Original Article

Adrenal Mass in Patients who Underwent Abdominal Computed Tomography Examination

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Abstract

Background: Adrenal masses are usually discovered incidentally (IAM) during abdominal computed tomography (CT). **Aims:** We aimed to describe the prevalence, management, and outcome of incidentally discovered adrenal mass on radiological investigation. **Materials and Methods:** A retrospective analysis was conducted to look for IAM identified by abdominal CT performed for other reasons between 2004 and 2008 and were followed for 4 years. IAM patients with known malignancy or clinically evident adrenal disease or overt disease originally missed due to insufficient clinical examination were excluded. **Results:** A total of 13,115 patients underwent abdominal CT, of which 136 were identified with adrenal mass (69 males and 67 females). Overall, 84 patients had benign IAM and six had primary adrenal carcinoma (all had tumor size ≥4 cm and five were males). Hormonal evaluation was performed in 80 cases, which revealed hypersecretion in 10 cases (six had Conn's syndrome and four had pheochromocytoma). Males had higher frequency of right-sided IAMs; whereas, left-sided IAM swere more common among females ($P = 0.02$). Seven patients underwent surgery and all were males (one Conn's syndrome, one pheochromocytoma, three primary adrenal adenocarcinoma, one benign nonfunctional adenoma, and one metastatic tumor). Only one patient died due to brain metastasis. **Conclusion:** The overall prevalence of adrenal incidentaloma is 1% in Qatar. Unfortunately, hormonal evaluation, surgical referral, and follow-up are not appropriate in this study. Moreover, screening of IAM warrants more attention to rule out malignancy. This work could be of value as a local auditing for the current management.

Keywords: Adrenal mass, Computed tomography, Incidentaloma, Malignancy

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Introduction

Adrenal masses are usually discovered incidentally (IAMs) during abdominal computed tomography (CT) performed for other indications. The reported incidence of IAM varies from 0.8 to 5% among general population during thoracic and abdominal CT.[1,2] According to prior IAM studies; abdominal pain, hypertension, and other nonspecific symptoms are the primary indications for abdominal CT.[3,4] In addition, IAMs are often detected during imaging of patients with other types of cancer or some inherited diseases.[5] The detection rate of adenomatous adrenal lesions by CT examination shows an association with advanced age; as young patients (20-29 years) have relatively lower (0.2%) rates as compared to elderly (7-10%) patients.[6,7] This higher rate of IAM in elderly could be explained in part by the fact that advanced age had higher comorbidities as well as more susceptibility for the development of adrenal mass. Libe and Bertherat[8] reported 6% prevalence of adrenal adenoma in elderly and the majority (80%) of these cases had nonfunctioning lesions. Though, adrenal gland is a common site for metastatic disease; only 26-36% of

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adrenal masses have tendency for metastasis.[9] Among adenomatous adrenal lesions, the majority (94%) have nonfunctioning cortical adenomas.[10] Furthermore, tumor size of >4 cm has been considered as an independent predictor of malignancy.[10] Frilling *et al*.,[11] reported a higher incidence of adrenal metastasis (71%) in patients with progressively increasing adrenal masses size (>4 cm) on follow-up.

The extensive use of CT and magnetic resonance imaging (MRI) has increased the incidental detection of adrenal masses and could also potentially differentiate benign and malignant adrenal lesions in noninvasive fashion.[10,12,13] Therefore, the detection and characterization of IAM by radiological workup is crucial for the risk assessment of metastasis in patients with no obvious indication of cancer. Moreover, Kandathil *et al*.,[14] reviewed the implications of positron emission tomography (PET) and CT using different radio compounds to differentiate benign and malignant IAM. The authors addressed the utility of PET/CT in difficult adrenal mass cases, otherwise, in most cases, CT and/or MRI would be enough for diagnosis. Herein, we reviewed and described the frequency, clinical presentation, and outcome of adrenal masses detected incidentally during abdominal CT for various indications in a small developing country in the Middle East.

Materials and Methods

It is a retrospective review of all patients who were screened by abdominal CT for various reasons at the Radiology Department, Hamad General Hospital (HGH) in Qatar, between March 2004 and March 2008. We included all adult patients referred from the Accident and Emergency Department or outpatient clinics to undergo abdominal CT examination for any indication. During the study period, HGH was the only tertiary care hospital in Qatar that deals with abdominal masses, so our cases are representative of the national population. IAM patients with known malignancy or clinically evident adrenal disease or overt disease originally missed due to insufficient clinical examination were excluded.[15] The diagnosis of IAM was based on abdominal CT findings and the identified IAMs were further evaluated for functional evaluation (hormonal assay) and the availability of histopathological findings.

The radiological criteria to distinguish benign and malignant adrenal masses includes mass size, CT attenuation value on an unenhanced CT, and the pattern of enhancement and de-enhancement (washouts).[16]

Patients diagnosed for IAM with hypersecretion were radiologically followed-up for 4 years to observe any change in the mass size and outcomes. The radiological and clinical follow-up has been obtained from patients medical records.

IAM was defined as the "incidental adrenal mass" of >1 cm, which is discovered during radiological examination for reasons other than to investigate for primary adrenal disease.[17] The diagnosis of primary adrenal carcinoma was confirmed by histological findings, if indicated. Ethical approval was obtained from the Medical Research Center (IRB# 12112/12) and waiver consent was approved at Hamad Medical Corporation, Qatar.

Statistical analysis

Patient characteristics are presented as percentages, mean ± standard deviation, and median and range, when applicable. Patients were categorized into three groups according to their age:

a. 18-44 years;
b. 45-59 years; and
c. ≥60 years.

In another analysis, IAM swere divided according to lesion size (≤4 and >4 cm). We also looked for the pattern of IAM in males and females. Comparison between respective groups was performed using Student's *t*-test for continuous variables and Pearson chi-square test for categorical variables. A significant difference was considered when the two-tailed *P*-value was less than 0.05. Data analysis was carried out using the Statistical Package for Social Sciences version 18 (SPSS Inc, Illinois).

Results

During the study period, a total of 13,115 patients were screened by abdominal CT for various reasons, of which 136 (69 males and 67 females) were found to have IAM. The mean age of patients was 57.2 ± 12.9 years and 62% were non-nationals, as expatriates represent around 80% of total population in Qatar [Table 1]. The main reasons for abdominal CT evaluation were abdominal pain (58%), road traffic accidents (25%), malignancy (11%), and stones (3%). The majority of cases (91%) were identified with unilateral IAM (62 left-sided and62 right-sided); whereas, only 9% cases had bilateral mass. Hormonal evaluation was recorded in80 cases; of which the majority (70 cases) revealed nonsecreting IAM and only 10 cases had hypersecreting IAM (six diagnosed with Conn's syndrome and four had pheochromocytoma) [Figure 1]. No surgical interventions or surgical referrals were reported in patients with hypersecreting adenomas.

At baseline, the median size of IAM was 2 cm (range: 1-12) and the follow-up that was available for half of the patients showed an increase in the mass size of 1.35 cm

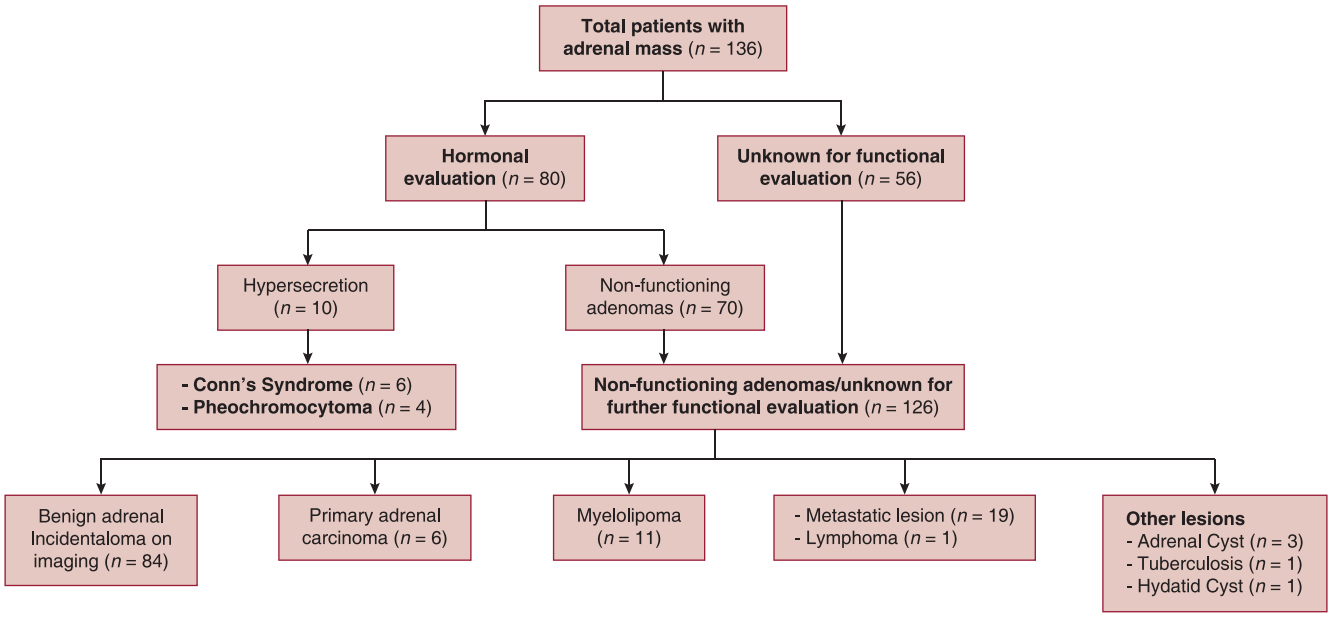

Figure 1: Study design

Table 1: Overall demographics and presentation; *n* = 136 (%)

Age (mean ± SD)	**57.2 ± 12.9**
Males	69 (50.7)
Nationals	52 (38.2)
Adrenal mass size (baseline) cm	2 (1-12)
Change in adrenal mass size (cm),*n = 22	1.35 (1-6)
Tumor size (>4 cm)	17 (13.1)
UnilateralIAM	124 (91.2)
Right	62 (45.6)
left	62 (45.6)
Bilateral IAM	12 (8.8)
Renal impairment/failure	17 (12.5)
Surgery	7 (5.1)
Malignancy	26 (19.0)
Functional IAM (hypersecretion)	10 (7.4)

*Median, range. IAM = Incidental adrenal mass, SD = standard deviation

(1-6). The frequency of IAM was found to increase with age [Figure 2]. However, a reverse trend was observed for the tumor size. Younger individuals (18-44 years) had significantly higher frequency of larger tumors (>4 cm) than the elderly patients (32 vs 7%; *P* = 0.02).

A total of 126 cases were identified to have either nonfunctioning adenomas (*n* = 70) or unknown for further functional evaluation (*n* = 56). Among these patients, 84 (61.8%)were found to have benign IAM and six (4.4%) patients had primary adrenal carcinoma (five diagnosed histologically by fine-needle aspiration (FNA)/biopsy and one by CT/MRI). Three of the carcinoma patients underwent surgery; one had brain metastasis and died without surgical intervention and two were lost to follow-up. In addition, 11 cases had myelolipoma, 19 had metastatic lesions (bronchogenic=10, breast cancer=3, ovarian cancer =2, hepatocellular carcinoma = 2, colonic cancer = 1, and cryptogenic = 1), one had lymphoma, and five had other lesions (adrenal cyst/tuberculosis/hydatid cyst) [Figure 1].

Two cases had history of surgical intervention (one for Conn's syndrome and other for pheochromocytoma) before the start of the study and found at the index study to have IAM on the other side. Three patients had surgery for primary adrenal adenocarcinoma; one for benign adenoma (nonfunctional) and one for mass histology to confirm metastatic tumor of bronchogenic cancer. The size of these three operated metastasis cases was ≥4 cm, when discovered. Postsurgical mortality was not reported in our study. Moreover, only one patient who had brain metastasis died without any surgical intervention.

Table 2 summarizes demographics and presentation according to gender in IAM patients. The majority of females with IAM were nationals (Qataris) as compared to males (53.7 vs 23.2%; *P* = 0.001). The frequency of right-sided IAM was higher in males (49.3 vs 41.8; *P* = 0.02); whereas, females were identified more with left-sided IAM (55.2 vs 36.2%; *P* = 0.02). In our series, seven patients underwent surgery and all of them were males. Moreover, five of the six primary adrenal carcinoma cases were also males and all had tumor size ≥4 except one case.

Discussion

This is a unique study from our region that describes the frequency, clinical presentation, and outcome of patients

with IAM discovered on abdominal CT examination performed for other indications. Cross-sectional imaging based on CT substantially increases the rate of adrenal incidentalomas.[3] In our series, the frequency of IAM reaches 1%.

Table 3 summarizes the characteristics of IAM cases from earlier studies.[18-25] The incidence of IAM varies according to the source of information. The autopsy-based studies reported a higher frequency of IAM (9%) as compared to investigations based on routine CT (0.8-5%).[2,6]

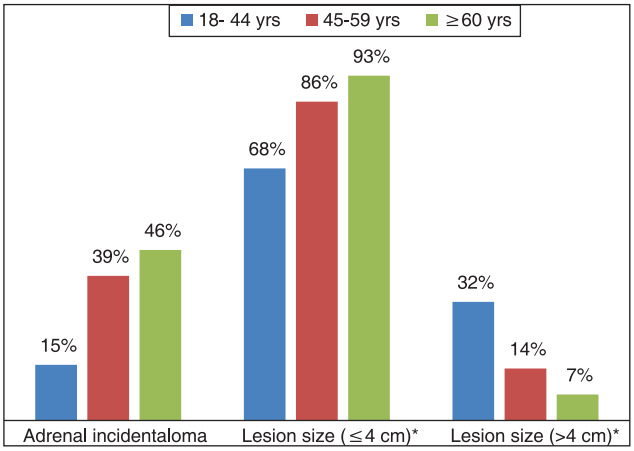

Figure 2: Frequency and size of lesions by different age groups (*$P = 0.02$)

Table 2: Demographics and presentation according to gender

Variable	Females $N = 67$ (%)	Males $N = 69$ (%)	*P*-value
Age	56.3 ± 14.1	58 ± 11.8	0.43
Nationals	36 (53.7)	16 (23.2)	0.001
Change in mass size (cm)	1.6 ± 1.2	2.2 ± 1.8	0.40
Size (>4 cm)	5 (8)	12 (18)	0.09
Unilateral IAM	65 (97.0)	61(88.4)	0.05
Right IAM	28 (41.8)	34 (49.3)	0.02
Left IAM	37 (55.2)	25 (36.2)	
Bilateral IAM	3 (4.5)	9 (13)	0.08
Surgery	0 (0)	7 (10.1)	0.007
Functional IAM (hypersecretion)	5 (7.5)	5 (7.2)	0.61

IAM = Incidental adrenal mass

Earlier investigators reported a variation in the prevalence of IAM based on age, gender, and location. Notably, the prevalence of IAM has been found to increase with age and be higher among elderly (7-10%) as compared to young patients (<1%).[6,7,15,16] In our series, the mean age was 57 years and a trend of higher frequency of IAM has been observed with advanced age (≥60 years). Grumbach *et al.*,[26] found no gender preference for adrenal incidentalomas which is in agreement with our findings. In contrast, other reports observed relatively higher prevalence of IAM among females.[20,24,25,27,28] These studies suggested that gender disparity could be partly explained by higher frequency of abdominal diagnostic procedures performed in females as compared to males. Other studies have also investigated the diagnoses of the IAM based on tumor size, malignant tendency, and age. Comlekci *et al.*,[24] reported an association of malignant incidentaloma with advanced age. Similarly, Tsvetov *et al.*,[21] observed a higher mean age in incidentaloma patients with extra-adrenal malignancy. Bülow *et al.*,[20] reported an association between risk of malignancy and elderly males. In addition, increased tumor size has been found to be an independent predictor of malignancy. In our study, a similar trend has been observed as majority of the primary adrenal carcinoma cases were males of age above 40 years and had tumor size greater than 4 cm.

Moreover, some investigators identified site-specific appearances of IAM using different diagnostic modalities. Cho *et al.*,[29] reported higher frequency of left-sided IAM (56%) on CT. While, studies based on ultrasonography[30-32] observed predominance of right-sided IAM, which might be attributed to greater visualization of the right-sided adrenal gland than the left side. However, other studies based on CT did not observe such trend.[27,33] Consistent with these reports, the detection rate of left-and right-sided IAM in our subjects was comparable.

Table 3: Review of adrenal incidentaloma cases

Authors	No. of cases	Malignancy	Hyperfunction	Follow-up (median; years)
Emral *et al.*[18]	70	0/60	0/60	2
Bernini *et al.*[19]	115	0/115	NC	4
Bülow*et al.*[20]	229	0/229	4/229	2.1
Tsvetov *et al.*[21]	100	1/88	0/88	2
Fagour *et al.*[22]	51	0/51	3/27	4.3
Vassilatou *et al.*[23]	77	0/77	NC	5.2
Comlekci *et al.*[24]	376	0/162	6/162	2
Giordano *et al.*[25]	118	0/118	0/102	3
Present study	136	26/136	10/80	4

Earlier studies have observed relatively higher rate of bilateral lesions (15-25%) using CT.[19,27] It has been suggested that bilateral tumors are often presented with metastatic disease, congenital adrenal hyperplasia, bilateral cortical adenomas, and infiltrative disease of the adrenal glands.[6] In our series, 8.8% of cases had bilateral masses, of which one-third was associated with metastatic lesions.

Figure 3 shows a proposed algorithm for the evaluation and follow-up of IAM based on the current consensus in literature.[15,34]. For the appropriate management of IAM, it is important to differentiate benign versus malignant and nonfunctional versus hyper secreting masses using clinical, radiological, and hormonal evaluation.

The major indications for surgery include lesion size >4 cm, adrenal hyperfunction, and IAM exhibiting suspicion of malignancy or pheochromocytoma on imaging. Laparoscopic adrenalectomy is preferred in patients who require surgical resection; whereas, open adrenalectomy is indicated in patients with large, malignant tumors.[35] Moreover, surveillance is recommended for nonfunctioning adenomas with mass size < 4 cm.[15] In our series, the mean size of IAM on initial diagnosis was 2.6 ± 1.9 cm, which is consistent with other studies that reported an average mass size of 2.5 cm at presentation.[19-21,23,24] In fact, the criterion for surgical removal varies from 3.5 to 6 cm. Adrenal masses greater than 5-6 cm in diameter are usually suspected for adrenocortical carcinoma[36] and most cases

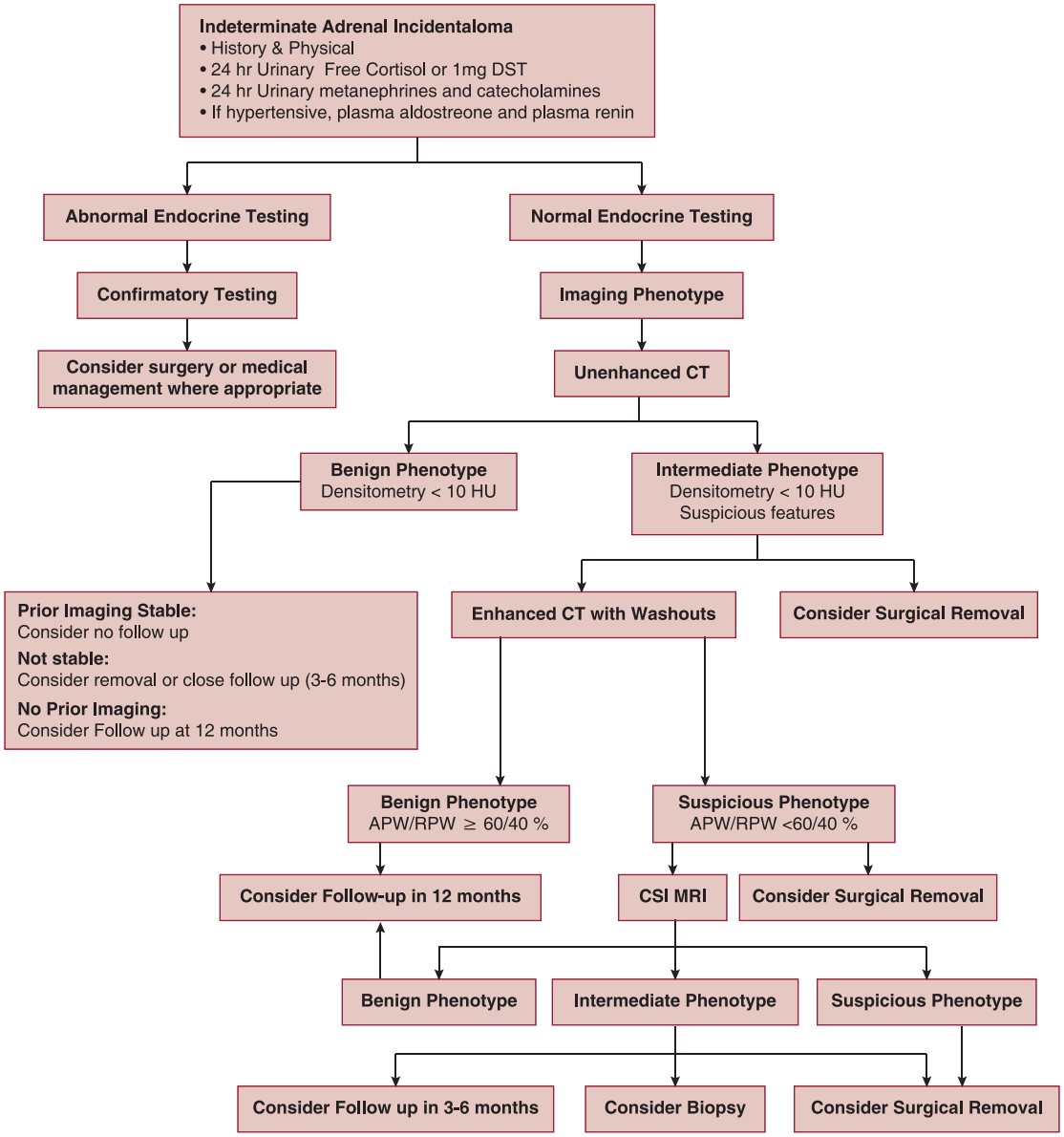

Figure 3: Algorithm for evaluation and follow-up of adrenal incidentalomas. APW = Absolute percent washout, RPW = relative percent washout, DST = Dexamethasone suppression test, CT = Computed tomography, CSI = Chemical shift magnetic resonance imaging, MRI = Magnetic resonance imaging. (Modified from Reference 15 with permission)

with mass size >4 cm requires surgical intervention.[15] It has been suggested that tumors <3 cm are mostly benign in nature and such patients require clinical and radiological follow-up.

In our series, the radiological follow-up revealed an increase in mass size in 16.2% cases which is in agreement with previous studies which reported change in mass size on prospective evaluation. A large review of 21 studies observed an increase in mass size among 12.5% of cases and identified very low risk of developing malignancy, subclinical hyperfunction, or overt disease on follow-up.[15] However, some investigators suggested a correlation between tumor size (>3 cm) at diagnosis, hormonal hyperfunction, and tumor growth.[31,37] Bernini *et al*.,[19] reportedthat the cumulative risk for increase in lesion size and development of endocrine abnormalities could be progressive for up to 80 months. The mass enlargement does not necessarily indicate malignant transformation that can be developed anytime. Therefore, the overall risk of progression should not be overlooked and patients with apparent benign masses need to be under radiological surveillance.

Sixty-two percent of our cases had benign IAM and only 4.4% cases had primary adrenal carcinoma, which is consistent with many previous reports. An earlier study observed a higher frequency (86%) of benign IAM and a lower rate (1.1%) of primary adrenocortical malignancy.[24] Although, most studies reported lower rate of malignancy, a study from Taiwan reported exceptionally higher rate of malignancy (47.6%) in incidentaloma cases.[33]

In our series, hormonal evaluation was performed in 80 cases; of which the majority was nonsecreting incidentaloma. Our findings are corroborated with an earlier study showing higher frequency of nonfunctioning adrenal (73.5%).[24] The functional IAM primarily includes pheochromocytoma (4-5%), Cushing's disease (5.3%), Conn's syndrome (1-3%), testosterone secreting lesions (<0.1%), estrogen secreting lesions (<1%), and adrenocortical carcinoma (4-5%).[15] Consistently, in our series, Conn's syndrome was observed in 3.7% cases, while 2.9% had pheochromocytoma. However, some studies reported relatively lower incidence of pheochromocytoma (0.3%)[3] and others identified a higher frequency of pheochromocytomas (20%).[33,38]

Fine-needle aspiration cytology (FNAC) is an invasive procedure which is indicated only in patients with potential metastases or infectious processes.[39] In our series, five patients were identified and confirmed for primary adrenal carcinoma by FNAC and one was diagnosed by CT. A recent study by Birsen *et al*.,[1] concluded that using the hormonal activity followed by a risk stratification algorithm based on tumor size and HU density will spare unnecessary diagnostic surgery for IAM.

Surgical removal of tumors is the only curative approach for malignant tumors regardless of the hormone status and functional adrenal tumors (with or without symptoms).[33] Some patients with IAM might develop postsurgical complications such as adrenal insufficiency, which is an indication for steroid substitutive therapy.[18] Wang *et al*.,[33] reported postoperative adrenal insufficiency in 18% cases, and the overall mortality was reported to be 0.4%. In our study, seven patients underwent surgery, but unfortunately the information regarding post surgical complications and mortality were not available.

The retrospective design is one of the limitations of the present study. However, there are no prospective controlled studies in the literature so far.[1] Information regarding hormonal evaluation was available for 80 cases and so functional status of adrenal masses remained underestimated in our series. Also, radiological follow-up based on CT evaluation was available only for 72 cases. We lack information on postsurgical complications and mortality and whether there is any potential association of IAM with hereditary syndromes. As there are no data on CT accuracy in characterizing adrenal masses <1 cm, the current analysis does not report it. Previous reports claimed that masses <1 cm do not require imaging workup because most are believed to beadenomas.[40] We do not have enough sample size to adopt robust comparison between males and females; however, our findings couldset platformfor further studies.

Furthermore, we could not get reasonable explanation for the lack of surgical referral of patients with positive hormonal status. This could reflect inappropriate management due to lack of hospital guidelines and awareness of this entity. Lastly, our study will be the basis to set up hospital guidelines for initial and follow-up workup for IAM cases for the appropriate diagnosis and management in our hospital.

In conclusion, the overall prevalence of IAM is 1% in Qatar. The most frequently observed lesions in our series are benign IAM, myelolipoma, and primary adrenal carcinoma. Our study demonstrates malignancy (primary adrenal carcinoma) in 4.4% IAM cases. Hormonal evaluation, surgical referral, and follow-up were not appropriate in this study. The hormone levels and metabolic workup should be done in all patients with adrenal masses. The screening of IAM warrants more attention to rule out malignancy. This work could be of value as a local auditing for the current management.

Acknowledgment

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