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Prevalence of Hereditary Pheochromocytoma and Paraganglioma and Associated Genotypes within a Paediatric and Adolescent Population: A Review of Patients Presenting to Familial Cancer Services within NSW, Australia, Between 1993-2018

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BACKGROUND: Phaeochromocytoma and paraganglioma (PC/PGL) syndromes associated with germline mutations are highly morbid. Published data has consistently demonstrated a high occurrence of tumours due to hereditary PC/PGL in childhood with a predominance of cluster 1 mutations. This cluster is associated with more aggressive features including bilateral, multiple and extra-adrenal tumours. As the occurrence of these tumours are scarce, data has not been systematically captured in the Australian Paediatric Cancer Registry. The objective of our study was to establish prevalence of hereditary PC/PGLs in patients under the age of 21 y who were investigated through Familial Cancer Services in New South Wales (NSW), Australia between 1993-2018.

METHODS: Information was collected through the statewide online genetic database known as 'TrakGene' which comprised of a network of 7 adult and 2 paediatric tertiary hospitals. Data collected included patient demographics and tumor features.

RESULTS: Of 31 patients assessed in our cohort 81% (25/31) harboured a germline mutation in one of the driver genes associated with hereditary PC/PGL: SDHB (n = 11), VHL (n = 12), NF1 (n = 1) and MAX (n = 1). The average age of PC/PGL in those with SDHB mutations was 14 y (ra. 7-21) and in those with VHL mutations was 14 y (ra. 5-18); the patients with NF1 or MAX mutations were aged 13 y and 21 y respectively. Of the SDHB group, eight presented with extra-adrenal PGL and two with PC. All tumors in patients with VHL were PCs. Longitudinal follow-up data demonstrated 23% (4/17) developed metachronous disease and 18% (3/17) developed metastatic disease.

CONCLUSION: Paediatric and adolescent patients with PC/PGL are highly likely to harbour a germline driver mutation, particularly in VHL or SDHB. Patients diagnosed with a PC/PGL at a young age should be referred to specialist services for comprehensive work-up to detect bilateral, multifocal or metastatic disease, and family counselling.