obesity and diabetes. Hyperglycaemia is the common denominator of both type-1 and type-2 diabetes and results in "glucose toxicity" that is closely linked to the high cardiovascular morbidity and mortality associated with diabetes. A reduction in the generation of NO -an important contributor to the endothelium regulation of blood flow and coagulation- in response to hyperglycaemia, is an early indicator of the onset of vascular disease. NO bioavailability is determined through the balance of its generation by eNOS and its quenching by reactive oxygen species, ROS. In response to hyperglycaemia and a variety of metabolic perturbations, eNOS produces predominately superoxide anions rather than NO and there is therefore an increase in oxidative stress and reduced bioactivity of NO. MicroRNAs (miRs) are small non-coding RNAs that inhibit gene expression and have also been implicated in the regulation of endothelial cell biology. A number of miRs including 221 & 222 have been implicated in endothelial cell function. They are involved in post-transcriptional control of major regulatory pathways.

Methods:
Mouse microvascular endothelial cells (MMECs) were cultured in normal (11mM) or high glucose (HG, 40mM) media and the ratio of coupled (dimeric) to uncoupled (monomeric) eNOS determined by immunoblot. ROS, NO and the expression of miR-221/miR-222 were also measured.

Results:
HG enhanced ROS, reduced the eNOS dimer/monomer ratio and reduced the generation of NO. Our data indicate that HG-induced ROS generation can be reversed in the presence of inhibitors of miR-221/miR-222.

Conclusion:
Hyperglycemia is associated with increased oxidative stress and decreased NO bioavailability. miR-221 and miR-222 play an important role in high glucose-induced increased oxidative stress and endothelial dysfunction.