## European Respiratory Society Annual Congress 2012

Abstract Number: 933 Publication Number: P4652

## Abstract Group: 7.6. Paediatric Respiratory Epidemiology Keyword 1: Epidemiology Keyword 2: Lung growth/development Keyword 3: Neonates

Title: Pregnancy complications and respiratory outcomes in very preterm infants

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**Body:** Very preterm infants have a high mortality and morbidity, due to a combination of immaturity per se, and of the underlying pathology causing preterm birth. The role of prenatal infection on increasing the risk of bronchopulmonary dysplasia (BPD) is still unsettled. Aim: To test the hypothesis that infection/inflammation disorders (I) (prelabor premature rupture of membranes, spontaneous preterm labor, infection and hemorrage) and hypertensive disorders (H) (maternal hypertension and intrauterine growth restriction) are differently associated to in-hospital mortality and BPD. Methods: A population-based prospective cohort of 2085 singleton infants 23 to 31 weeks gestational age (GA) born in 6 Italian regions in 2003-2005 (ACTION study), was analyzed. Infants born of mothers with H (31%) were contrasted with those born after I (63%) with respect to mortality and BPD. Multivariable logistic analyses (generalized estimating equations) were used. Results: Mortality was 14.3%, with 48.7 % of deaths occurring in the first 5 days of life, largely due to respiratory causes. Infants born after H had more respiratory distress syndrome than the I group (odds ratio (OR)= 1.41, 95% confidence interval (CI): 1.1-1.8, adjusted for GA, sex and antenatal steroids). 12.8 % of neonates had BPD. After adjustment for GA, H disorders had a higher risk of mortality (OR=1.4; 95% CI:1.0, 2.0) and of BPD (OR=2.5; CI: 1.8, 3.6). Further adjustment for maternal age, education, citizenship, and antenatal steroids did not change results. Conclusions: Our results support the hypothesis that pathogenetic mechanisms involving the regulation of lung/airways size and vessels are more important than I in the development of BPD.