TITLE: Enhanced vulnerability of diabetic mice to *Streptococcus agalactiae* infection

AUTHORS: MENDONCA, J.C.; PENA, J.M.S.; RODRIGUES, D.S.; SANTOS, N.O.; JONATHAN, G.S.; MORAES, J.A.; TORRES, E.J.L.; NAGAO, P.E.

INSTITUTION: UNIVERSIDADE DO ESTADO DO RIO DE JANEIRO, RIO DE JANEIRO, RJ (RUA SÃO FRANCISCO XAVIER, 524, PAVILHÃO HAROLDO LISBOA, INSTITUTO DE BIOLOGIA ROBERTO ALCANTARA GOMES, DEPARTAMENTO DE BIOLOGIA CELULAR,5º ANDAR, SALA 501B, CEP 20550-013, RIO DE JANEIRO – RJ, BRAZIL).

ABSTRACT:

Streptococcus agalactiae is an invasive pathogen known for causing severe infections in pregnant woman, newborns and infants. Most recently the number of imunocompromised adults and elderly presenting comorbitidies caused by *S. agalactiae* are increasing and this is a huge concern, mainly for diabetic patients. Diabetes is a metabolic condition associated with a higher risk of developing multiple infections, such as pneumonia and cardiovascular diseases. There is a correlation between GBS, diabetes and both lung/heart diseases according to literature, but it's still not very much elucidated. Then, our aim in this study was to understand how an hipervirulent GBS strain can increase the risk of developing sepsis and pulmonary infections in diabetic Swiss mice. Male and female mice were treated with streptozotocin, drug that deplete all β cells, 48h prior to intranasally infect mice with $1x10^5$ CFU/mL of GBS. They were divided in four groups (NDNI, NDI, DNI, DI). After 1 week, the animals were sacrificed for tissue CFU count, bronchoalveolar lavage fluid and histological analysis. All diabetic mice presented severe hyperglycemia. Body weight of those mice were significantly reduced and food consumption was increased when compared to non-diabetic mice GBS infection or not. After CFU counting, all organs presented higher number of viable cells on diabetic mice, showing GBS spread in lungs, kidney and bladder. Macrophages from bronchoaveolar lavage were cultured and divided for two experiments. Part of the fluid was treated with CM-H2DCFDA probe, which showed overproduction of reactive oxide species after 30 minutes and 1 hour post-infection, mainly in diabetic infected group. The invasion assays with the macrophages demonstrated high GBS survival in macrophages from diabetic mice after one week. Together, the data showed that diabetic mice infected with the hypervirulent strain of GBS spread to organs more efficiently, and could develop severe and rapid manifestations in multiple organs. Increased points of lung inflammation were identified, probably due to the ability of GBS to bypass the immune system.

KEYWORDS: *Streptococcus agalactiae*, diabetes, sepsis, lung macrophages.

FINANCIAL SUPPORT: CNPq, Capes, FAPERJ and SR2/UERJ.