Spectrum of adrenal disorders in a referral hospital of Bangladesh
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ABSTRACT

\textbf{Background:} Adrenal diseases are common and their presentations are variable. This study aimed to determine the frequency and presenting features of various adrenal diseases in a tertiary care hospital of Bangladesh.

\textbf{Methods:} This retrospective descriptive study was carried out in Endocrinology in-patient department of BIRDEM General Hospital, Dhaka, Bangladesh, from October 2017 to December 2018. During this time, total 745 patients were screened; out of whom 91 had adrenal diseases.

\textbf{Results:} Mean age of the study population was 39.6±11.5 years. Among them, 65.9\% were male. Most (75.8\%) cases had adrenal insufficiency, followed by endogenous Cushing’s syndrome (8.8\%), Conn’s syndrome (6.6\%), non-functioning adenoma (3.3\%), congenital adrenal hyperplasia (CAH) (2.2\%), pheochromocytoma (1\%), myelolipoma (1\%) and adrenal carcinoma (1\%). According to functional status, most (73.8\%) were hypofunctional. Of the patients with adrenal insufficiency, secondary adrenal insufficiency was the most common (78.3\%). Among the secondary adrenal insufficiencies, 75.9\% had iatrogenic adrenal insufficiency and 24.1\% had pituitary diseases. Regarding the cases of primary adrenal insufficiency, 20\% cases were due to adrenal tuberculosis, 6.6\% were due to adrenal histoplasmosis and 73.3\% were idiopathic. Most of the adrenal insufficiency patients presented with hypotension (66.7\%), followed by gastrointestinal symptoms (76.8\%), weight loss (55.1\%), hyponatraemia (42\%), pigmentation (13\%) and hypoglycemia (10\%). In this study, 9.9\% patients had adrenal incidentaloma. Most of them (88.9\%) were benign. Causes of Cushing’s syndrome among the study population were, iatrogenic (66.7\%), adrenal (16.7\%) and pituitary cause (16.7\%). In this study, 16.5\% patients had endocrine hypertension and the causes were endogenous Cushing’s syndrome (53.3\%), Conn’s syndrome (40\%) and pheochromocytoma (6.7\%). Of the hypertensive patients, 60\% had co-existing hypokalemia.

\textbf{Conclusion:} Adrenal insufficiency was the most common adrenal disorder followed by endogenous Cushing’s syndrome, Conn’s syndrome, non-functioning adenoma and other adrenal disorders. Presentations of adrenal disorders are variable. Among the cause of adrenal insufficiency iatrogenic adrenal insufficiency was the most common.

\textbf{Keywords:} adrenal insufficiency, adrenal disorder, Conn’s Syndrome, Cushing’s syndrome, pheochromocytoma.

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INTRODUCTION

Adrenal diseases present with a variety of medical and endocrine issues, ranging from partial or complete gland insufficiency to several kinds of adrenal hyperfunction.\textsuperscript{1} Not only it is important for the endocrinologists, but it has special importance in the surgical field also, in cases of adrenal adenoma, incidentaloma, carcinoma and metastases. Presentations of adrenal diseases are variable. Some of the diseases present with typical and dramatic features, while, many others have subtle symptoms and signs. Many cases are diagnosed incidentally on routine biochemical or radiological investigations.

Adrenal insufficiency presents in a vague, indolent manner with abdominal, flank or back pain; decreased
hematocrit or electrolyte abnormalities. Adrenal hemorrhage or infarction is increasingly identified as a cause of adrenal insufficiency.\(^2\)\(^-\)\(^5\) Among the genetic causes commonest is congenital adrenal hyperplasia which describes a group of autosomal recessive disorders characterised by enzyme defects in the steroidogenic pathways involved in the biosynthesis of cortisol, aldosterone and androgens. 21-hydroxylase (21-OH) is the most common of these enzyme deficiencies being found in up to 95% of cases.\(^7\)

On the other hand cases with excess of adrenal hormones are classically that of steroid or mineralocorticoid excess, phaeochromocytoma being rare. Signs and symptoms of Cushing’s syndrome overlap with common diseases, such as the metabolic syndrome, obesity, osteoporosis, and depression. Therefore, it can take years to finally diagnose Cushing’s syndrome, although early diagnosis is important for prevention of complications.\(^8\)\(^\)\(^-\)\(^9\) Primary hyperaldosteronism commonly results in refractory hypokalemia, which can be severe enough to cause myalgias, paralysis, or rhabdomyolysis.\(^9\) Phaeochromocytomas are catecholamine producing chromaffin cell tumours arising from the adrenal medulla,\(^10\)\(^-\)\(^11\) with an incidence of around 0.3 per 100,000.\(^12\) The treatment of choice is minimally invasive surgical resection of the affected adrenal gland, which effectively normalizes blood pressure and cures symptoms.\(^13\)\(^-\)\(^17\) Paroxysmal catecholamine release by a phaeochromocytoma can cause severe blood pressure fluctuations and headaches, but also lead to fatal cardiovascular events during hypertensive crisis leading to myocardial infarction or stroke.\(^18\)\(^,\)\(^19\)

In our country there is scanty data regarding the frequency of different adrenal diseases and their manifestations. Therefore, the purpose of this study was done to find out the frequency and presenting features of various adrenal diseases.

**METHODS**

This was a retrospective study, carried out in Endocrinology in-patient department of BIRDEM General Hospital, Dhaka, Bangladesh, from October 2017 to December 2018. Patients who were admitted with different endocrine diseases in Endocrinology Department of BIRDEM General Hospital were screened. Total 745 patients were screened, out of whom 91 had adrenal diseases. Data were retracted from previous hospital records. Diagnosis of each case was confirmed by clinical presentation, hormonal assay and other biochemical investigations and imaging as required.

**RESULTS**

Total patients were 91 with a mean age of 39.6±11.5 years. Among them, 65.93% were male. In the study population most (75.8%) cases had adrenal insufficiency, followed by endogenous Cushing’s syndrome (8.8%), Conn’s syndrome (6.6%), non-functioning adenoma (3.3%), congenital adrenal hyperplasia (CAH) (2.2%), phaeochromocytoma (1%), myelolipoma (1%) and adrenal carcinoma (1%) (Table I). According to functional status, most (75.8%) were hypofunctional, 18.7% were hyperfunctional and 5.5% were non-functional.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number</th>
<th>Percentage</th>
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<tr>
<td>Adrenal insufficiency</td>
<td>69</td>
<td>75.8</td>
</tr>
<tr>
<td>Endogenous Cushing’s syndrome</td>
<td>8</td>
<td>8.8</td>
</tr>
<tr>
<td>Conn’s syndrome</td>
<td>6</td>
<td>6.6</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Non functioning adrenal adenoma</td>
<td>3</td>
<td>3.3</td>
</tr>
<tr>
<td>CAH</td>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>Adrenal myelolipoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Adrenal carcinoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>91</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Of the patients with adrenal insufficiency, 54 (78.3%) had secondary adrenal insufficiency and rest 15 (21.7%) had primary adrenal insufficiency. Again, of the secondary adrenal insufficiencies, 41 (75.9%) had iatrogenic adrenal insufficiency and 13 (24.1%) had pituitary cause. Regarding the cases with primary adrenal insufficiency, 3 (20%) cases were due to adrenal tuberculosis, 1 (6.6%) due to adrenal histoplasmosis and 11 (73.3%) were idiopathic (Figure 1). Most (46, 66.7%) of the adrenal insufficiency patients presented with hypotension, followed by gastrointestinal symptoms (76.8%), weight loss (55.1%), hyponaeraemia (42%), pigmentation (13%) and hypoglycemia (10%) (Figure 2).
In our study, 9 (9.9%) cases of incidentaloma were found, most of them were benign (88.9%) and 11.1% were malignant. Among the incidentaloma, majority of the case were diagnosed as non-functional adenomas (55.6%). In this study, there were 24 patients with Cushing’s syndrome. Causes of Cushing’s syndrome were iatrogenic (66.7%), adrenal (16.7%) and pituitary (16.7%) (Figure 3). Fifteen patients (16.5%) had endocrine hypertension. Causes of endocrine hypertension were, endogenous Cushing’s syndrome (53.3%), Conn’s syndrome (40%) and pheochromocytoma (6.7%) (Figure 4). Of the hypertensive patients, 9 (60%) had hypokalemia.

**DISCUSSION**

In this study, among the case of adrenal insufficiency, secondary adrenal insufficiency was common and most of them were iatrogenic. These data corresponds to the findings of Chabre et al, who found that prevalence of primary adrenal insufficiency of 82-144/million, with auto-immunity being the most common cause in adults and genetic causes being the most common cause in children. Prevalence of secondary adrenal deficiency was estimated to be between 150-280/million. Corticosteroid-induced adrenal insufficiency is often cited as the most frequent cause of adrenal insufficiency, but its incidence is in reality not well known likely due to ambiguity about its definition as biological and biochemical anomalies are more or less constant during treatment with corticosteroids.

In our study, among the group of adrenal insufficiency, gastrointestinal symptoms were the most common presenting feature. Other common presenting features were hypotension and weight loss. Burke found that in adrenal insufficiency, weight loss was present in 60% cases, hypoglycemia in 30%, asthenia in 87%, hypotension in 13%, syncope in 27%, vomiting in 20%, diarrhea in 7%, hyponatremia in 27% cases.

In our study, less than ten percent cases were incidentaloma, most of them were benign. Among the incidentaloma majority of the case were diagnosed as non-functional adenomas. Chatzellis et al found that mean prevalence of adrenal incidentalomas in a total of 71,206 cases was found to be 2.3%, ranging from 1 to 8.7%. Burzon et al in a review of the literature including 3868 patients with adrenal incidentalomas from 26 non-surgical series found that 70% of cases were apparently non-functioning cortical adenoma, 5% adrenocortical carcinoma, 2% metastases, 16% hyperfunctioning tumors and 8% other lesions (i.e. myelolipomas, cysts, hemorrhage, etc.).
Exogenous steroid use was the most common cause of Cushing’s syndrome. Remaining were pituitary and adrenal origin. Sharma et al stated that administration of supraphysiologic doses of glucocorticoids is the most common cause of Cushing’s syndrome (exogenous or iatrogenic Cushing’s syndrome). Endogenous Cushing’s syndrome is rare, with an incidence of 0.7–2.4 per million population per year. A study from Denmark reported a diagnosis of Cushing’s syndrome in 166 patients over an 11-year period (1985–1995), yielding an incidence of two cases per million inhabitants per year. A similar study from Spain reported 49 cases of Cushing’s syndrome over 18 years, yielding an incidence of 2.4 cases per million inhabitants per year. In another review by Feelders et al, Cushing disease had an incidence of 1.2–2.4 per million and the prevalence of diagnosed cases were around 39 per million population.

In our study, we found that among the case of adrenal hypertension, 60% patient had hypokalemia and most of them are due to Conn’s syndrome. However spontaneous hypokalemia is not always a common presenting manifestation of Conn’s syndrome, occurring in only 9-37% of cases. In an retrospective observational study by Burrello et al, hypokalemia was present in 15.8% of 5100 patients with hypertension, whereas 76.9% were normokalemic and 7.3% hyperkalemic. The prevalence of primary aldosteronism in patients with hypokalemia was 28.1% and increased with decreasing potassium concentrations up to 88.5% of patients with spontaneous hypokalemia and potassium concentrations <2.5 mmol/L. In another study by Huang et al it was found that hypokalemia was a recognized feature of Conn’s syndrome and was seen more commonly in Asian patients and possible provocative factors were high carbohydrate intake, heavy exercise etc.

Limitation
This study was performed in a tertiary care institute, on hospitalized patients, which may not be representative of the whole population. Sample size was also small.

Conclusion
In this study adrenal insufficiency was most common adrenal disorder. Other adrenal disorders encountered in this study were Cushing’s syndrome, Conn’s syndrome, non-functioning adenoma, CAH, pheochromocytoma, myelolipoma and adrenal carcinoma. Presentations of adrenal disorders were variable.

Authors’ contribution: Each author has participate in management of the patients. The principal author has compiled all the data and performed statistical analysis for publication. All authors have read and approved the final manuscript to be submitted.

Conflicts of interest: Nothing to declare.

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REFERENCES