Rare Causes of Primary Adrenal Insufficiency at King Faisal Specialist Hospital - Retrospective Study

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Introduction:

- Adrenal insufficiency is a rare, but potentially fatal medical condition [1].
- In children, the cause is most commonly congenital adrenal hyperplasia (CAH) but in recent years a growing number of causative gene mutations have been identified resulting in syndromes that share primary adrenal insufficiency (PAI) characteristics.
- PAI Incidence in Europe reported 82–144/million [2].
- Higher CAH incidence has been reported in Saudi Arabia (1/7908) and 44 cases have reported for other causes [3].
- Underline causes for a lot of cases have not been identified till Whole exome sequencing have been applied.

Objectives:

- **Primary:** To Identify Causes for primary adrenal insufficiency at KFSHRC.
- **Secondary:** To Identify causative genes and common features of PAI.

Methodology:

- Study Design is retrospective cross-sectional study by reviewing Medical records.
- Inclusion criteria: All patients following with Pediatric Endocrinology clinics at KFSHRC during 2018 with PAI.
- Exclusion criteria: All cases of Congenital adrenal hyperplasia and Autoimmune Polyglandular disease were excluded.
- IRB approved the research with RAC Number: (2181 257).
- Data were collected and entered by using Excel Sheet then analyzed by SPSS.

Result and Discussion:

- The most common causes of PAI are Adrenoleukodystrophy then Familial Glucocorticoid Deficiency and Adrenal Hypoplasia which is different from Hsieh and White study [4].
- X-lined diseases account for 56% of them which explains predominance of male on the study.
- Adrenoleukodystrophy is common on our hospital due to availability of transplant and screening of other family members which is recommended [5].
- ACTH resistance and Adrenal Hypoplasia present early on life but majority present late.

Conclusion:

- Causes other than CAH should be suspected during evaluation of primary adrenal insufficiency.
- Whole exome sequencing helped in diagnosing majority of cases.
- More researches are needed to identify common genes in our society for developing Primary Adrenal Insufficiency panel.
- All male patients presenting with PAI to be screened for Adrenoleukodystrophy (VLCFFA) and Adrenal Hypoplasia (CK, Lipid, US, DAX1 gene). Also, Karyotyping is recommended for female patients.
- Consider screening all patients with PAI for proteinuria to Role out Nephrotic Syndrome type 14.

References:

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Figure 1: Causes of primary adrenal insufficiency

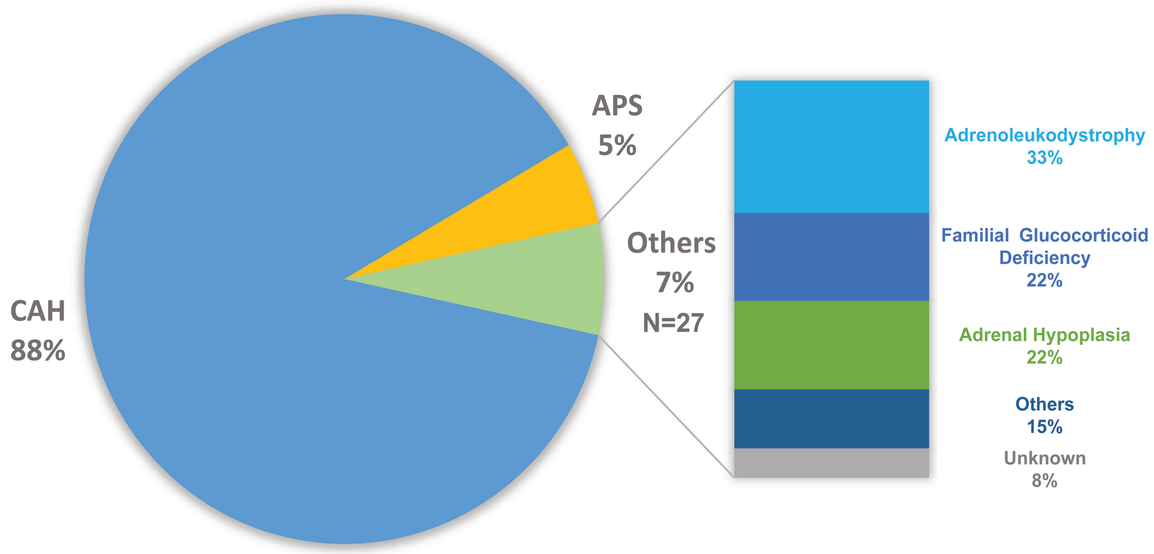


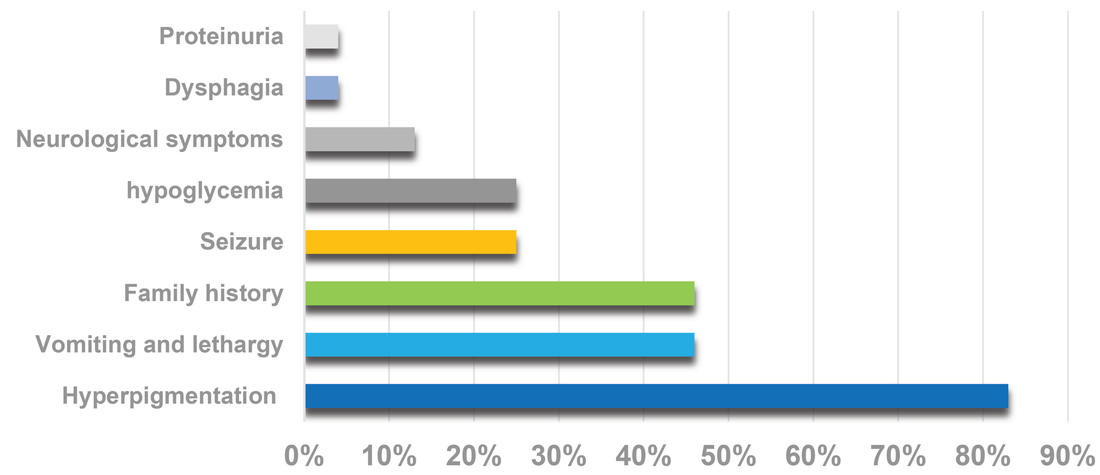
Table 1: Clinical Characteristic of PAI

Causes	Gender M	Gender F	Mean age at presentation	Electrolyte disturbance
Overall	81 %	19 %	60% > 3 Y	55 %
Adrenoleukodystrophy	100%	0	8 Y	50%
Familial Glucocorticoid Deficiency	71%	29%	NNT 6 M MC2R 1 M PDE8B 3 Y	100% None None
Adrenal Hypoplasia	100%	0	1 M	83%
Others	25%	75%	5 Y	50%
Unknown	100%	0	1 W	50%

Table 2: Molecular Genetic Defects

Phenotype	Gene	Inheritance	Percentage
Adrenoleukodystrophy	ABCD1	X-linked	43%
Pigmented Nodular Adrenocortical Disease	PDE8B	AR	14%
Glucocorticoid Deficiency 4	NNT	AR	10%
Adrenal Hypoplasia	NRB01	X-linked	9%
ACTH resistance	MC2R	AR	9%
Nephrotic Syndrome 14	SGPL1	AR	5%
IMAGe Syndrome	CDKN1C	AD	5%
Immune Dysregulation	PIK3CD	AD	5%

Figure 2: Presentation of PAI cases



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