Type: Oral Presentation

Final Abstract Number: Pre.018
Session: Pre-Congress Symposium: Emerging African Investigators Symposium
Date: Wednesday, April 2, 2014
Time: 13:00-17:00
Room: Room Roof Terrace

The prevalence and incidence of diabetes mellitus and other disorders of glycaemia in South African black patients on antiretroviral therapy

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Background: While opportunistic infections and mortality related to Human Immunodeficiency Virus (HIV) infection has reduced significantly following antiretroviral therapy (ART) scale-up, non-AIDS events are emerging causes of death. This study determined the prevalence and incidence of dysglycaemia in adult South African black subjects of second generation Zulu descent.

Methods & Materials: The study included HIV infected ART naive patients who were eligible for ART (group 1, n = 150), and age, gender, and ethnically matched HIV infected subjects who were not eligible for ART (group 2, n = 88) and HIV negative subjects (group 3, n = 88). WHO criteria for disorders of glycaemia were used to compare the three groups for the prevalence of diabetes mellitus (DM), impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), using the oral glucose tolerance test and HBA1c at baseline (Yr 0) prior to group 1 commencing ART (tenofovir, lamivudine, efavirenz/nevirapine). Group 1 was followed for 24 months or longer on ART to determine the incidence of dysglycaemia. Poisson approximations were used to estimate incidence.

Results: At baseline, the prevalence of DM was 0% in group 1and 2, 4.94% in group 3 (p = 0.005).The prevalence of IGT was 2.96%, 2.4% and 3.7% and of IFG, 0.7%. 1.2% and 0% in group 1, 2 and 3, respectively. Multivariate analysis showed that systolic blood pressure (OR 1.3 [95% CI 1.1-1.6] p = 0.002) and triglycerides (OR 4.1[95% CI 1.0-16.6] p = 0.05) were significant risk factors for DM. In the follow-up study, of 150 HIV infected persons on ART, 13 developed DM during 219.2 person-years follow up (PYFU), with an incidence of 5.9 cases per 100 PYFU (95% CI 3.2 – 10.1); 11 developed IGT during 217.9 PYFU (incidence: 5.0 cases per 100 PYFU [95% CI 2.5 to 9]) and 8 developed IFG during 216.3 PYFU (incidence: 3.7 cases per 100 PYFU [95% CI 1.6 – 7.3]). In multivariate analysis, systolic blood pressure was a significant predictor of IGT and IFG

Conclusion: The incidence of DM in HIV infected patients on ART is high. Patient monitoring in developing countries must also focus on metabolic complications of ART.

http://dx.doi.org/10.1016/j.ijid.2014.03.425

Type: Invited Presentation

Final Abstract Number: Mte.001
Session: Meet-the-Expert: Invasive Non-typhoid Salmonellosis (iNTS): Increasing Awareness and Future Vaccines
Date: Thursday, April 3, 2014
Time: 07:45-08:45
Room: Room 1.40

Bivalent vaccine strategies for invasive non-typhoidal Salmonella infections

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While non-typhoidal *Salmonella* (NTS) have long been known to be a cause of self-limited gastroenteritis, it is becoming increasingly recognized that multiple antibiotic-resistant strains are also emerging as important causes of invasive bacteremia and focal infections, resulting in hospitalizations and deaths. Surveys from multiple sites in sub-Saharan Africa reveal that ~ 75-90% of NTS from cases of invasive disease are *Salmonella* Typhimurium (and the monophasic *S.* Typhimurium variant *S.* I 4,[5],12:i:-), serovars that fall into *Salmonella* group B, or *Salmonella* Enteritidis, a group D *Salmonella* serovar. An effective NTS vaccine directed against these serovars could thus provide broad protection. We have constructed attenuated *S.* Typhimurium and *S.* Enteritidis strains that can serve as live oral vaccines as well as "reagent strains" for improved production of conjugate vaccine components. Live oral vaccine strains CVD 1931 (*S.* Typhimurium D65 Δ*guaBA* Δ*clpX*) and CVD 1944 (*S.* Enteritidis R11 Δ*guaBA* Δ*clpX*) were shown to protect mice against a high challenge dose (10,000 X LD_{50}) with invasive African clinical isolates. Cross-protection experiments revealed that these live NTS vaccines also protect mice against other invasive Group B and D serovars. In parallel, we have developed *S.* Enteritidis conjugate vaccines using *S.* Enteritidis flagellin FliC as a carrier protein, chemically linked to homologous lipopolysaccharide-derived Core and O-polysaccharide (COPS), purified from *S.* Enteritidis R11 Δ*guaBA* Δ*clpPX* expressing flagellin at high levels. Various candidate conjugates were constructed by linkage to solvent-exposed lysines on FliC either at random COPS hydroxyls with CDAP chemistry, or at the Core-KDO terminus with thioether chemistry. Mice immunized with COPS:FliC conjugates were significantly protected from lethal challenge with an invasive African *S.* Enteritidis clinical isolate, demonstrating 80-100% vaccine efficacy. Protection was further maintained in mice immunized with fractional COPS:FliC doses that did not stimulate high COPS-specific antibody levels, indicating the potency of our conjugate vaccines. Since *S.* Typhimurium and *S.* Enteritidis are the most common NTS serovars associated with invasive disease, this research can pave the way for development of highly effective, broad spectrum vaccines against NTS.

http://dx.doi.org/10.1016/j.ijid.2014.03.426