



STUDY OF CLINICAL AND LABORATORY PROFILE OF PATIENTS WITH ADRENAL MASS.

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ABSTRACT **Aims and objectives:** AIM of this study was to observe and correlate clinical and laboratory profile of patients with adrenal mass. The objective was to study clinical and laboratory profile of patients with adrenal mass with the secondary objective to establish the etiological diagnosis with adrenal mass **Methods:** This observational study was carried out at tertiary care government hospital in north India from Jul 2020 to June 2022. Based on prevalence 4.4 of the disease as per previous study sample size for 95% confidence level & 5% precision works out 43. The inclusion Criteria were patients detected to have adrenal mass or symptoms related with adrenal mass. The exclusion criteria were any pre-existing known malignancy other than adrenal gland. Subsequent to enrolment the demographic data, clinical data, laboratory data, hormonal assays and radiological data was recorded as per predesigned proforma. The adrenal CT imaging protocol consists of three phases together are used for calculating absolute percentage washout and/or relative percentage washout to differentiate lipid-poor adenomas from primary carcinoma and metastases. **Results:** The mean age was 39± 15.41. Majority of patients were males 35(77.8%). 86.7% subjects had no comorbidity, 7.9 % had HTN. 6.7% patients were noted to have clinical cushings whereas in 4.4% subject acanthosis nigricans and goiter was seen. On Overnight dexamethasone suppression test, 16/45 patients were observed with value higher than <2.01 ug/dl, similar was the case with low dose dexamethasone suppression test. There was a significant rise in the mean plasma free metanephrine and urinary metanephrine noted in 12/ 45 patients. The minimum size of adrenal mass detected in the USG abdomen was 2.5 cm. The minimum size of adrenal mass detected in the CT abdomen was 1.21 cm. There is a significant association noted between absolute percentage washout (APW) outcome and hormonal activity with p-value <0.001. **Conclusion:** 6.7 % had features of cushing's disease and 4.4 % had acanthosis nigricans. On hormonal assays elevated metanephrine levels were seen in 26% subjects. On hormonal assays of ONDST and LDDST 35.5 % subjects were seen with elevated levels. Other hormonal assays aldosterone, renin and ACTH were normal. CECT was sensitive to identify a small adrenal mass up to 0.633 cm. 34 % of adrenal mass were hyper functional and 2 % were found malignant in this study.

KEYWORDS : ONDST, LDDST, APW, RPW, Adrenal mass, metanephrine, normetanephrine, renin

INTRODUCTION:

Early diagnosis and management of adrenal tumors has undergone a significant change with the advances in biochemical evaluation, diagnostic imaging techniques, and progress in the field of minimally invasive surgery. [1,2] Usually, the patient has no signs of hormonal excess or obvious underlying malignancy. Incidence has been increasing proportionally to the use of radiographic imaging. The differential diagnosis of adrenal mass includes adrenal adenoma, adrenal myelolipoma, adrenal cyst, adrenal lipoma, pheochromocytoma, primary or secondary adrenal malignancy, and tuberculosis. Half of adrenal mass are hyperfunctioning which require further evaluation. Cyst and different type of lipomas are characteristic lesions on CT scan [3]. It is not easy to answer a patient's questions when adrenal mass is detected. This study was attempt to workup and simplify evaluation of the mass.

AIM and objective

Aim of this study was to observe and correlate clinical and laboratory profile of patients with adrenal mass. The objective was to study clinical and laboratory profile of patients with adrenal mass with the secondary objective to establish the etiological diagnosis with adrenal mass.

Methodology

This was a cross sectional observational study conducted at tertiary care government hospital in Delhi from 01 Jul 2020 to 30 June 2022.

Based on prevalence 4.4 (per 100000 persons) of the disease as per previous studies [4, 5] and with the above assumptions the sample size for 95% confidence level & 5% precision works out 43. Patients attending medical emergency, OPD and indoor patients were screened. The inclusion Criteria was patients detected to have adrenal mass or symptoms related to adrenal mass. The exclusion criteria was any pre-existing known malignancy other than adrenal gland.

Subsequent to enrollment in this study the demographic data, clinical data, laboratory data, hormonal assays and radiological data was recorded as per predesigned proforma. The PET CT or MRI was done on case-to-case basis. The adrenal CT imaging protocol consists of a multiphase study including an unenhanced scan followed by a 1-min

delayed enhanced scan and a 15-min delayed de enhanced scan. The APW was calculated using the formula: $APW = \frac{(\text{enhanced HU}) - (15 \text{ min delayed HU})}{(15 \text{ min delayed HU})} \times 100\%$ (enhanced HU) – (unenhanced HU). An APW value of greater than 60 % was considered diagnostic of an adenoma. In the absence of an unenhanced phase, a RPW was calculated as follows: $RPW = \frac{(\text{enhanced HU}) - (15 \text{ min delayed HU})}{(15 \text{ min delayed HU})} \times 100\%$ (enhanced HU).

The descriptive analysis of quantitative parameters was expressed as means and standard deviation. The categorical data was expressed as absolute number and percentage. Independent Student t – test was used for testing of mean between independent groups. All analysis has been done using SPSS software, version 24.0.

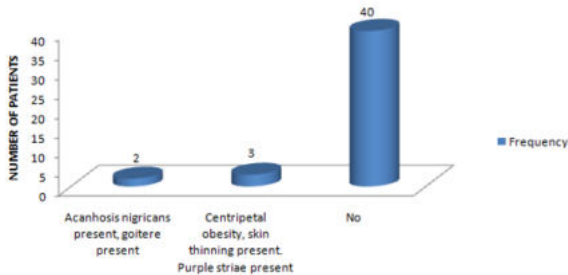
Results:

In this study 45 patients were included. The majority of patients 16 (35.6%) were in the age group between 31-40 years and the remaining 14(31.1%) were in the age group between 41-50 years. The mean age was 39 years with standard deviation 15.41. The minimum age was 23 years and maximum was 52 years. Majority of patients were males 35(77.8%). On history taking, the various comorbidities seen in this study were, 6.7% subjects had primary hypertension, 2.2% subjects each had HTN / CKDV, HTN / CKD-V, DCMP with HTN and 86.7% subjects had any comorbidity. On clinical examination, 6.6 % had features of cushing's disease and 4.4 % had acanthosis nigricans . This study found the mean height of patients included in this study was 170.87 cm with standard deviation 5.26. The minimum height was 152 cm and maximum was 179 cm. The mean weight of patients was 70.71 kg with standard deviation 6.21. The minimum weight was 55 kg and maximum was 79 kg. The details are shown in table 5, figure 4. The mean pulse rate of patients in this study was 79.71 with standard deviation 8.50. The minimum pulse rate was 62 and maximum was 95. The mean respiratory rate of patients was 16.62 with standard deviation 1.46. The minimum respiratory rate was 14 and maximum was 18. Out of the 45 patients, 3(6.7%) patients had clinical cushings where centripetal obesity, skin thinning and purple striae were present whereas in 2 (4.4%) had acanthosis nigricans and goiter was seen.

On laboratory examination, this study noted hemo-concentration in 02 patients, normal metabolic profiles, RFT, LFT and serum electrolytes.

On hormonal assays, the mean value of T3, T4 and TSH were 2.86 mIU/l, 3.75 pg/ml and 2.12 ng/dl respectively with standard deviation 1.01, 2.43 and 1.06 respectively. The minimum value of ONDST was 0.16 µg/dl and maximum was 9.16 µg/dl. The mean of Overnight dexamethasone suppression test (ONDST) was 2.48 µg/dl with standard deviation 1.56 µg/dl. The minimum value was 12.8 µg/dl and maximum was 26.06 µg/dl for low-dose dexamethasone suppression test (LDDST). The mean value was 20.41 with standard deviation 2.91. There was 16/45 patients who was observed with higher cortisol levels. The similar number of patients were also observed to have elevated cortisol levels after LDDST.

Features of Cushing Syndrome



The mean of ACTH was 27.88 pg/ml with standard deviation 7.55 pg/ml. The minimum value was 14.67 and maximum was 42.4. The mean plasma aldosterone was 11.35 ng/ml with standard deviation 60.06. The minimum plasma aldosterone was 20.5 ng/ml and maximum was 192 ng/ml. The minimum renin concentration was 4.86 and maximum was 66.86. The mean direct rennin concentration was 22.92 (ng/ml) with standard deviation 18.02.

There was a significant rise in the mean plasma free metanephrine and urinary metanephrine in 12/ 45 patients. The mean of 24-hour urine metanephrine was 268.55 ug/l for 24hrs with standard deviation 693.22. The minimum urine metanephrine was 12 ug/l for 24hrs and maximum was 2461.5 ug/l for 24hrs whereas, the mean of plasma free metanephrine was 35.05 ng/L with standard deviation 26.46 ng/L. The minimum was 2.9 and maximum was 78.8. the mean of 24-hour urine normetanephrine was 2581.58 ng/L with standard deviation 4348.61 ng/L. The minimum urine metanephrine was 40.2 ng/L and maximum was 13500 whereas, the mean of plasma free normetanephrine was 73.31 ng/L with standard deviation 73.31 ng/L. The minimum was 7.97 ng/L and maximum was 233.4 ng/L. The details of various hormonal assays noted in the cohort are placed in table 1.

Table 1: Distribution of Patients According To Hormonal Assays In The Cohort.

Hormonal Assays	N	Mean	Std.dev	Minimum	Maximum
ONDST µg/dl	45	2.48	1.56	0.16	9.16
LDDST µg/dl	45	20.41	2.91	12.8	26.06
ACTH pg/ml	45	27.88	7.55	14.67	42.4
Plasma Aldosterone Concentration ng/dl	45	115.32	60.06	20.5	192
Direct Renin Concentration ng/ml/h	45	22.92	18.02	4.86	66.86
24 Hours Urine Metanephrine ug/L for 24hrs	45	268.55	693.22	12	2461.5
24 Hours Plasma Free Metanephrine ng/L	45	35.05	26.46	2.9	78.8
24 Hours Urine Normetanephrine ng/L	45	2581.58	4348.61	40.2	13500
24 Hours Plasma Free Normetanephrine ng/L	45	72.59	73.31	7.97	233.4

On radiological examination in this study, the minimum size of adrenal mass detected in USG abdomen was 2.5 cm and maximum size was 6.3 cm with standard deviation mean is 3.81 cm. The minimum size of adrenal mass detected in CT abdomen was 1.21 cm and maximum size was 3.86 cm with standard deviation mean is 0.633 cm.

On direct correlation between radiological and pathological examination findings, there is a significant association noted between absolute percentage washout (APW) outcome and pathological result with p-value <0.001. 19 / 21 (95%) patients had test positive in adenoma whereas, 2 / 21 (8%) patients had test positive in non-

adenoma. The details are depicted in table 2.

Table 2: Comparison of Patients Between APW Outcomes and Pathological Result

APW	ADENOMA	NON ADENOMA	TOTAL
Test +ve	19 (95%)	2 (8%)	21 (46.7%)
Test -ve	1 (5%)	23 (92%)	24 (53.3%)
Total	20 (100%)	25 (100%)	45 (100%)

Chi-Square Value-33.70; P-Value<0.001; Significant

Similarly, this study noted significant association between RPW outcome and pathological result with p-value been <0.001. Majority of 18 (90%) patients had test positive in adenoma whereas 3(12%) patients had test positive in non-adenoma. The details are depicted in table 3.

Table 3: Comparison of Patients Between RPW Outcomes and Pathological Result

	ADENOMA	NON ADENOMA	TOTAL
Test +Ve	18 (90%)	3 (12%)	21 (46.7%)
Test -Ve	2 (10%)	22 (88%)	24 (53.3%)
Total	20 (100%)	25 (100%)	45 (100%)

CHI-SQUARE VALUE-27.16; P-VALUE <0.001

DISCUSSION

The adrenal gland is a common site of disease, with a prevalence of abnormality reported to be as much as 9% in autopsy series. Prevalence of adrenal abnormalities is important to understand because the adrenal gland is a common site of disorders, and the increased use of cross sectional imaging has increased the frequency of detection of adrenal lesions [4]. The total number of 45 patients was evaluated in the present study with the mean age of 39 years. The minimum age was 23 years and maximum was 52 years. J.H. Song et al. [3] in 2007 found the mean age of the patients in their study of 967 patients was 64 years. Ebbehøj A et al. [6] in 2020 found the average age more than 65 years among adults. In this study, 35 (77.8%) patients were male. The National Institute of Health Office of Rare Diseases Research reports found that adrenal mass affects women more frequently than men (female to male ratio is between 2.5 and 3 to 1). Vural V et al. (2020) [7] found female population of 71.1% were having adrenal mass. This study found 86.7% subjects did not have any comorbidity, 6.7% subjects had primary hypertension. The other comorbidities were CKD and DCMP with HTN. Similarly, Nandra et al. [8] in his study found no comorbidity in his cohort. Boland GW et al. [9] did a study Adrenal masses: characterization with delayed contrast-enhanced CT in which only 2% of subjects showed comorbidity, rest did not have any comorbidity. In this study, out of 3 / 45 patients had features of cushing syndrome in the form of centripetal obesity, skin thinning and purple striae. 2 / 45 (4.4%) patients had acanthosis nigricans and goiter. C. A. Stratakis in his study recorded similar signs like obesity, skin thinning and purple striae. Ya-ling et al. in 2019 [10] found signs of fat redistribution and protein-wasting features. The 38.4% patients in this study had primary hypertension whereas, 8.9% had Dilated cardiomyopathy. Petramala L et al. [11] concluded cardiomyopathies due to adrenal hormone excess are interesting clinical entities. Previously, a coexistent cardiomyopathy associated with mineralocorticoid, glucocorticoid, or amine excess was reported.

In this study on Overnight dexamethasone suppression test (ONDST), the mean was 2.48 nmol/l with standard deviation 1.56 nmol/l. Zaman S et al (2021) [12] noted a Transient Regression of Adrenal Lymphoma After a Single Dose of 1 mg Dexamethasone with values of cortisol of <28 nmol/L (0-50) after overnight dexamethasone suppression test with 1 mg of dexamethasone. The minimum value of ACTH was 14.67 ng/L and maximum was 42.4 ng/L in this study. Puvaneshwaringam S [13] conducted a study on ACTH following overnight dexamethasone suppression in patients with adrenal incidentalomas. He found Cortisol level after (ONDST) was ≥ 50 nmol/l in 140 out of 373 patients. In patients with cortisol (ONDST) Zaman S et al done a case report in which the finding of Adrenocorticotrophic Hormone (ACTH) was 74.8 ng/L. The minimum plasma aldosterone was 20.5 (ng/ml), maximum was 192 (ng/ml) with the mean plasma aldosterone of 11.35 (ng/ml). Ganguly A [14] has done a study on Anomalous Postural Response of Plasma Aldosterone Concentration In Patients With aldosterone-producing adrenal adenoma. He found plasma aldosterone concentration in recumbent normotensive controls on high-sodium intake was below 5 ng /100 ml, averaging less than 3 ng/100 ml. After 4 hours in the up- right posture, the average plasma aldosterone was 8.5 ng/ 100 ml. According to this study the direct renin concentration did

not fall with fall in plasma renin levels, the minimum plasma renin was 4.86 ng/ml and maximum was 66.86 ng/ml and the mean direct rennin concentration was 22.92 (ng/ml) with standard deviation 18.02 ng/ml. The mean of 24-hour urine metanephrine was 268.55 ng/l for 24 hours with standard deviation 693.22 ng/l for 24 hours. The minimum urine metanephrine was 12 and maximum was 2461.5 ng/l for 24 hours. Ahmed, AA et al. [15] in his study found borderline elevations of Urine or Plasma Metanephrine Levels, and the "Subclinical" Pheochromocytoma shows the results 10 / 45 patients (24%) had borderline elevations in urine or plasma metanephrine levels. Sawka et al. [16] found the urinary values, a sensitivity of 90% was noted, with a specificity of 98%. False negative urinary results were reported in 3 patients, two of whom had MEN2. Hickman et al. [17] assessed plasma and urine markers in 22 patients with pheochromocytoma. metanephrine was superior in this study to catecholamines, which showed plasma sensitivity of 79% (specificity 71%), compared to urinary catecholamine sensitivity of 79% (specificity of 88%). The mean Normetanephrine level in this study at 2 hours was 2581.58 ng/ml with standard deviation 4348.61 ng/ml. The minimum urine metanephrine was 40.2 ng/ml and maximum was 13500 ng/ml whereas, the mean of plasma free normetanephrine was 73.31 ng/ml. JC Carr, [18] in his study concluded plasma metanephrines with a sensitivity of 91% and specificity of 99%.

On radiographic examination in this study USG showed minimum size of adrenal mass was 2.5 and maximum was 6.3 cm. Similar findings were documented by Suzuki Y et al. [19] There is a significant association between absolute percentage washout (APW) and/or relative percentage washout (RPW) and pathological result with p-value < 0.001 in this study. Song J H. et al [3] done a study that concluded that there were 788 adenomas constituting 75% of all lesions. Michael A B et al. [20] By using an RPW of 37.5% and excluding cysts and myelolipomas, all malignant lesions were detected with a sensitivity of 100% (17 of 17 lesions) and a specificity of 95% (90 of 95 lesions).

CONCLUSIONS

In this study, out of 45 patients of adrenal mass, 6.7 % had features of cushing's disease and 4.4 % had acanthosis nigricans. On laboratory parameters none of them were found to have disturbances in RFT, LFT or in metabolic parameters. On hormonal assays elevated metanephrine levels were seen in 26% subjects. The hormonal assays of ONDST and LDDST 35.5 % subjects were seen with elevated levels of serum cortisol. The hormonal assays aldosterone, renin and ACTH were found to be normal. CECT was sensitive to identify a small adrenal mass up to 0.633 cm. 34 % of adrenal mass were hyper functional and 2% were found malignant in this study.

Recommendation of this study:

The absolute percentage washout APW outcome is a significant test in identifying hormonally active tumors when correlated with hormonal assays.

STUDY PROFORMA

Patient's details:

Date of Birth:

Age: Sex: Male/Female

Comorbidities

Diabetes/Hypertension/IHD/Others/None
Specify, other Comorbidities

Height Cm Weight Kg

Baseline Parameters

Systemic examination

CBC

LFT AND RFT

Na/K/Ca/ PO4

Hormone profile

Cortisol Basal

24 hours urinary free cortisol (If required)

ONDST (Over night dexamethasone suppression test)

Low DOSE dexamethasone suppression test

High DOSE dexamethasone suppression test (If required)

ACTH (If required)

Plasma aldosterone concentration (If required)

Plasma renin activity / Direct Renin concentration (If required)

24 hour urine metanephrine/normetanephrine test

Ultrasound abdomen

CT scan abdomen

MRI abdomen (If required)

MIBG scan (If required)

PET scan (If required)

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