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Pheochromocytoma
- An experience from a single centre in South India

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Background

WHO (2004) define pheochromocytomas as an intra-adrenal paraganglioma, whereas closely related tumours of extra-adrenal sympathetic or parasympathetic paraganglia are classified as extra-adrenal paragangliomas. The prevalence of pheochromocytoma is 0.05% to 0.1% in patients with sustained hypertension. About 24% to 27% of patients are associated with known genetic mutations. Among the children, prevalence of mutation may be as high as 40%. Upto 20% of pheochromocytomas are extra-adrenal in nature, while 13-26% are malignant.

Study Design

Retrospective Data : 1994-2014 (21-years)

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Outpatient and inpatient hospital records, discharge summaries, operation notes, laboratory reports and follow-up records.

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203 patients with pheochromocytoma/paraganglioma

- 23 excluded– lack of complete data
- 180 patients included in the study

Patient profile: 1994-2014

	1994-2006 (n=94)	2007-2014 (n=86)
Age (yrs)	35 (11- 71)	36 (18-72)
Male – n(%)	45 (48 %)	41 (48%)
Female – n(%)	49(52%)	45 (52%)

- **Age of onset is earlier as compared to the Western literature (43.9 years)**
- **Male : female ratio = 1:1**

Presenting symptoms

SYMPTOMS	NUMBER (%)
Paroxysmal episodes	104 (58 %)
Headache	112 (62 %)
Palpitation	53 (29 %)
Sweating	36 (20 %)
Pain abdomen	72 (41%)
Weight loss	63(38%)
Abdominal mass	19 (12%)
Vomiting	23 (13%)
Seizures	22 (12%)

Presenting symptoms

- Classical triad of symptoms 22%
- Paroxysmal episodes -60%
- Hypertension -78%
- Orthostatic Hypotension – 16%
- Hypertensive crisis-5%
- Overt Diabetes Mellitus – 35%
- Prolonged QTc -38%

Incidentally detected pheochromocytoma

Incidental detection	1994-2006 (n=86)	2007-2014 (n=94)
Number of patients	22 (26%)	24 (25%)
HTN present / On antihypertensive medications	13 (54%)	12 (55%)
Normotensives/ Not on antihypertensive	11 (46%)	10 (45%)

Investigations profile: 1994 - 2014

INVESTIGATIONS	POSITIVE
Urinary metanephrines/normetanephrines	**119/136 (88%)**
Predominant metanephrines	**24%**
Predominant normetanephrines	**12%**
Urinary Vanillyl Madelic Acid (VMA)	**32 / 44 (72%)**

Predominant normetanephrine group

- Had **significantly more normotensives** than metanephrine group (42% vs 17%, p=0.001)
- Had **more extra-adrenal tumour** than the metanephrine group (59% vs 33%)

Imaging characteristics

INVESTIGATIONS	POSITIVE
CECT ABDOMEN	177/180 (98%)
MRI HEAD AND NECK (PGL)	3/180 (2%)
I-131 MIBG SCAN	120/137 (88) %

- **Central haemorrhage / necrosis are commonest radiological finding**
- **Mean largest diameter on CT : 6.4 ± 1.5 cm**
- **MIBG positive in 82% of biochemically negative tumours**
- **MIBG negative – 48% extraadrenal, 25% malignant**

Tumour Characteristics

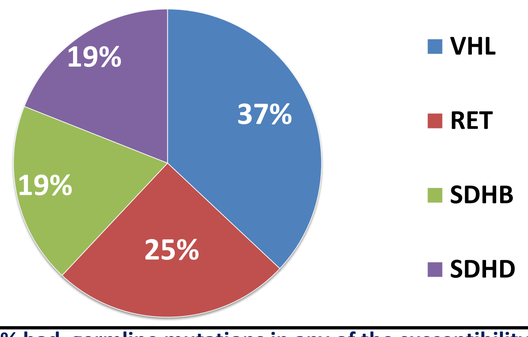
	Numbers (n=180)
Adrenal	150(85%)
Extra-adrenal (± adrenal)	**48 (27%)**
Unilateral (Right sided)	104 (58%)
Bilateral	**16 (9%)**
Bladder	5 (3 %)
Malignancy	**25(14%)**

- Adrenal tumours slightly larger than extra-adrenal (7.4 vs 6.9 cm)
- 38% of extra-adrenal had pain abdomen, 28% were normotensive
- Malignant tumours were more common in the extra-adrenal tumours (18% vs 10%)
- Malignant tumours had significantly larger mean diameter (11.4 cm)

Sites of distribution of metastasis

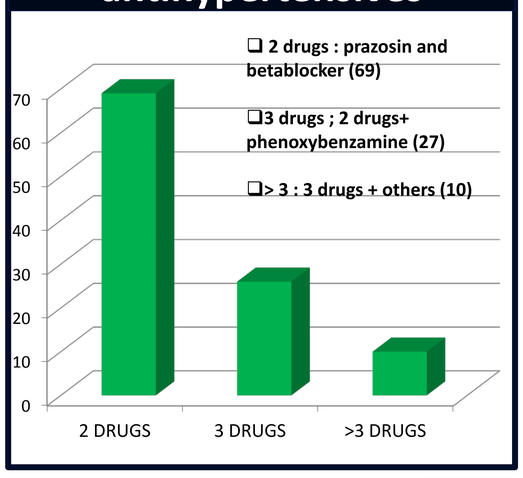
METASTASIS SITES (Malignant tumours)	DISTRIBUTION (25) N(%)
Liver	**19 (78%)**
Bone	**11 (45%)**
Pelvis	08 (33%)
Pancreas	01 (4%)
Spleen	01 (4%)
Lungs	01 (4%)

Spectrum of Genetic Mutation (N=50)



- 32% had germline mutations in any of the susceptibility genes
- VHL was more common in young age < 22 yrs & b/l tumour
- One of the malignant tumours had SDH-B positive and one had SDH-D mutation

Pre-operative antihypertensives



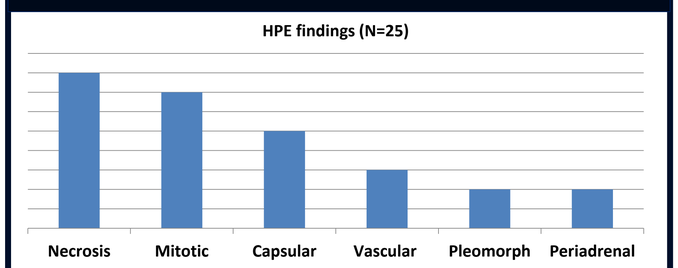
Types of Treatment received

TREATMENT MODALITY		DISTRIBUTION (180) N (%)
Surgery	Completed successfully	176 (97%)
	Recurrence Initial operation elsewhere	26 (15%) 16 (8.8%)
	Mortality	01 (0.5%)
MIBG therapy	Primary Post-surgery	01 (0.5%) 12 (7%)
Lutetium therapy	Post-surgery	01

Histopathological features

HPE	Percentage of patients
Cell nests – zellballen pattern	93 %
Focal necrosis	21%
Diffuse necrosis	10%
Capsular invasion	19%
Vascular invasion	11%
Mitotic figures	20%
Nuclear hyperchromasia	7%
Nuclear pleomorphism	5%
Periadrenal extension	8%
Chromogranin staining	94%
Synaptophysin staining	83%

Biopsy features in malignant lesion



- Tumour necrosis (88.8%), mitotic figures (77.7%) , capsular invasion (55.5%): Most common biopsy findings in > 50% malignant tumours.

Follow-up

FOLLOW-UP	FEATURES
Median Duration (months)	52 months (06- 242 months)
Persistent hypertension	51(29%)

- **50% had reduction in antihypertensives post surgery**
- **Pre-operative duration of HTN longer → persistent postoperative hypertension**

Conclusion

- The median age of presentation of Pheo/PGL at diagnosis was 36 years (range- 16-72 years).
- Pheochromocytoma was Incidentally detected in 22-24 % patients.
- Malignancy was seen in 14% and was more common with larger tumours(>10 cm), extra adrenal tumours and in patients with higher normetanephrine levels.
- VHL was the most common genetic mutation, more common younger subjects and in patients with bilateral tumors.

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