

# Usefulness of assessment of urinal metoxycatecholamines secretion in everyday clinical practice - Pheochromocytoma as diagnostic challenge.



Authors: Elwira Przybylik- Mazurek, Ewelina Rzepka, Monika Buziak-Bereza, Alicja Hubalewska-Dydejczyk

Department of Endocrinology, Medical College Jagiellonian University, Krakow, Poland



## OBJECTIVES

Adrenal incidentaloma is an adrenal mass found on imaging studies done for other reason than suspected adrenal disease.

The majority of them are non-functioning adenomas, however pheochromocytomas could be also observed.

Currently, in diagnosis of incidentalomas, the assessment of hormones of adrenal cortex and medulla is performed.

The aim of the study was to assess the incidence of pheochromocytoma in patients with incidentaloma.

## METHODS

Medical records of 380 patients with incidentaloma, hospitalized during 14 months (between April 2014 and July 2015) in our Clinic were retrospectively reviewed.

Diagnostic imaging pictures (magnetic resonance imaging - MRI or computed tomography - CT), the incidence of hypertension, urine metoxycatecholamines secretion (normetanefrine or metanefrine), as well as hormonal assessment of adrenal cortex were analyzed.

## RESULTS

Seventy eight percent of patients (296 of 380) were hypertensive.

Most of lesions have benign features on imaging study (281 patients of 339 cases with known description of tumors in CT or MRI, which contains 82.8% of that cases - in the rest 41 patients only CT scans without assesment of density were performed.) In this group were patients with adenoma-like tumors and lesions characterised clearly as myelolipoma.

There were only nine histologically confirmed pheochromocytomas, which comprises 2.37% of all cases. In the literature, the prevalence of pheochromocytoma in adrenal incidentalomas is higher and stands at 3.1% [1]. In those 9 patients, only one person have adenoma-like characteristic on imaging study. However, the attenuation value on unenhanced CT in this case were higher than 10HU. Some cases of pheochromocytoma which mimics adrenal adenoma have been already reported [2]. Nevertheless, the likelihood of a pheochromocytoma in adrenal lesions with imaging criteria of an adenoma is extremely low [3].

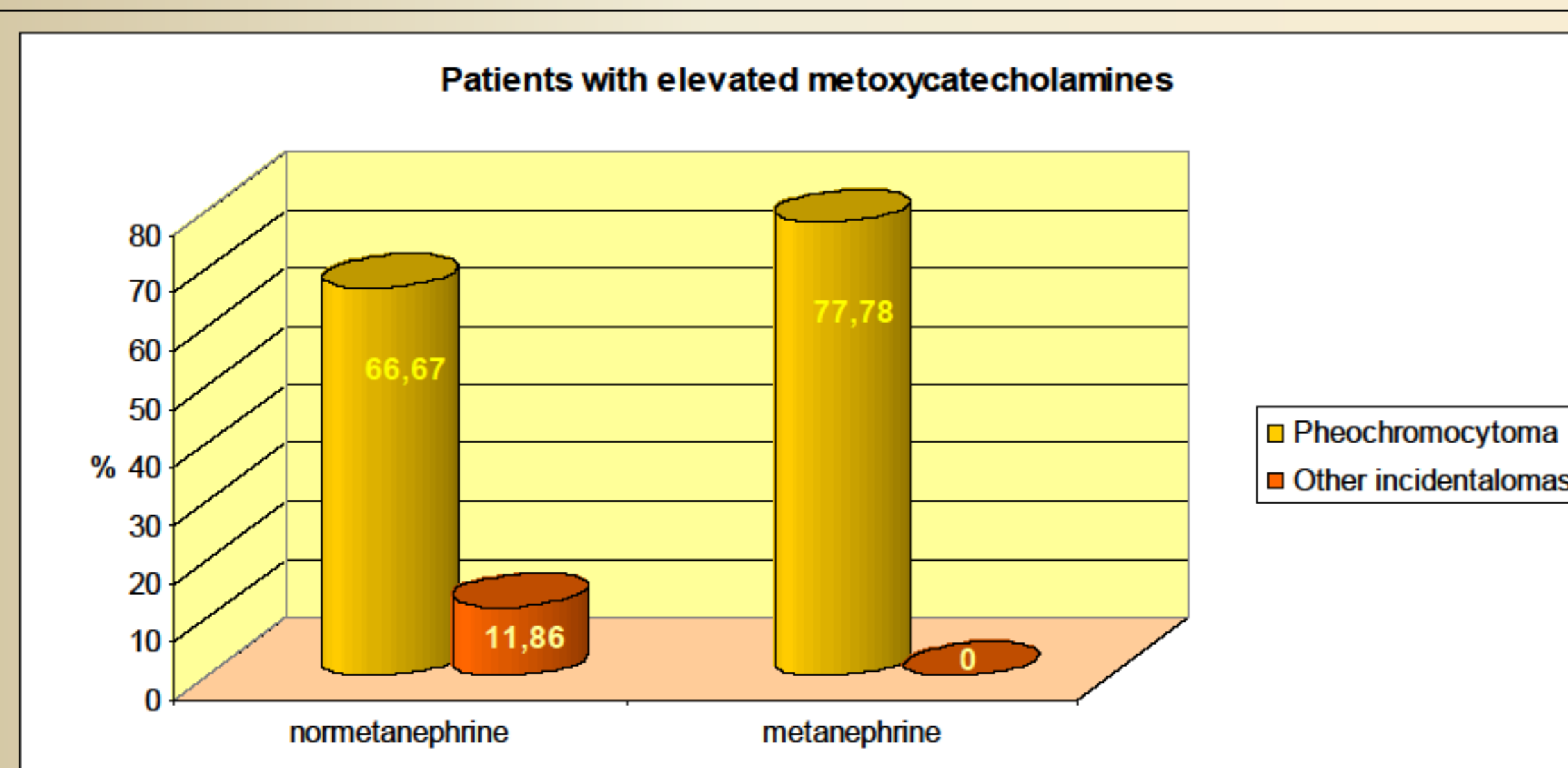
Accurate levels of metoxycatecholamines were known in 304 patients of total 380. Forty three patients (14.1%) have elevated level of metoxycatecholamines (normetanefrine [N:88.0-440.0ug/24h] or metanefrine [N:52.0-341.0ug/24h]). Positive value was specified as higher than the upper limit of normal. In this group of 43 patients, seven (16.3%) patients have histologically confirmed pheochromocytoma.

Thirty five patients don't have pheochromocytoma in spite of elevated metoxycatecholamines. The percentage of false positive results in our study was significantly higher (81.4%), compared to 34% presented in another article [4]. It was probably related with larger group (seventy patients) and different characteristics of the patients (including not only incidentalomas, but also tumors with suspicion of pheochromocytoma) in cited study.

Thirty two patients with elevated metoxycatecholamines have hypertension. Only 3 patients with elevated normetanefrine weren't hypertensive. Patients with hypertension have higher level of normetanefrine (maximum result was 832 ug/24h, compared to 512.6 ug/h in normotensive patients). None of patients with false positive results has elevated metanefrine, contrary to patients with confirmed pheochromocytoma. The opposite results were showed by Carr et al.[4]

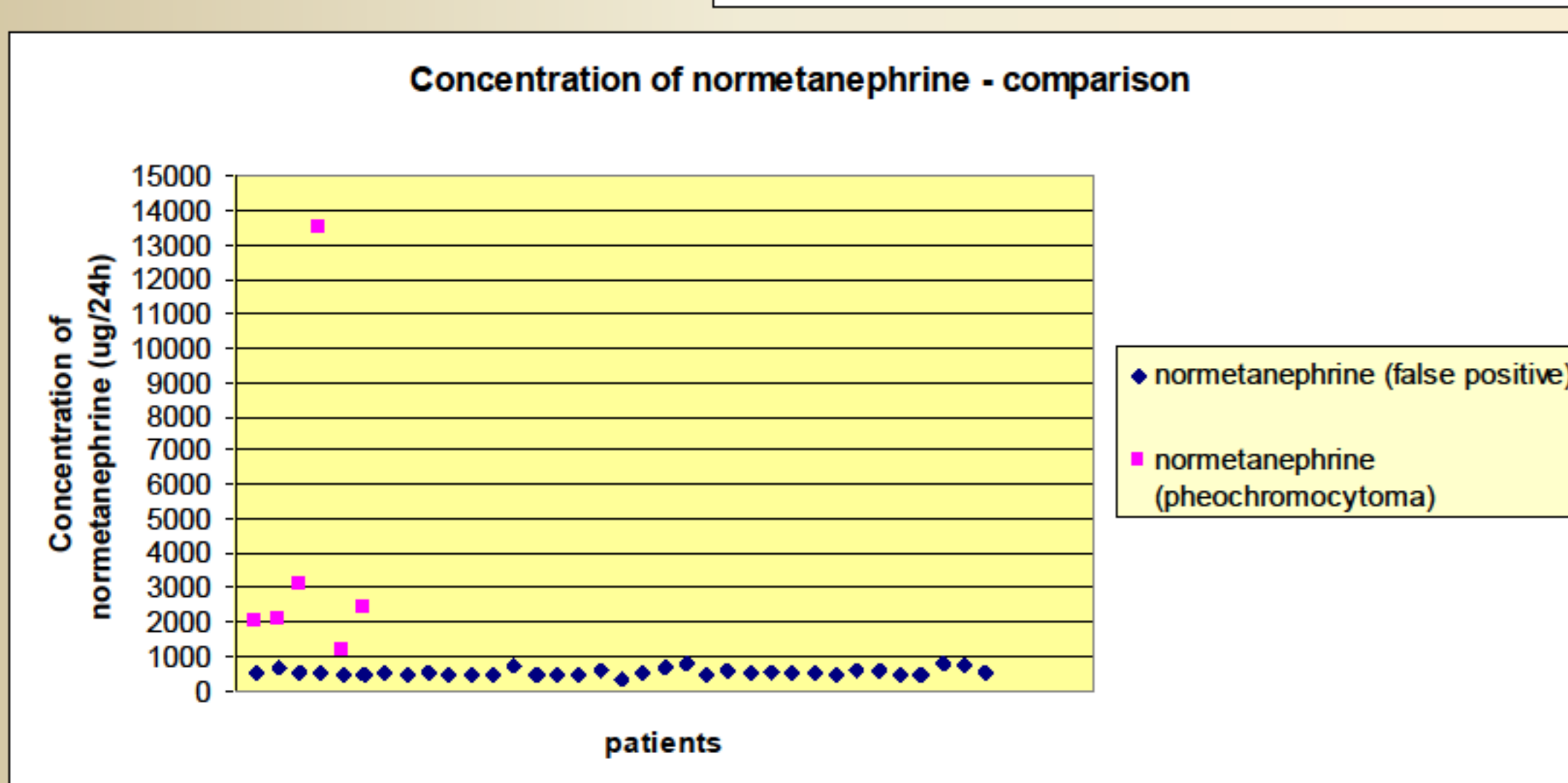
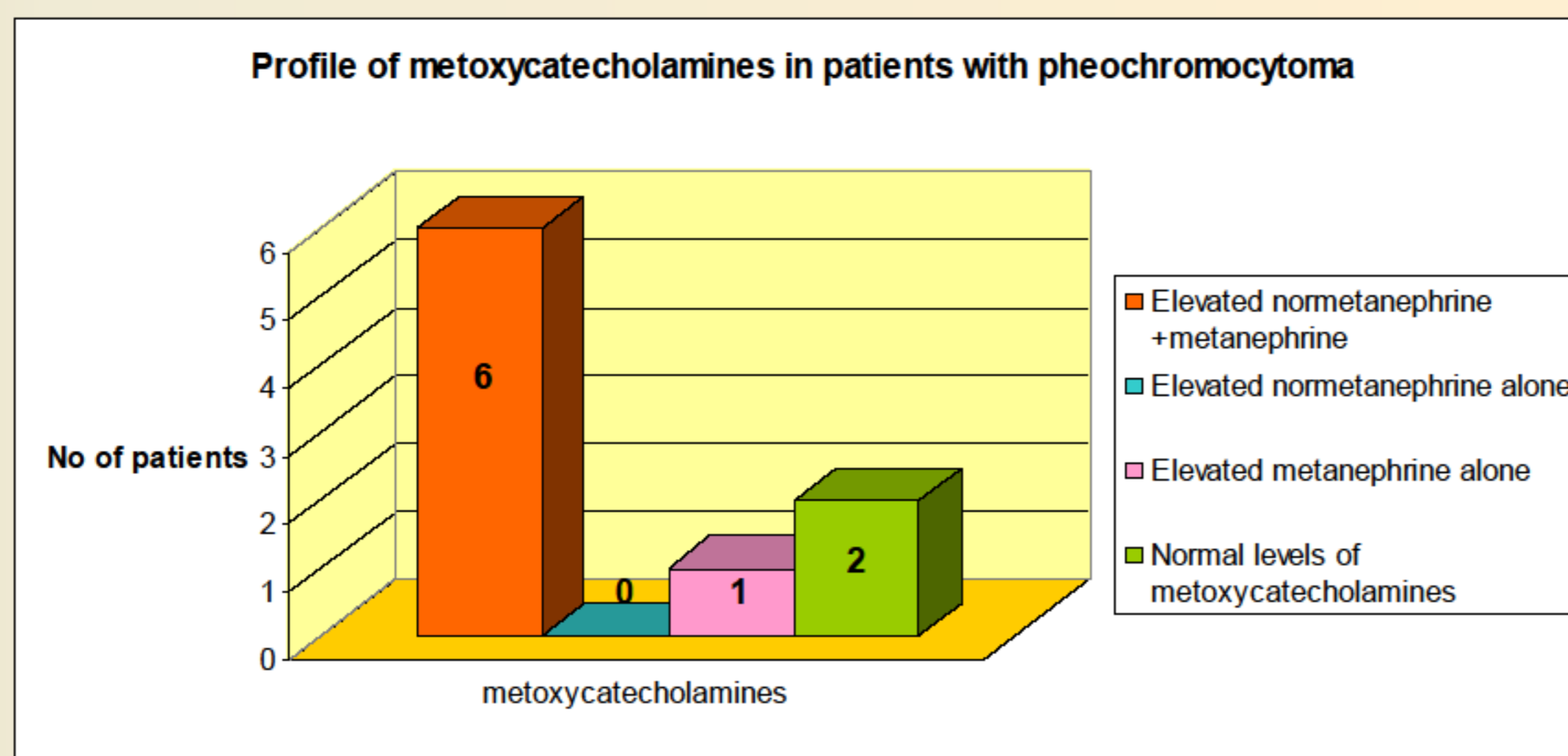
The differences in concentration of normetanefrine were also observed between group of cases with false positive results and pheochromocytomas, as it was shown on graph 3. The cut-off point of elevated normetanefrine diagnostic for pheochromocytoma in our study was comparable to that noticed in other article [5].

Moreover, 2 patients with pheochromocytoma have unelevated metoxycatecholamines secretion with benign features on imaging study in one of those patients. Few retrospective studies suggest that metanephrines may be normal in up to 25% of patients with normotensive incidentally discovered pheochromocytomas [3].



Graph 1

Graph 2



Graph 3

## CONCLUSIONS

1. The assessment of urine metoxycatecholamines secretion seems to have limited usefulness in diagnosis of pheochromocytoma in incidentalomas, mainly because of low incidence of elevated level of metoxycatecholamines and possibility of false positive results.
2. Normal level of urine metoxycatecholamines secretion were also observed in some patients with pheochromocytoma.
3. In diagnosis of pheochromocytoma, clinical symptoms and radiological imaging picture should play the most important role.
4. Assessment of urine metoxycatecholamines secretion should be performed in justified cases.

## REFERENCES:

1. Cawood TJ, Hunt PJ, O'Shea D, et al. Recommended evaluation of adrenal incidentalomas is costly, has high false-positive rates and confers a risk of fatal cancer that is similar to the risk of the adrenal lesion becoming malignant; time for a rethink? *Eur J Endocrinol.* 2009 Oct;161(4):513-27.
2. Blake MA, Krishnamoorthy SK, Boland GW, et al. Low density pheochromocytoma on CT: a mimicker of adrenal adenoma. *AJR Am J Roentgenol* 2003; 181:1663-1668.
3. Fassnacht M, Arita W, Bancos I, et al. Management of adrenal incidentalomas - a European Society of Endocrinology Clinical Practice Guideline in collaboration with the European Network for the Study of Adrenal Tumors. *ESE and ENSAT guidelines on adrenal incidentaloma v.21.12.2015.*
4. Carr JC, Spanheimer PM, Rajput M, et al. Discriminating Pheochromocytomas from Other Adrenal Lesions: The Dilemma of Elevated Catecholamines. *Ann Surg Oncol.* 2013 Nov; 20(12): 3855-3861.
5. Young WF Jr. Pheochromocytoma: 1926-1993. *Trends in Endocrinology and Metabolism*, vol 4, Elsevier Science, Inc 1993. p.122.

