

ORAL SESSION 06 (BEST ORAL PRESENTATION) SESSION-POPULATION SCIENCE

MONDAY ORAL

OS 06-01 **DEVELOPMENTAL STAGES OF HYPERTENSION BETWEEN MALES AND FEMALES- ARE THERE DIFFERENT MECHANISMS?**

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Objective: The objectives of this study are to investigate the developmental stages of hypertension between males and females and identify why young males have higher blood pressure than young females.

Design and method: The study used a sub-sample of 2000 offspring from the original cohort of the Mater University of Queensland Study of Pregnancy (MUSP) and its outcomes. The MUSP is a prospective birth cohort study which commenced in early 1980s in Brisbane, Australia and followed their offspring till young adulthood. Anthropometric and blood pressure data were measured at 5, 14, 21 and 30 year; and socio-economic, obstetric history and lifestyle of mothers were prospectively collected around pregnancy and offspring characteristics were prospectively collected at childhood, adolescent and young adulthood. Multivariable analyses were conducted to determine the developmental stages and differential impact of males and females were investigated.

Results: Maternal pregnancy exposures including obesity and hypertensive disorder in pregnancy and offspring growth trajectories prospectively associated with offspring blood pressure development at age 5 and 14 years. Although mean difference of systolic (SBP) and diastolic blood pressure (DBP) were not considerable at age 5 and 14 between males and females but by age 21 it was substantial (e.g. over 10 unit in SBP and 4 units in DBP). The prevalence of hypertension was much higher among males than females by age 21 year. None of the confounding or mediating factors, including maternal blood pressure, parental obesity, socioeconomic status, offspring physical inactivity and diets did not explain this substantial blood pressure difference between young males and females.

Conclusions: This study shows that maternal pregnancy exposures and offspring early growth trajectories prospectively associated the development of childhood and adolescent blood pressure. Blood pressure difference between males and females are substantial and it mainly exhibits from adolescent to young adulthood. Mechanisms behind this will be discussed.

OS 06-02 **MULTIPLE ANTIHYPERTENSIVE MEDICATION USE, RESISTANT HYPERTENSION AND OUTCOMES IN THE UNITED STATES: FINDINGS FROM NHANES 1988 TO 2012**

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Objective: Multiple medication use in patients with hypertension (HTN) is a common clinical problem faced by both primary and specialists. Patients who remain to have higher BP in spite of the concurrent use of 3 antihypertensive agents of different classes are defined as resistant hypertension (RH). In the study we aimed to identify the prevalence of RH, and examined its association with mortality from all-cause and cardiovascular disease (CVD).

Design and method: Data from the U.S. National Health and Nutrition Examination Surveys (NHANES) 1988–2012 were analyzed cross-sectionally on the burden of RH using logistical regression models, and analyzed prospectively on its association with mortality using Cox regression models.

Results: Of 18,471 patients with HTN (M: 8411, F: 10060), 72.8% in males and 75.9% in females took antihypertensive medications. Whites had the highest prevalence (77.4%), followed by Blacks (74.8%), and Hispanics (67.2%), ($p < 0.001$). The prevalence of males who took 1, 2 or ≥ 3 antihypertensive medications were 67.1%, 25.0%, and 8%, and the corresponding values were 68.7%, 25.3%, and 6% in females. Blacks has the highest prevalence of RH (9.4%), followed by Whites (6.1%), and Hispanics (5.8%), ($p < 0.001$). Patients with RH had significantly higher risk of mortality from all-cause (hazard ratio, HR = 1.82, 95%CI 1.21-3.45, $p < 0.001$), and CVD (HR: 2.16, 95%CI: 1.72-4.65, $p < 0.001$).

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Conclusions: The study, using the U.S. nationally representative data, indicates that RH poses a serious clinical and public health problem for all racial and ethnic groups. Further large-scale prospective studies are needed to extend and confirm the current findings.

OS 06-03 **DIURNAL BLOOD PRESSURE RHYTHMICITY IN RELATION TO ENVIRONMENTAL AND GENETIC CUES**

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Objective: No previous study addressed the relative contributions of environmental and genetic cues to the diurnal blood pressure rhythmicity. We firstly investigated the explained variance of environmental and clock genes in relation to the night-to-day ratio (NDR) and morning surge (MS), respectively.

Design and method: From 24-h ambulatory recordings of systolic blood pressure (SBP) obtained in untreated Chinese patients (51% women; mean age, 51 years), we computed NDR in 897 and MS in 637. Environmental cues included season, mean daily outdoor temperature, atmospheric pressure, humidity and weekday and the genetic cues variation in the clock genes BMAL1 (rs6486121), CRY2 (rs10838524) and CLOCK (rs1801260).

Results: SBP averaged (\pm SD) 126.7 \pm 11.9 mm Hg, NDR 0.86 \pm 0.07 and MS 24.8 \pm 10.7 mm Hg. In adjusted analyses, NDR was 2.4% higher in summer and 1.8% lower in winter ($P < 0.001$) compared with the annual average with a small effect of temperature ($P = 0.079$); MS was 1.7 mm Hg lower in summer and 1.1 mm Hg higher in winter ($P < 0.001$). The other environmental cues did not add to NDR or MS variance ($P \geq 0.37$). With adjustment for season and temperature, NDR was 3.30% ($P = 0.017$) higher in TT homozygotes ($n = 27$) compared with C allele carriers ($n = 870$) of BMAL1 rs6486121. In CLOCK rs1801260 C carriers ($n = 83$), MS was 3.7 mm Hg ($P = 0.003$) higher than in TT homozygotes ($n = 554$). Of NDR and MS variance, season and temperature explained ~8% and ~3%, while for genetic cues these proportions were ~1% or less.

Conclusions: In conclusion, environmental compared with genetic cues are substantially stronger drivers of the diurnal blood pressure rhythmicity probably because the former also change the expression of the proteins encoded in clock genes.

Table 1. The Night-to-Day Ratio and Morning Pressure Surge in Relation to Host Factors and Environmental and Genetic Cues in Stepwise Regression

Genetic/Environmental variables	NDR (NDR ratio) (95% CI)	P	MS (mm Hg) (95% CI)	P
Sex				
Female (ref)	0.92 (0.92 to 0.93)	<0.001	0.00	NS
Age (100 years)	0.89 (0.87 to 0.90)	<0.001	0.03	NS
24-h blood pressure (>135 mm Hg)	NS	NS	0.05 (0.04 to 0.07)	<0.001
Total cholesterol (>200 mg/dL)	-0.03 (-0.12 to -0.11)	0.01	0.00	NS
R ²			0.016	
Environmental cues				
Season				
Spring	-0.00 (-0.01 to 0.02)	NS	0.00 (0.02 to 0.11)	NS
Summer	2.38 (0.91 to 3.77)	<0.001	-0.05 (-0.10 to 0.00)	NS
Autumn	-0.02 (-0.02 to 0.00)	<0.001	-0.05 (-0.10 to 0.00)	NS
Winter	-1.72 (-2.09 to -0.34)	<0.001	0.02 (0.01 to 0.03)	<0.001
Mean daily temperature (>14°C)	0.02 (0.01 to 0.03)	<0.001	0.00	NS
R ²			0.017	

Adjusted mean and their 95% confidence interval (CI) indicate the change in the night-to-day blood pressure ratio or morning blood pressure surge associated with a 1 SD increase in traditional variables or with a categorical factor. Season: first factors considered for entry in the stepwise regression procedure. Data are mean (SD) or median (IQR) for continuous variables. NS indicates non-significant. Boldface indicates statistical significance. * indicates $p < 0.05$. The values in the table with the P-value set at 0.10. Models for environmental cues included sex, age, 24-h ambulatory blood pressure and total cholesterol. CI and 95% CI are the 95% confidence interval and 95% CI, respectively. NS and NS are the not significant and not applicable, respectively. R² and R² are the coefficients of partial and multiple determination.

OS 06-04 **CHANGES IN GENE EXPRESSION PATHWAYS PREDICT DELAYED SODIUM EXCRETION DURING SALINE INFUSION**

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