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**PROSPECTIVE CROSS-SECTIONAL STUDY ON THE CLINICAL PROFILE AND MYOCARDIAL FUNCTION OF SEVERELY AND MODERATELY MALNOURISHED CHILDREN 2 MONTHS TO 18 YEARS OLD IN PHILIPPINE CHILDREN’S MEDICAL CENTRE (PCMC)**

Odessa Bayani*. Philippine Children’s Medical Center, Philippines

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**Background** Malnutrition in children produces visceral protein loss and consequent cardiac atrophy. There are conflicting studies if this cardiac atrophy results in myocardial dysfunction.

This study aims to determine the prevalence of myocardial dysfunction and describe the demographic, clinical, electrolyte changes, electrocardiographic and structural and myocardial function in severely and moderately malnourished children.

**Methods** This is a prospective cross-sectional study conducted on severely and moderately malnourished children 2 months to 18 years old in Philippine Children’s Medical Center. Serum potassium, magnesium, ionised calcium and phosphorus determination, 2D echocardiography and electrocardiogram (ECG) were done.

**Results** 73 subjects (43 moderately and 30 severely malnourished) were recruited. Majority had neurologic diseases (n=18, 25%), followed by tuberculosis (n=13, 18%). 2 had pneumonia, 2 had diarrhoea.

Hypokalemia was found in 5/30 or 16% severely malnourished (Potassium 2.21–2.96 mmol/L) and 4/42 or 9% moderately malnourished (Potassium 2.5–2.89 mmol/L) (p>0.05). Only one marasmic child had hypomagnesemia (0.5 mmol/L). Ionised calcium and phosphorus were normal. Both groups demonstrated prolonged QT interval, short and prolonged PR interval, prolonged QRS duration with no statistical significance. The most common ECG finding is short PR interval in moderately (n=29/42 or 69%) and severely malnourished (n=18/29 or 62%) subjects. (p>0.05)

The systolic and diastolic functions were normal in both the severely and moderately malnourished. Although the left ventricular mass (LVM) was low with no statistical significance between the two groups, the LVM index remained to be normal. The presence of pericardial effusion in severely malnourished (n=5/29, 17%) compared with only 1 in moderately malnourished had a statistical significance of P.

**Conclusions** Hypokalemia, hypomagnesemia and shortened PR interval are common in malnutrition. Hence, vigilant monitoring of electrolytes and ECG should be done in all malnourished children. Even if the left ventricular mass was reduced in malnutrition, the left ventricular mass index remained to be normal. No myocardial dysfunction was found in the moderately and severely malnourished children. This suggests a possible compensatory mechanism of a malnourished heart.

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**MAJOR GENETIC ALTERATIONS IN SPORADIC COLORECTAL CANCER IN THE CHINESE POPULATION**

Po Man Tsang*. The Chinese University of Hong Kong, Hong Kong

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**Background** Sporadic colorectal cancer accounts for 80% of all colorectal cancer. The 2 major mechanisms of genetic alteration are chromosomal instability (CIN) and microsatellite instability (MSI). The prevalence of KRAS, NRAS, BRAF and CTNNB1 mutations in western population was 42.4%, 5.1%, 15.2% and 1.1%. BRAF mutations in Chinese population were much lower (3.1%). RNF43 mutation was recently reported with a high prevalence of 18%. It was found mutually exclusive with APC inactivation and was associated with MSI-H tumours.

In this study, the prevalence of APC, KRAS, NRAS, BRAF, CTNNB1 and RNF43 mutations in Chinese sporadic colorectal cancer patients was confirmed by next generation sequencing (NGS). The association of RNF43 mutation with APC, BRAF mutations and MSI status of tumours, was analysed. Clinical-pathological correlation was evaluated.

**Methods** NGS was used to investigate the prevalence of major mutations in 55 subject samples. Data analysis was done by Statistical Package of the Social Sciences (SPSS) statistics. Clinical-pathological correlation was analysed by Cox regression and Kaplan-Meier estimate.

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**HYPERPROLACTINEMIA, BEWARE OF PROKINETIC DRUGS!**

Unknown Shivam*, Akli Sridevi. Vidyahi Institute of Medical Sciences and Research Center, India

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**Background** Hyperprolactinemia is the most common cause of galactorrhoea in women. Levosulpride an atypical neuroleptic and a prokinetic drug acting only on the D2 receptors can cause significant hyperprolactinemia which may be associated with galactorrhoea. However, it is often under- or misdiagnosed. Hence, we describe a case of drug induced hyperprolactinemia presenting with galactorrhoea.

**Methods** A 31 years old lady presented with complaints of menstrual irregularity and galactorrhoea since 18 months. She consulted an Endocrinologist in the USA who started her on Cabergoline 0.25 mg twice a week. However, galactorrhoea did not subside. MRI of the pituitary gland was unremarkable. Cabergoline dose was increased to 0.5 mg twice a week and then gradually to 2 mg per week. After few months of treatment, she was shifted to Bromocriptine in view of persistent galactorrhoea and hyperprolactinemia not responding to cabergoline. She presented to us in April 2017 with unabated symptoms and elevated serum prolactin (152 ng/ml). A review of drug history revealed intake of Esomeprazole (40 mg) and Levosulpride (75 mg) combination pill since January 2016 for dyspepsia. Levosulpride induced hyperprolactinemia was suspected and hence it was stopped.

**Results** After a week of stopping levosulpride serum prolactin level reduced to 13.48 ng/ml whereas galactorrhoea subsided completely. These findings confirmed levosulpride induced hyperprolactinemia.

**Conclusions** We have made significant advances in the field of medicine, but this case teaches us to never forget the basics of medicine – A detailed history and clinical examination. Careful drug history and awareness about levosulpride and its effect on serum prolactin levels would avoid unnecessary costly investigations and treatment.
Results The frequency of APC, KRAS, NRAS, BRAF, CTNNB1 and RNF43 mutations were 76.4%, 61.8%, 9.1%, 3.6%, 1.8% and 9.1%. The most common RNF43 mutation was p.Gly659fs. RNF43 mutation was associated with MSI-H status (p<0.001) and BRAF V600E mutation (p<0.001). RNF43 and APC mutations were likely mutually exclusive. High pre-operative CEA level ≥10 (p=0.013), high grade (p=0.005), T4 tumours (p=0.006), Stage IV cancer (p<0.001) with distant metastasis (p<0.001) were poor predictors of disease-free survival. High grade (p<0.001), T4 tumours (p<0.001), Stage IV cancers (p<0.001) with distant metastasis (p<0.001) were poor predictors of overall survival.

Conclusions The frequency of major mutations in Chinese population was stable. RNF43 mutation is likely anti-EGFR therapy resistant and is an alternative to targeted therapy. The current clinical classification of colorectal cancer and blood tests for disease monitoring were the most effective way to predict clinical prognosis. More research of larger sample size on the pathogenicity of RNF43 mutation and clinical correlation of major mutations is required.