

**Macroscopic and Microscopic examination of adrenal gland in medico legal autopsies****Kuntal Roy<sup>1</sup>, Sujoy Kumar De<sup>2</sup>, Soumi Pradhan<sup>3\*</sup>, Tushar Kanti Das<sup>4</sup>, Somnath Das<sup>5</sup>**<sup>1</sup>*Junior Consultant Pathologist, Calcutta Medical Research Institute 7/2 Diamond Harbour Road Kolkata 700027, West Bengal, India*<sup>2</sup>*Medical Officer, Uluberia SDH and SSH, Station Road, Uluberia 711315, West Bengal, India*<sup>3</sup>*Junior Consultant, AMRI Hospitals - Mukundapur, 230 Barakhola Lane Purba Jadavpur, Mukundapur, Kolkata 700099, West Bengal, India*<sup>4</sup>*Professor and Head, Department of Forensic Medicine and Toxicology, R G Kar Medical College & Hospital, Khudiram Bose Sarani, Kolkata, West Bengal 700004, India*<sup>5</sup>*Associate Professor, Department of Forensic Medicine and Toxicology, R G Kar Medical College & Hospital, Khudiram Bose Sarani, Kolkata, West Bengal 700004, India***Received: 29-09-2020 / Revised: 16-10-2020 / Accepted: 30-10-2020****Abstract**

**Background:** Medico legal autopsy are performed to identify the cause of death, time of death, determine or confirm medical diagnosis that remained unknown or unclear prior to the patient's death. Various histopathological finding not related to the cause of death are observed in the routine histopathological examination of medico legal autopsies. These findings are important learning tools for the pathologist and forensic expert and have immense academic and research value. **Materials & Methods:** The adrenals were examined meticulously after removal from the deceased at autopsy to find out any gross abnormalities and the findings were noted in the case record forms. On the day of removal of organ; weight and measurement of the specimen were noted, the adrenals were cut, and carefully opened. Photographs of the specimen were taken accordingly. The specimen was then placed in 10% buffered formalin saline for fixation. After overnight fixation the specimen were examined and parameters noted. Total bilateral adrenalectomy was done. **Results:** Around 38.7% of autopsy cases were seen to have adrenal lesions. In present study the most common age group was seen to be 31-40 yrs with male(71%) being more than females(29%). Among the adrenal lesions, we found 22.64% cases of adrenal cortical nodule, 16.03% cases of adrenal lymphocyte infiltration, 3.77% cases of adrenal haemorrhage, 1.88% cases of adrenal cortical adenoma and 0.94% cases adrenal myelolipoma. In the present study, incidentally detected adrenal mass found in 2.8% of cases, comprising of adrenal cortical adenoma and myelolipoma, in the age group of above 60 yrs gave some guideline that it is found in aged group and the sex distribution in male and female was 2:1. This study shows that prevalence of adrenal cortical nodule is 22.64%. Prevalence increases with increase of age. So this is an ageing process and number of nodule increase with ageing. In most of the cases multiple nodules were found and at the same time they were mostly bilateral. The present study shows percent of cases of adrenal lymphocyte infiltrate increases with increase of age. It is also an ageing process. Most of the cases were present above 70yr. **Conclusion:** The compilation of these data from autopsies with major unexpected findings that would have contributed to death emphasizes the importance of incorporating autopsy information into institutional quality care and improvement programmes.

**Keywords:** Medico legal autopsy, adrenal gland, incidental findings, histopathology

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**Introduction**

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Autopsies are important in clinical medicine as they can identify medical error and assist continuous improvement. Clinical or Pathological autopsies are performed to diagnose a particular disease or for research purposes [1]. They aim to determine, clarify, or confirm medical diagnoses that remained unknown or unclear prior to the patient's death. They help us to gain more insight into pathological processes that contributed to a patient's death. Autopsies are also performed to ensure the standard of care at hospitals and thus help us to answer how patient deaths can be prevented in the future [2]. Autopsies are also carried out for determination of manner of death, evaluation of ante-mortem and post-mortem diagnosis, epidemiological purposes, survey outbreaks, medical audit, and teaching, forensic purposes and to enlighten/reassure families or inform them of hereditary disease [3]. Diseases of the adrenal gland are responsible for great deal of mortality and morbidity. A large number of people are affected every year by adrenal disease. Early diagnosis of some adrenal disease allows the clinicians to treat the patient at an early stage and help to reduce sufferings of the patient [4]. But each and every pathological lesion does not necessarily manifest overt clinical features and the patients with minor pathological lesions do not seek medical advice. Some of this pathological lesion can be identified only incidentally at autopsy [5]. Asymptomatic adrenal pathology may be overlooked in routine autopsy examination unless the clinico-pathological correlation is urgently needed (pathological autopsy). This research has further included the possible role of adrenal in a death due to apparently unknown etiology. A few studies have been done in India and abroad in the field of adrenal autopsy and hardly any recent work can be found out through thorough search. Actual weight, volume, gross and microscopical findings of adrenal gland can be studied more accurately by medicolegal autopsy method which cannot be done so accurately by imaging method [2, 6]. It is well known that the formulation of health care planning is very much dependent on incidence, prevalence, frequency and distribution of a particular disease. But data of those parameters regarding adrenal diseases in Indian subcontinent are not adequate. There is tremendous wealth of natural pathology to be learnt from medicolegal autopsy. The medico legal autopsy has been studied to find out the occurrence of adrenal lesions like, normal age related change in the adrenal gland, cystic lesion, benign and malignant tumor of adrenal gland etc. In this era of dwindling pathological autopsy, the medico-legal autopsy will be a supplement to record the occurrence of adrenal disease in the study

population. As studies on adrenal lesions in autopsy cases are limited this very study was taken to find out the occurrence of various pathological lesions of adrenal.

### Materials & methods

Current observational, descriptive, cross sectional study was conducted in Department of Pathology, R. G. Kar Medical College and Hospital, Kolkata (a tertiary care hospital in eastern India, Department of Forensic Medicine and Toxicology, R.G. Kar Medical College and Hospital, Kolkata and the police morgue attached to R. G. Kar Medical College and Hospital, Kolkata, India. It was done for 12 month (1st April 2013 to 31st March 2014) on sample 106. Cases were selected by random sampling method, taking all cadavers meeting the inclusion and exclusion criteria on the particular days in which autopsies were conducted. After approval from institutional ethical committee and informed written consent from the relatives of the deceased, the study was initiated. The medico-legal autopsies performed at the Police Morgue attached to R.G. Kar Medical College & Hospital was attended; detailed history was obtained from the investigating officer and/or relatives of the deceased. Meticulous autopsy was conducted with special reference to the gross findings in the adrenal of both sides. All the important findings were noted down in the predesigned case record form and later included in the master chart. At the time of autopsy the specimens of adrenal were examined thoroughly to find out any pathological lesion grossly. The gross description like, size, weight, surface, dimension, cut surface etc. were noted. Photographs of the specimens were taken. After gross examination sections from the apparently abnormal site were taken. These sections were prepared for microscopic examination through multi-step process. The slides thus prepared were examined to detect the pathological lesions. After examination the results were analyzed accordingly. The adrenals were examined meticulously after removal from the deceased at autopsy to find out any gross abnormalities and the findings were noted in the case record forms. On the day of removal of organ; weight and measurement of the specimen were noted, the adrenals were cut, and carefully opened. Photographs of the specimen were taken accordingly. The specimen was then placed in 10% buffered formalin saline for fixation. After overnight fixation the specimen were examined and parameters noted. Total bilateral adrenalectomy was done. All data were collected, compiled and subjected to suitable statistical analysis

(Independent sample test). Statistical analysis was done using “SPSS version 20 software”. If the null-hypothesis is rejected ( $P < 0.05$ ), then the conclusion is that there is a statistically significant difference between at least two of the subgroups.

### Results

This present study shows 71% were male and 29% were female out of 106 cases. (Table 1). This study deals with incidental findings of lesions of adrenal

glands in victims whose autopsies were done at police morgue of R G Kar Medical College & Hospital. Detail history about the mode of death was obtained from diseased relatives, BHT, post mortem form and police inquest form. After getting permission from institutional ethical committee the study was conducted and adrenal tissue was obtained and processed as described earlier and screened for various lesions of adrenal gland.

**Table 1: Distribution of cases according to sex (n=106)**

Sex	Number of Case	Percentage(%)
Male	75	70.75
Female	31	29.24

**Table 2: Distribution of cases according to histopathological change (N=106)**

Histopathologic Change	Number of Case	Percentage (%)
Normal	65	61.3
With change	41	38.7
Total	106	100

In this present study out of 106 cases, we found 38.7% of cases with histopathological change and 61.3% of normal cases (Table 2).

**Table 3: Average age of study subject normal or with adrenal change**

Age	Group	Number	Mean	Std. Deviation	Std. Error of Mean
	1.Normal	65	31.92	11.730	1.455
2.With Change	41	57.32	15.842	2.474	

Here in 65 normal cases the mean age was  $31.92 \pm 11.730$  and in 41 cases with histopathological change the mean age was  $57.32 \pm 15.842$ . The mean between normal and with change cases show statistically significant difference (Table 3).

**Table 4: Distribution of cases according to spectrum of histopathological change**

Histopathological Change	Number of Case	Percentage (%)
Adrenal cortical nodule	24	22.64
Lymphocyte infiltration	17	16.03
Adrenal haemorrhage	4	3.77
Adreno cortical adenoma	2	1.88
Myelolipoma	1	0.94

In this present study, we found 24 (22.64%) cases of adrenal cortical nodule, 17 (16.03%) cases of lymphocyte infiltration, 4 (3.77%) cases of haemorrhage, 2 (1.88%) cases of cortical adenoma and 01 (0.94%) cases myelolipoma (Table 4).

**Table 5: Mean age of different adrenal lesions**

Histopathological Changes	Min Age	Max Age	Mean Age	Standard Deviation
Normal (n=65)	10	57	31.92	11.73
Cortical Nodule (n=24)	40	96	61.87	14.69
Lymphocyte infiltration (n=17)	34	85	61.35	17.25
Haemorrhage (n=4)	35	45	36.25	6.29
Adrenocortical Adenoma (n=2)	68	72	70	2.82
Myelolipoma (n=1)	--	--	62	--

In this study, the mean age of adrenocortical nodule was 61.87 yrs with standard deviation of 14.69. In case of Lymphocyte infiltrate in adrenal gland, the mean age was 61.35yrs with standard deviation of 17.25. Adrenal haemorrhage shows mean age was 36.25 yrs with

standard deviation of 6.25. In case of adrenocortical adenoma the mean age and standard deviation were respectively 70 yrs and 2.82. Adrenal myelolipoma was showing mean age of 62 yrs (Table 5).

**Table 6: Prevalence of incidentally detected Adrenal Mass (n=3)**

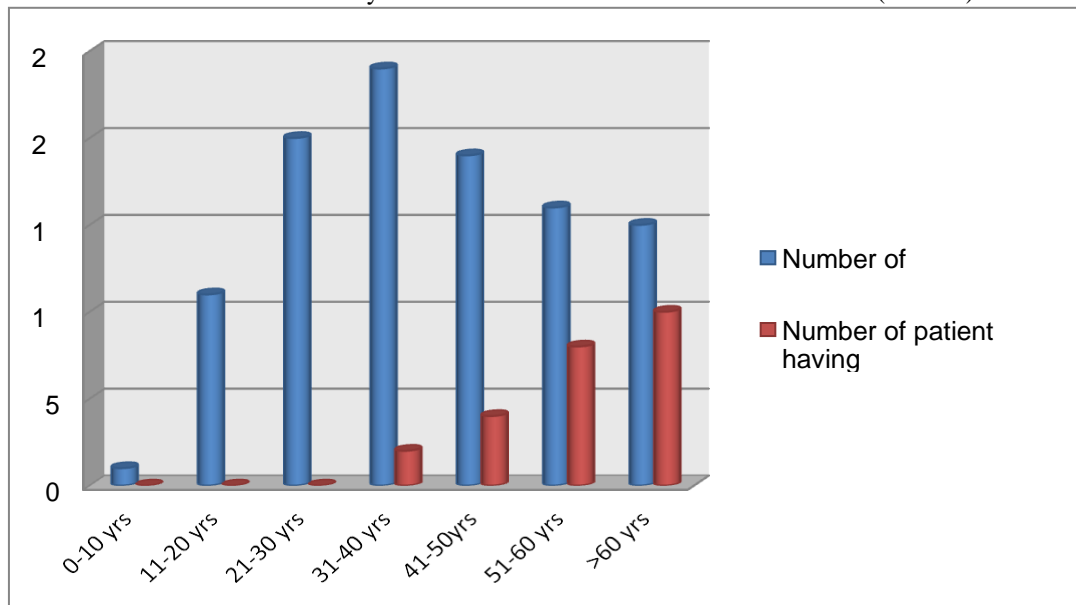
Total Number of Cases	Incidentally Detected Adrenal Mass	Percentage (%)
106	3	2.8%

Incidentally detected adrenal mass has been found in 2.8% of cases in the present study (Table 6).

**Table 7: Distribution of cases of incidentally detected adrenal mass according to sex (n=3)**

Sex	Number of cases	Percentage (%)
Male	2	66.67
Female	1	33.33

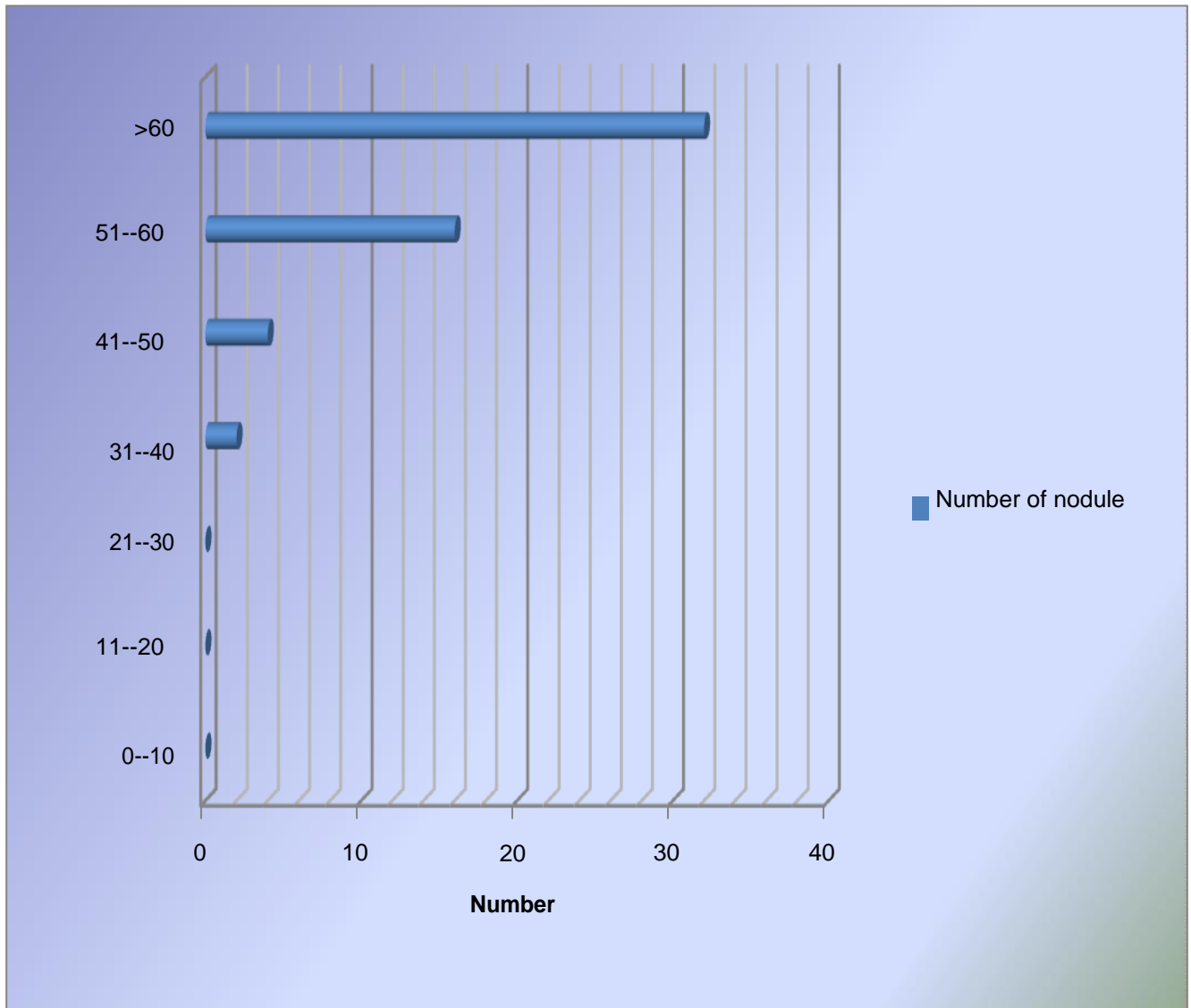
The sex distribution of incidentally detected adrenal mass was male:female = 2:1 (Table 7).

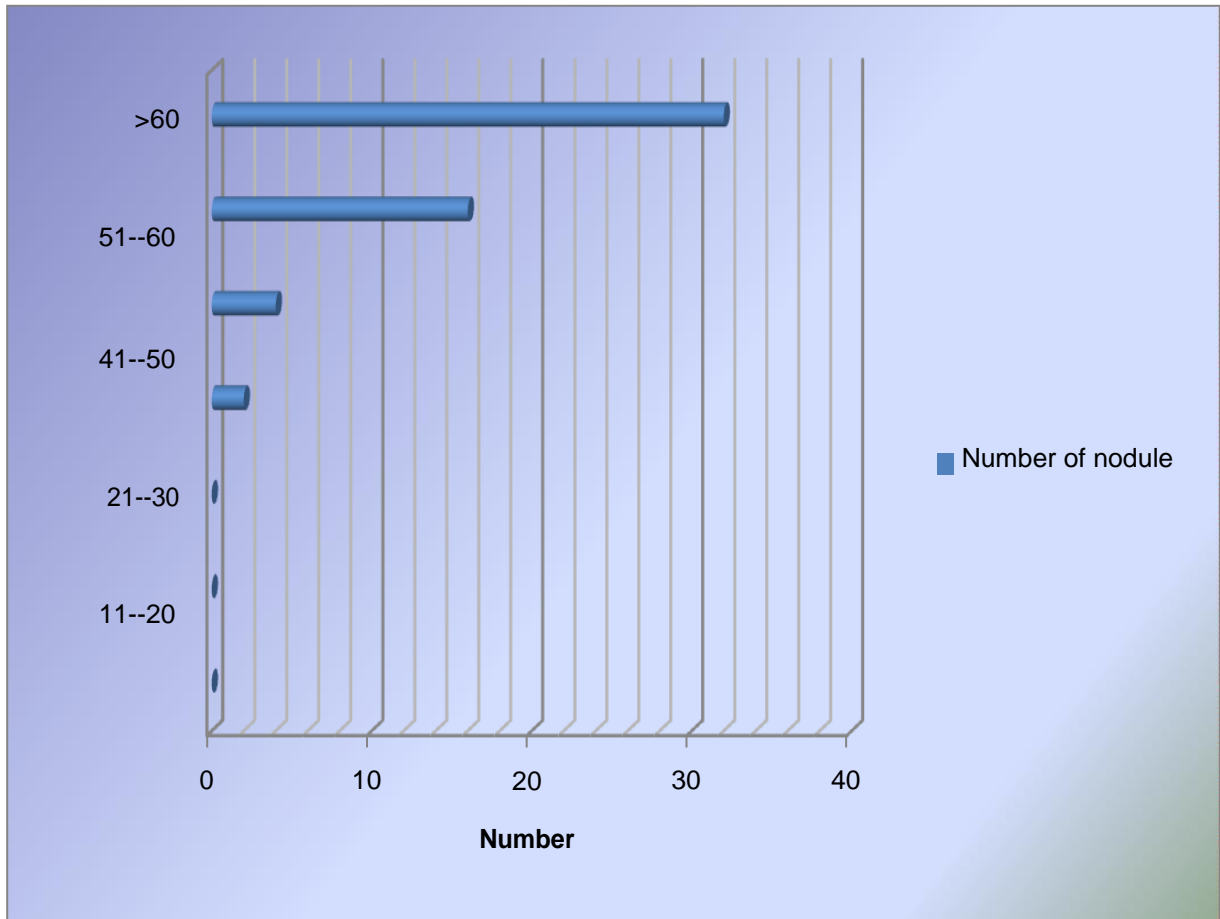


**Fig 1: Distribution of cases of adrenal cortical nodule according to age.**

There were no cases of adrenocortical nodule in the age group of 0-10 yrs, 11-20 yrs and 21-30 yrs but it has been found in the following cases: 2 (8.33%) out of 24 cases in the age group of 31-40 yrs; 4 (21.05%) out of 19 cases in the age group of 41-50 yrs; 8 (50%) out of

16 cases in the age group of 51-60 yrs and 10 (66.66%) out of 15 cases in the age group of above 60 yrs. So it is revealed that such cases increase with increasing of age. Hence this is ageing process (Figure 1).





**Fig 2: Distribution of number of adrenal cortical nodule according to age.**

In this study we got 2 nodules in the age group of 31-40, 4 nodules in the age group of 41-50, 16 nodules in the age group of 51-60 and 32 nodules in greater than 60 yrs of age. Average number of nodule per case in the age group of 31-40 yrs, 41-50yrs, 51- 60 yrs and above 60 yrs was respectively 1, 1, 2 and 3.2. So, number of nodule increase as the age increases (Figure 2).

**Table 8: Distribution of cases according to number of nodule (n=24)**

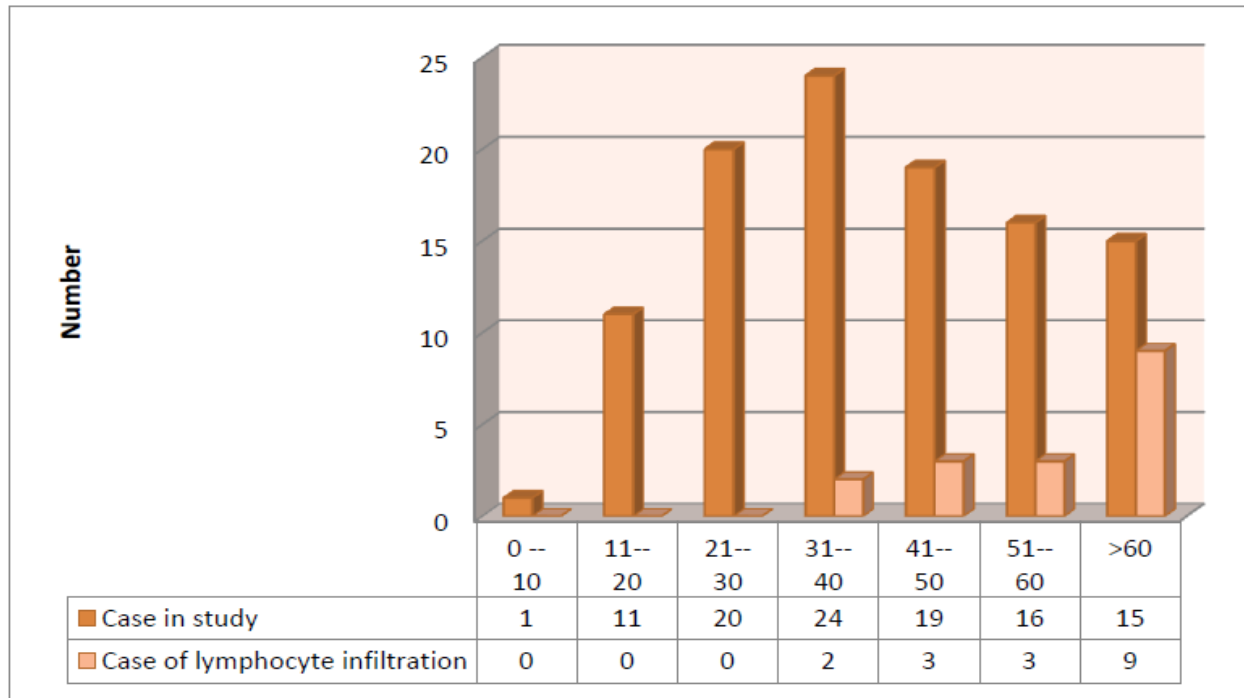
Number of Nodule	Number of Case	Percentage (%)
One nodule	8	33.33
Two nodule	4	16.66
Three or more nodule	12	50

In the present study one nodule found in 33% of cases, two nodules found in 17% of cases and three or more number of nodule found in 50% of cases. So in most of the cases multiple nodule were found (Table 8).

**Table 9: Distribution of cases according to laterality of nodule in cases adrenal cortical nodule (n=24)**

Laterality of Nodule	Number of Cases	Percentage (%)
Unilateral nodule	9	37.5
Bilateral nodule	15	62.5

The study shows that in 37.5% of cases adrenocortical nodule was present unilaterally and in 62.5% of cases that was bilateral. So most of the case, nodules were present bilaterally (Table 9).



**Fig 3: Distribution of cases of adrenal cortical lymphocyte infiltration according to age.**

Among the study population in the age group of 0-30 yrs adrenal shows no lymphocyte infiltration. In the age group of 31-40 yrs 2 cases show adrenal lymphocyte infiltration. In the age group of 41-50 yrs 3 cases show adrenal lymphocyte infiltration.

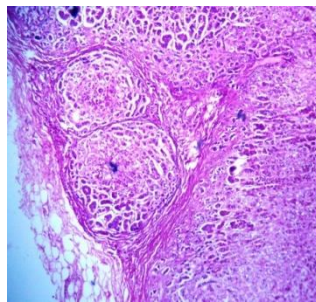
Respectively 3 and 9 cases of adrenal lymphocyte infiltration show in the age group of 51-60 yrs and above 60 yrs. So cases of adrenal lymphocyte infiltration increase with increase of age. So it is an ageing process (Figure 3).



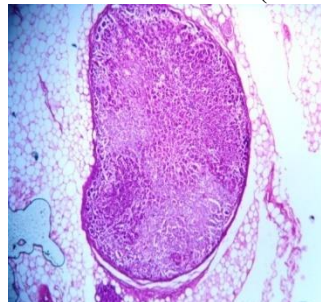
**Fig 4: Cut section of normal adrenal**



**Fig 5: Gross appearance of myelolipoma**

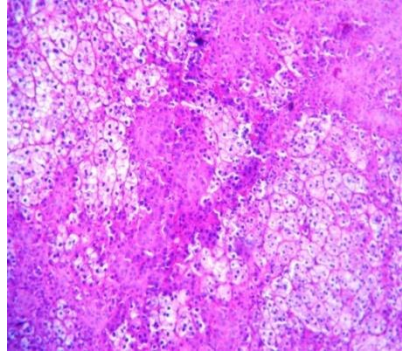


**Fig 6: Two adrenal cortical nodules (H&E, Mag: X 100)**



**Fig 7: Adrenal cortical nodule in adjacent fat (H&E, Mag: X 100).**





**Fig 8: Histopathology of adrenal cortical adenoma (H&E, Mag: X 100).**

### Discussion

Most of adrenal diseases are asymptomatic. Adrenal pathologic findings are said to be common in autopsy population; however their nature and true prevalence is not well documented. Autopsy provides unique insight into the prevalence of asymptomatic adrenal diseases in community. Thus, in present study 106 medico legal autopsy cases were included to know the various adrenal lesions in asymptomatic cases. The study was done in R.G. Kar Medical College & Hospital, Police Morgue from April 2013 to March 2014. The data were recorded; results were inferred, analyzed and further compared with available studies and literature regarding the same. In this present study, out of 106 cases, 38.7% of cases were found with histopathological change, while rests 61.3% were found to be normal. Among the histopathological changes, we found 24(22.64%) cases of adrenal cortical nodule, 17(16.03%) cases of adrenal lymphocyte infiltration, 4(3.77%) cases of adrenal haemorrhage, 2(1.88%) cases of adrenal cortical adenoma and one (0.94%) case of adrenal myelolipoma. In the present study of 106 cases, incidentally detected adrenal mass was found in 2.8% of cases. In the age group of 0 to 60 yrs, there was no incidentally detected adrenal mass but in the age group of above 60 yrs, there were three (20%) incidentally detected adrenal masses (two adrenal cortical adenoma and one myelolipoma) noted out of 15 cases. So it is found in older age group. And the sex distribution in male and female was 2:1. Brazon L et al [7] in their study of total 71, 206 cases from the literature the mean prevalence of incidentally detected adrenal mass was 2.3%, ranging from 1 to 8.7%, without significant differences between females and males. According to Kloos RT [8] et al, the prevalence of incidentally detected adrenal mass increases with the patients' age, being 0.2% in young subjects as compared with 6.9%

in subjects older than 70 years of age. Rineheart et al.[9] in their study of 100 cases, found that the prevalence of incidentally detected adrenal mass was 3%. In the study of Russi et al [10] out of 9000 cases the prevalence of incidentally detected adrenal mass was 1.45% with female male ratio 2.0:1.2. The study done by Commons & Callaway [11] revealed that among 7437 cases the prevalence of incidentally detected adrenal mass was 2.88% and among them female were 2.84% and male were 2.88%. The research of Schroede [12] showed that out of 4000 cases the prevalence of incidentally detected adrenal mass was 1.38%. Devenyi [13] in his study of 5120 cases found that the prevalence of incidentally detected adrenal mass was 3.55% with a sex distribution of 3.62:3.61 (female: male). As per the study of Kokko et al.[14] of 2000 cases the prevalence of incidentally detected adrenal mass was 1.05% but they did not mention about the sex distribution. Hedeland et al.[15] in their study of 739 cases found that the prevalence of incidentally detected adrenal mass was 8.70%. Among them 7.16% was female and 10.34% was male. The prevalence of incidentally detected adrenal mass was shown as 5.40% among 94 cases in the study of Yamada & Fukunaga [16]. Granger & Genes [17] found that the prevalence of incidentally detected adrenal mass was 2.52% and male female ratio was 2.58:2.43, among 2425 cases. Russell et al. [18] in their research of 35000 cases found the prevalence of incidentally detected adrenal mass was 1.97%, of which 2.05% was female and 1.92% was male. In the study of Abecassis et al. [19] among 988 cases the prevalence of incidentally detected adrenal mass was found 1.9%. The study concerning 2951 cases by Meagher et al. [20] revealed that the prevalence of incidentally detected adrenal mass was 5%. The study of Reinhard et al. [21] dealing with 498 cases indicated that the prevalence of incidentally detected adrenal mass was 5.00%. Our study correlates with the study of

Brazon L et al [7], Rineheart et al [9], Commons & Callaway [11], and Granger & Genes [17]. In this present study we found 24 (22.64%) cases of adrenal cortical nodule out of 106 cases. In the age group of 0-10 yrs, 11-20 yrs and 21-30 yrs there was no case of adrenal cortical nodule but in the age group of 31-40yrs, 2(8.33%) out of 24 cases; 41-50 yrs, 4(21.05%) out of 19 cases; 51-60 yrs, 8(50%) out of 16 cases and above 60yrs, 10(66.66%) out of 15 cases had shown adrenal cortical nodule. Number of cases increase with increase of age. So this is an ageing process. In this study, average number of nodule per case in the age group of 31-40 yrs, 41-50yrs, 51-60 yrs and above 60 yrs was respectively 1, 1, 2 and 3.2. So, number of nodules increase with increase in age. Majority of the cases had multiple nodules. We found one nodule in 33% of cases, two nodules in 17% of cases and three or more nodules in 50% of cases. Regarding laterality, most of the cases (62.5%) were bilateral. This study resembled the studies of DeLellis RA, Mangray S [22], Rosai J [23] and Neville AM [24]. DeLellis RA, Mangray S [22] concluded the incidence of cortical nodule in autopsy studies was 25% and it was multicentric, bilateral and according to Rosai J cortical nodules were usually multiple. Neville AM [24] concluded it as part of ageing process.

According to Lloyd RV, Douglas BR, Young WF [25] focal aggregates of lymphocytes are an incidental finding in the adrenal cortices of normal adults and increase in frequency with the age of the patient. Hayashi Y et al [26] studied the incidence of mononuclear cell infiltration in the adrenal cortex in autopsy cases of young and old subjects. Histologically, 110 of 174 autopsy cases with age greater than 60 years (63.2%) were shown to have mononuclear cell infiltration of varying degree within the adrenal cortex, whereas such a lesion was observed in lesser incidence (7.4%) in the 54 younger, control subjects aged less than 49 years. In addition, severely infiltrating lesions in the adrenal cortex were found frequently in the elderly greater than 70 years. It has been found from the present study in the age group of (0-30) yrs shows no cases of lymphocyte infiltration. In the age group of (31-40) yrs, (41-50) yrs, (51-60) yrs and >60 yrs show 2(8.33%), 3(15.78%), 3(18.75%) and 9(60%) cases of lymphocyte infiltration respectively. So it is an ageing process. We found 9 cases of lymphocyte infiltration of above 60 yrs, of which 3(50%) cases were between 61-70 yrs and 6(66.67%) cases were above 70 yrs. So this study correlates with the study of Lloyd RV, Douglas BR, Young WF [25] and Hayashi Y et al [26].

## Conclusion

Very few studies have been undertaken on adrenal gland itself. Our present study can illuminate and provide necessary feedback to the clinician in charge of patient care with increase accuracy and effectiveness. The study of common as well as uncommon asymptomatic lesions of adrenal is an extremely difficult task in a vast number of living subjects and autopsy study is the best possible way to work on it. This study emphasizes the importance of forensic autopsies for epidemiological and clinical analysis.

We have some peculiar observations. Adrenal cortex of many aged patients with lymphocyte infiltration may represent a preclinical manifestation of organ specific autoimmune adrenalitis. This data may give insight into further search of pathogenesis of autoimmune Addison's disease. Finding of adrenal cortical adenoma and cortical nodule are best regarded as part of the aging process and may have association with essential hypertension in older age group. We were severely constrained by limitation of sample size, duration of study and financial backup. Therefore, we need to study larger sample size to achieve more realistic incidence of asymptomatic adrenal lesions more in general population.

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