DOI: 10.7860/JCDR/2026/80913.22377

Original Article

Pathology Section

Comparison of the Pheochromocytoma of the Adrenal Gland Scaled Score (PASS), Grading of Adrenal Pheochromocytoma and Paraganglioma (GAPP) and Modified GAPP: A Cross-sectional Study

NIYOR DUTTA[1], ELANTHENRAL SIGAMANI[2], A SANTHOSH RAJ[3], MARIE THERESE MANIPADAM[4], SHAWN THOMAS SAM[5], ANISH JACOB CHERIAN[6], MAZHUVANCHARY JACOB PAUL[7], DEEPAK THOMAS ABRAHAM[8]

ABSTRACT

Introduction: Pheochromocytoma (PCC) is a rare adrenal tumour with variable biological behaviour. Several histopathological scoring systems have been proposed to predict metastatic potential, including the Pheochromocytoma of the Adrenal Gland Scaled Score (PASS), the Grading of Adrenal Pheochromocytoma and Paraganglioma (GAPP), and the Modified GAPP (M-GAPP) incorporating Succinate Dehydrogenase Subunit B (SDHB) Immunohistochemistry (IHC). The present study focused to compare the performance of these scoring systems in an Indian single-centre series of adrenal PCC.

Aim: To evaluate and compare the prognostic performance of PASS, GAPP, and M-GAPP scoring systems in predicting the malignant potential of adrenal PCC.

Materials and Methods: This retrospective cross-sectional study was conducted at tertiary care centre,India, and included 111 histopathologically confirmed adrenal PCC cases diagnosed between 2000 and 2020 at a tertiary care centre in India. Clinical, biochemical, histopathological, and follow-up data were analysed. Sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and Receiver Operating Characteristic (ROC) curve analysis, with the Area Under the Curve (AUC), was used to calculate at predefined cut-offs (PASS ≥4; GAPP ≥3; M-GAPP high-risk). Chi-square test, Fisher's exact test, Student's t-test, or Mann-Whitney U test was used where appropriate, with significance set at p-value <0.05.

Results: The mean age at diagnosis was 36.8±14.8 years. Tumours were right-sided in 45.05%, left-sided in 39.64%, and bilateral in 15.31%. Metastasis occurred in 8.11% of cases, while recurrence was seen in 3.60%. Among syndromic cases, Von Hippel–Lindau (VHL) mutation was associated with metastasis in 11.76% of patients. Comedo-type necrosis showed a significant correlation with metastasis (p-value = 0.008). PASS (≥4) showed a sensitivity of 55.56% and specificity of 67.60%. GAPP (≥3) showed a sensitivity of 66.67% and specificity of 59.80%. M-GAPP incorporating SDHB loss showed higher specificity (71.40%) and NPV (98.00%), though sensitivity was 21.30%. ROC curve analysis demonstrated M-GAPP had the highest AUC compared to PASS and GAPP.

Conclusion: In this Indian Institutional series, M-GAPP outperformed PASS and GAPP by demonstrating better specificity and NPV, making it more reliable in excluding aggressive tumours. Incorporating SDHB IHC into histopathological assessment may improve risk stratification. Limitations include the retrospective, single-centre design and small number of metastatic events.

Keywords: Grading of Adrenal Pheochromocytoma and Paraganglioma score, Immunohistochemistry, Ki-67 proliferative index, Prognostic scoring, Succinate Dehydrogenase

INTRODUCTION

Pheochromocytomas are rare catecholamine-producing tumours arising from chromaffin cells of the adrenal medulla, with an incidence of approximately 2-8 cases per million population per year [1]. These tumours are clinically significant because of their potential to cause life-threatening cardiovascular complications and their unpredictable malignant potential [2,3].

Histopathological examination remains the gold standard for diagnosis; however, distinguishing benign from malignant pheochromocytomas at initial presentation is challenging [4,5]. Traditional features such as capsular and vascular invasion, necrosis, and mitotic activity are associated with aggressive behaviour, but are not entirely reliable predictors [6].

To address this limitation, various histopathological scoring systems have been proposed. The Pheochromocytoma of the Adrenal Gland Scaled Score (PASS) was introduced by Thompson LDR in 2002 [4], incorporating 12 morphological criteria to stratify risk. Later, the Grading of Adrenal Pheochromocytoma and Paraganglioma (GAPP) system was developed, which combined histological parameters with catecholamine phenotype and Ki-67 proliferative index [7]. Although both systems are widely used, their prognostic accuracy has been questioned, with inconsistent results across studies [8,9].

The Modified GAPP (M-GAPP) score further refines the GAPP system by including Succinate Dehydrogenase Subunit B (SDHB) Immunohistochemistry (IHC), which helps identify tumours associated with germline mutations and poorer prognosis [10,11]. Incorporating SDHB status may improve specificity and guide long-term follow-up strategies [12].

Given the variability in predictive accuracy among these scoring systems, especially in different ethnic and geographic populations, there is a need to evaluate their performance in an Indian single Institution series of adrenal pheochromocytomas [13-15]. Hence,

the present study aimed to compare the prognostic performance of the PASS, GAPP, and M-GAPP scoring systems in adrenal pheochromocytomas and to evaluate the utility of the M-GAPP system in predicting metastatic potential in an Indian single Institution series.

MATERIALS AND METHODS

This was a retrospective cross-sectional study conducted at a tertiary care centre in India. A total of 111 histopathologically confirmed cases of adrenal pheochromocytoma diagnosed between January 2000 and December 2020 were included. This study was approved by the Institutional Review Board (IRB minute number 12898, dated 8th June 2020).

Inclusion criteria: Cases with complete clinical, biochemical, histopathological, and follow-up data were included.

Exclusion criteria: Cases with incomplete data or inadequate tissue for the scoring system evaluation were excluded from the study.

Study Procedure

Histopathological evaluation: Haematoxylin and Eosin (H&E) stained slides were reviewed. Two pathologists independently applied the PASS [Table/Fig-1] and GAPP [Table/Fig-2] scoring systems. Discrepancies were resolved by consensus. The M-GAPP score was calculated by incorporating SDHB IHC findings [Table/Fig-3].

Immunohistochemistry (IHC): SDHB and Ki-67 (MIB-1) IHC were performed using standard protocols. Ki-67 index was categorised as <1%, 1–3%, and >3% (as per GAPP criteria). A threshold of >3% was considered high proliferation. Loss of SDHB expression was interpreted as cytoplasmic negativity in tumour cells with retained staining in internal controls.

Application of scoring systems

- PASS ≥4 was considered suspicious for malignancy.
- GAPP ≥3 was considered intermediate/high risk.
- M-GAPP ≥3 with SDHB loss was considered high risk.

A summary of parameters included in each system is provided in [Table/Fig-4].

PASS Features	Score (if present)
Nuclear hyperchromasia	1
Profound nuclear pleomorphism	1
Capsular invasion	1
Vascular invasion	1
Extension into periadrenal adipose tissue	2
Atypical mitotic figures	2
>3 mitoses per 10 high power fields (HPF)	2
Tumour cell spindling	2
Cellular monotony	2
High cellularity	2
Central or confluent tumour necrosis	2
Large nests or diffuse growth (>10% of volume)	2
Maximum possible score	20

[Table/Fig-1]: Pheochromocytoma of the Adrenal Gland Scaled Score (PASS).

Parameters	Category	Points
Histological pattern	Zellballen	0
	Large/Irregular Nest	1
	Pseudorosette (even if focal)	1
Cellularity	Low (<150 cells/0.05 mm²)	0
	Moderate (150–250 cells/0.05 mm²)	1
	High (>250 cells/0.05 mm²)	2
Necrosis	Absent	0
	Comedo-type necrosis	2
Capsular/Vascular Invasion	Absent	0
	Present	1
Ki-67 Labelling index	<1%	0
	1–3%	1
	>3%	2
Catecholamine Type	Adrenergic (E or E+NE) or non-functional	0
	Nor adrenergic (NE or NE+DA)	1
Maximum Possible Score		10

[Table/Fig-2]: Grading System for Adrenal Pheochromocytoma and Paraganglioma (GAPP).
Note: Cellularity assessed per 0.05 mm² field under 400X magnification. Catecholamine type was determined based on biochemical and clinical records.

GAPP Score	Histological grade
0–2	Well-differentiated type
3–6	Moderately differentiated
7–10	Poorly differentiated type

[Table/Fig-3]: GAPP Score and Histological Grade.

Scoring system	Key parameters	Additional markers	Score range	Interpretation
PASS	12 histological features	None	0–20	≥4 Suggests malignant potential
GAPP	Histology+ Biochemistry + Ki-67	Catecholamine type, Ki-67	0–10	Well (0-2), Moderate (3-6), Poor (7-10)
M-GAPP	GAPP + SDHB IHC	Loss of SDHB staining	0–11	Improved specificity for metastasis

[Table/Fig-4]: Summary of PASS, GAPP, and Modified GAPP (M-GAPP) Scoring Systems.
Note: This table compares the components and scoring interpretations of PASS, GAPP, and M-GAPP systems used for risk stratification of pheochromocytoma.

STATISTICAL ANALYSIS

Categorical variables were compared using the Chi-square test or Fisher's-exact test, as appropriate. Continuous variables were analysed using the independent Student's t-test or Mann-Whitney U test. Diagnostic performance was evaluated using sensitivity, specificity, Positive Predictive value (PPV), and Negative Predictive Value (NPV) derived from 2×2 contingency tables at predefined cut-offs. Receiver Operating Characteristic (ROC) curve analysis, with the Area Under the Curve (AUC), was used to illustrate comparative performance. All analyses were performed using Statistical Package for Social Sciences version 21.0 (IBM Corp., Armonk, NY, USA), with significance set at p-value <0.05.

RESULTS

A total of 111 cases of adrenal pheochromocytoma were included. The mean age at diagnosis was 36.80±14.80 years (range: 8-69). The male-to-female ratio was approximately equal (M:F=1.05:1). Tumours were in the right adrenal in 50 (45.05%), left adrenal in 44 (39.64%), and bilateral in 17 (15.31%).

Metastasis and recurrence: Metastasis was documented in 9/111 cases (8.11%). Metastatic sites included regional lymph nodes (pararenal, retrocaval, para-aortic) and extra-nodal sites (renal artery, inferior vena cava, duodenum, omentum, skeletal muscle, and pancreas). Recurrence occurred in 4/111 cases (3.60%), two of which also developed metastasis. One patient later developed an extra-adrenal paraganglioma.

Syndromic cases: A total of 17 patients harboured Von Hippel–Lindau (VHL) mutations; 2 (11.76%) developed metastasis (p-value=0.33, Fisher's-exact test). Twelve patients with, Multiple Endocrine Neoplasia type 2 (MEN2) (RET mutations) commonly had bilateral tumours, but none metastasised (p-value=0.65, Fisher's-

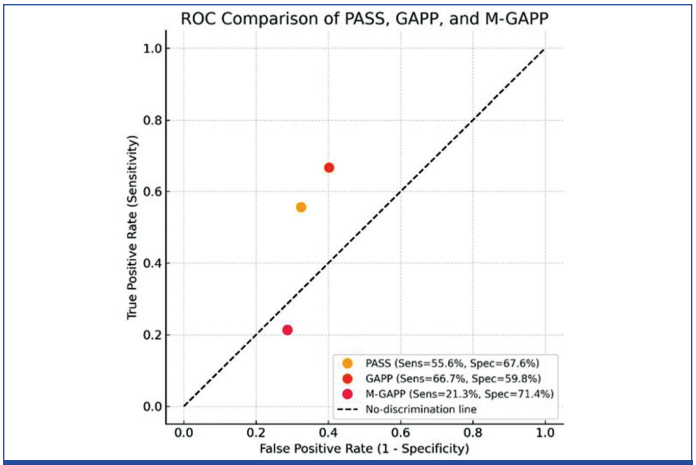
exact test). Two patients with Neurofibromatosis type 1 (NF1) and one with SDHD mutation did not show metastasis or recurrence.

Histopathological features: On review, comedo-type necrosis was the only feature significantly associated with metastasis (p-value=0.008, Chi-square test). Capsular invasion, vascular invasion, cellular monotony, and increased mitotic activity were more frequent in metastatic cases but did not reach significance.

Performance of scoring systems

- PASS ≥4 was seen in 40/111 cases (36.04%). It showed a sensitivity of 55.56%, specificity of 67.60%, PPV- 13.20%, and NPV-94.50%.
- GAPP ≥3 was observed in 68/111 cases (61.26%). It demonstrated a sensitivity of 66.67%, specificity 59.80%, PPV 12.80%, and NPV 95.30%. Among its parameters, comedo-type necrosis was significant.
- M-GAPP incorporating SDHB loss showed sensitivity 21.30%, specificity 71.40%, PPV 14.70%, and NPV 98.00%. Loss of SDHB expression was observed in five metastatic cases.

ROC curve analysis: ROC analysis showed M-GAPP had the highest AUC compared to PASS and GAPP, supporting its superior specificity and NPV [Table/Fig-5].



[Table/Fig-5]: ROC Comparison of PASS, GAPP, and M-GAPP.

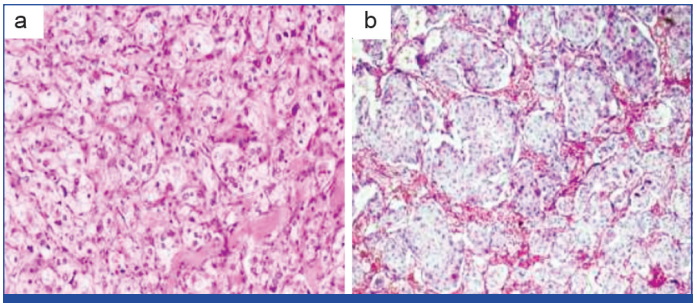
Histopathological features (Illustrative): Histologically, the tumours displayed classic Zellballen architecture [Table/Fig-6]. Comedo-type necrosis was the only feature significantly correlated with metastasis (p-value=0.008). Other adverse histological features-capsular invasion [Table/Fig-7], nuclear hyperchromasia and marked pleomorphism [Table/Fig-8], vascular invasion [Table/Fig-9], increased mitotic activity [Table/Fig-10], atypical mitotic figures [Table/Fig-11], and tumour cell spindling [Table/Fig-12] were more frequent in metastatic cases but did not reach statistical significance [Table/Fig-13].

PASS score: A PASS score ≥4 was observed in 40/111 cases (36.0%). Correlation with metastasis showed a sensitivity of 55.6%, specificity of 67.6%, PPV of 13.2%, and NPV of 94.5%.

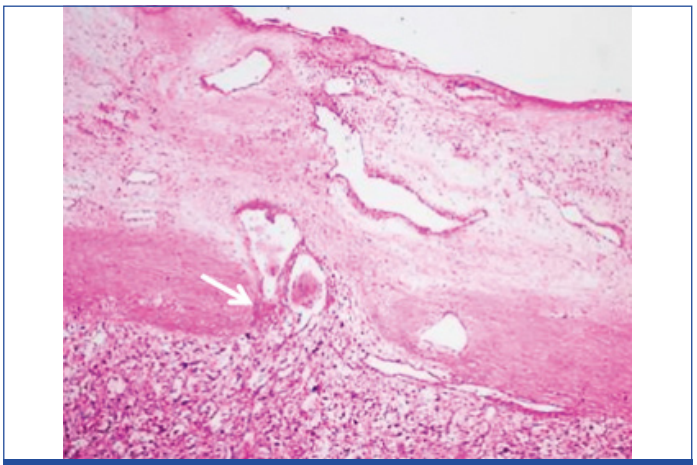
GAPP score: A GAPP score ≥3 was seen in 68/111 cases (61.3%). Among individual GAPP parameters, comedo-type necrosis remained the only statistically significant predictor. Overall, GAPP had a sensitivity of 66.7%, specificity of 59.8%, PPV of 12.8%, and NPV of 95.3%.

Ki-67 proliferative index: A Ki-67 index >3% was recorded in metastatic cases, showing high specificity (93.1%) but low sensitivity (22.2%) for predicting malignancy.

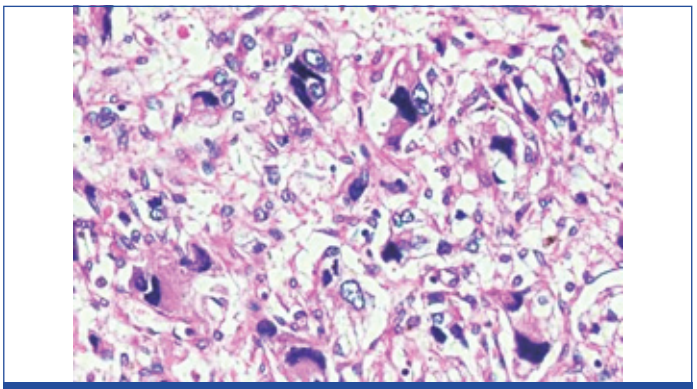
Modified GAPP (M-GAPP): Incorporating SDHB IHC into the GAPP score improved predictive performance. Loss of SDHB expression was observed in five metastatic cases [Table/Fig-14]. M-GAPP yielded a sensitivity of 55.6%, specificity 71.4%, PPV 14.7%, and NPV 98.0%the highest specificity and NPV among the three scoring systems [Table/Fig-15,16].



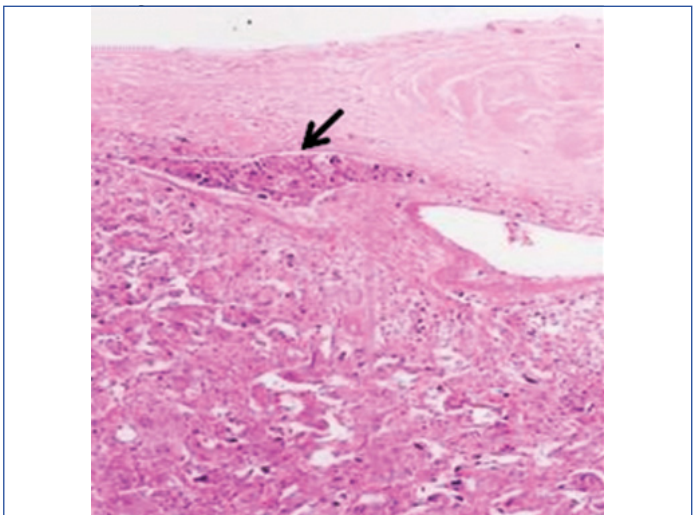
[Table/Fig-6]: Pheochromocytoma showing classic Zellballen pattern. (a) & (b) tumour cells arranged in nests surrounded by fibrovascular stroma (H&E, 100X).



[Table/Fig-7]: Capsular invasion by pheochromocytoma. Arrow indicates tumour cells infiltrating the capsule (H&E, 200X).



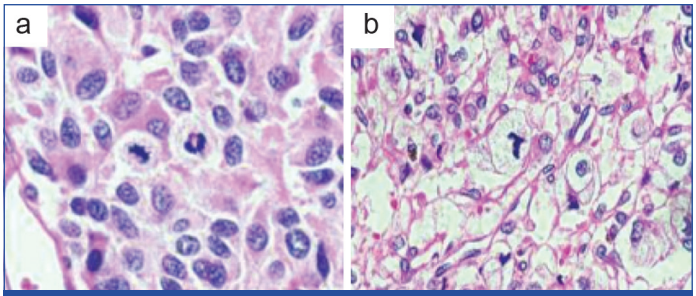
[Table/Fig-8]: Pheochromocytoma showing nuclear hyperchromasia and marked pleomorphism (H&E, 400X).



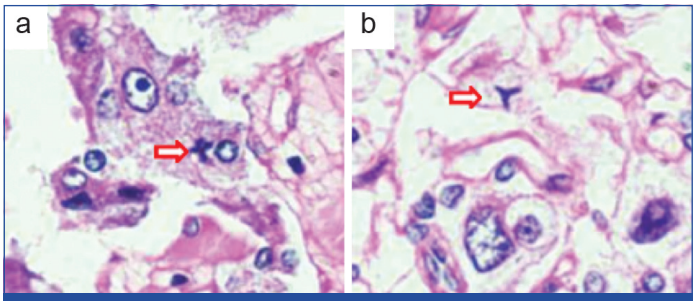
[Table/Fig-9]: Vascular invasion by pheochromocytoma. Black arrow shows tumour cells protruding into the vascular lumen (H&E, 100X).

DISCUSSION

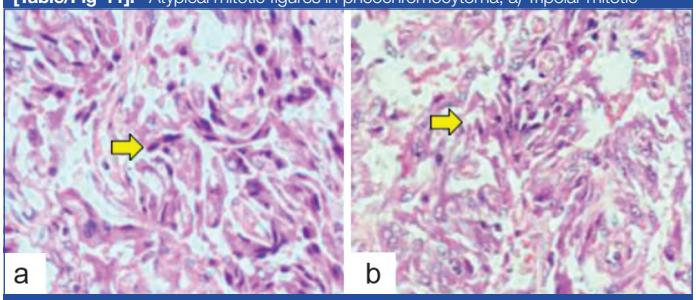
In the present study, the prognostic performance of PASS, GAPP, and M-GAPP scoring systems in adrenal pheochromocytomas



[Table/Fig-10]: Mitotic activity in pheochromocytoma; a) Brisk mitotic figures observed (H&E, 400X); b) Frequent mitotic figures in tumour nests (H&E, 400X).



[Table/Fig-11]: Atypical mitotic figures in pheochromocytoma; a) Tripolar mitotic

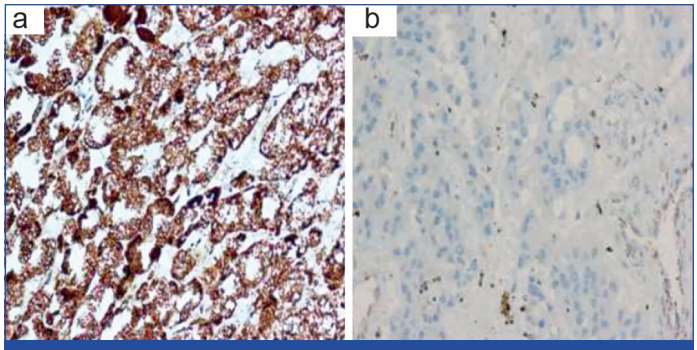


[Table/Fig-12]: Tumour cell spindling in pheochromocytoma. (a) Fascicular arrangement of elongated tumour cells (H&E, 200X). (b) Spindle-shaped tumour cells with tapered nuclei (H&E, 400X)

Parameters	Metastatic cases (n=9)	Non metastatic cases (n=102)	p-value
Mean age (years)	35.2±12.5	36.9±14.9	NS
Male:Female ratio	1.25:1	1.03:1	NS
Bilateral tumours	1 (11.1%)	16 (15.7%)	NS
Comedo-type necrosis	5 (55.6%)	15 (14.7%)	0.008
Capsular invasion	4 (44.4%)	24 (23.5%)	NS
Vascular invasion	3 (33.3%)	21 (20.6%)	NS
Cellular monotony	4 (44.4%)	27 (26.5%)	NS
Increased mitotic activity	3 (33.3%)	19 (18.6%)	NS
SDHB loss	5 (55.6%)	4 (3.9%)	<0.05

[Table/Fig-13]: Clinicopathological and histological features in metastatic vs non metastatic PCCs.(N=111).

was evaluated. The current study findings showed that while PASS and GAPP demonstrated moderate sensitivity, M-GAPP provided higher specificity and NPV, making it more reliable for excluding aggressive behaviour.



[Table/Fig-14]: SDHB IHC in pheochromocytoma; a) Retained granular cytoplasmic staining in tumour cells; b) Complete loss of staining in tumour cells with positive internal control in endothelial cells (400X).

Scoring system	Cut-off value	No. of cases above cut-off n (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
PASS	≥ 4	40 (36.0)	55.6	67.6	13.2	94.5
GAPP	≥ 3	68 (61.3)	66.7	59.8	12.8	95.3
M-GAPP	High risk*	34 (30.6)	55.6	71.4	14.7	98.0

[Table/Fig-15]: Distribution of cases according to PASS, GAPP, and M-GAPP scores.

Scoring System	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
PASS	55.6	67.6	13.2	94.5
GAPP	66.7	59.8	12.8	95.3
M-GAPP	55.6	71.4	14.7	98.0

[Table/Fig-16]: Diagnostic performance of PASS, GAPP, and M-GAPP.

Previous studies have reported variable predictive accuracy for PASS. Thompson originally proposed PASS ≥4 as a cut-off [4], but subsequent studies, including those by Kimura N et al., [6] and Wu D et al., [7], found inconsistent sensitivity and specificity. In the present series, PASS had limited utility (sensitivity 55.56%, specificity 67.60%), consistent with these reports.

Similarly, GAPP, which incorporates histological features with Ki-67 and catecholamine phenotype, has been shown to improve risk stratification [6]. However, several studies noted low reproducibility across populations [9,10]. In the present study, GAPP achieved higher sensitivity (66.67%) but lower specificity (59.80%), reflecting its limitations in excluding malignancy.

The inclusion of SDHB IHC in M-GAPP has been reported to improve prognostic accuracy, particularly in patients with germline mutations and syndromic associations [11,8]. The present series findings support this observation, as loss of SDHB was noted in five metastatic cases, and M-GAPP showed the highest specificity (71.40%) and NPV (98.00%). ROC analysis further demonstrated that M-GAPP had the largest AUC compared to PASS and GAPP. The comparative performance of PASS, GAPP, and M-GAPP across published studies is summarised in [Table/Fig-17].

The present series findings closely parallel the observations of Wu D et al., [7] and Kimura N et al., [6], who reported moderate sensitivity and specificity for PASS. GAPP showed consistently higher sensitivity

Authors (Year of study)	Scoring system	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Key observations
Present study (2025)	PASS	≥4	55.56	67.60	13.20	94.50	Moderate sensitivity and specificity; high NPV; comedo-type necrosis significant
	GAPP	≥3	66.67	59.80	12.80	95.30	Slightly higher sensitivity than PASS but lower specificity
	M-GAPP	≥3	55.56	71.40	14.70	98.00	Highest specificity and NPV; SDHB loss seen in >50% metastatic cases
Wu D et al., (2015) [7]	PASS	≥4	55.00	72.00	18.00	94.00	PASS overestimated risk in some benign cases
Kimura N et al., (2014) [6]	PASS	≥4	60.00	67.00	20.00	93.00	Comparable specificity; moderate sensitivity
Koh JM et al., (2017) [9]	GAPP	≥3	65.00	60.00	15.00	94.00	Similar sensitivity to present study; reproducibility issues
Amar L et al., (2005) [10]	GAPP	≥3	68.00	59.00	14.00	95.00	Catecholamine phenotype inclusion improved model fit

Gill AJ et al., (2010) [11]	M-GAPP	≥3	56.00	73.00	16.00	97.00	SDHB loss significantly correlated with metastasis
Van Nederveen FH et al., (2009) [8]	M-GAPP	≥3	58.00	72.00	15.00	97.00	Supports adding SDHB IHC to improve prediction

[Table/Fig-17]: Comparative diagnostic performance of PASS, GAPP, and Modified GAPP (M-GAPP) scoring systems in predicting malignant potential of adrenal pheochromocytomas across different studies.

but limited specificity across studies by Koh JM et al., [9] and Amar L et al., [10], like our results. Importantly, Van Nederveen FH et al. [8] and Gill AJ et al., [11] also demonstrated that M-GAPP, through incorporation of SDHB IHC, significantly improved specificity and NPV, which agrees with current findings.

Among histological features, comedo-type necrosis was significantly associated with metastasis (p-value=0.008), echoing findings from previous studies [12,13]. Other features, such as vascular invasion, capsular invasion, and cellular monotony, showed trends but did not reach statistical significance, consistent with prior literature [13].

Syndromic cases in the present study (VHL,MEN2,NF1,SDHD) largely paralleled international reports, where VHL mutation carriers have increased metastatic risk [16-18]. Although numbers were small, current results highlight the importance of integrating clinical, genetic, and morphological data in risk assessment.

Limitation(s)

Its retrospective, single-centre nature and the small number of metastatic events, may limit statistical power and generalisability. Nevertheless, current findings contribute valuable insights from an Indian single Institution series and underscore the practical value of incorporating SDHB IHC into the routine evaluation of pheochromocytomas. Future multi-institutional studies with larger sample sizes are warranted to confirm these results and to refine prognostic stratification systems.

CONCLUSION(S)

In this Indian single Institution series, the M-GAPP score, incorporating succinate dehydrogenase subunit B immunohistochemistry, outperformed both PASS and GAPP in predicting the malignant potential of adrenal pheochromocytomas. While PASS and GAPP demonstrated only moderate sensitivity and specificity, M-GAPP provided higher specificity and negative predictive value, making it more reliable for excluding aggressive tumours. Incorporating SDHB IHC into routine histopathological assessment may therefore, enhance prognostic risk stratification and guide long-term surveillance.

REFERENCES

[1] Beard CM, Sheps SG, Kurland LT, Carney JA, Lie JT. Occurrence of pheochromocytoma in Rochester, Minnesota, 1950-1979. Mayo Clin Proc. 1983;58(12):802-04.
[2] Neumann HPH, Young WF Jr, Eng C. Pheochromocytoma and paraganglioma. N Engl J Med. 2019;381(6):552-65.
[3] Lam AK. Update on adrenal tumours in 2017 World Health Organization (WHO) of Endocrine Tumours. Endocr Pathol. 2017;28(3):213-27.
[4] Thompson LDR. Pheochromocytoma of the adrenal gland scaled score (PASS) to separate benign from malignant neoplasms. Am J Surg Pathol. 2002;26(5):551-66.
[5] Strong VE, Kennedy T, Al-Ahmadie H, Tang L, Coleman J, Fong Y, et al. Prognostic indicators of malignancy in adrenal pheochromocytomas: Clinical, histopathologic, and cell cycle/apoptosis markers. Surgery. 2008;143(6):759-68.
[6][Kimura N, Takayanagi R, Takizawa N, Itagaki E, Katabami T, Kakoi N, et al. Pathological grading for predicting metastasis in phaeochromocytoma and paraganglioma. Endocr Relat Cancer. 2014;21(3):405-14.
[7] Wu D, Tischler AS, Lloyd RV, DeLellis RA, de Krijger R, van Nederveen F, et al. Observer variation in the application of the PASS and GAPP scoring systems. Am J Surg Pathol. 2015;39(6):759-64.
[8] Van Nederveen FH, Gaal J, Favier J, Korpershoek E, Oldenburg RA, de Bruyn EM, et al. An immunohistochemical procedure to detect patients with paraganglioma and SDHB germline mutations: A multicentre test of 200 cases. Lancet Oncol. 2009;10(8):764-71.
[9] Koh JM, Ahn SH, Kim H, Kim BJ, Sung TY, Kim YH, et al. Validation of pathological grading systems for predicting metastatic potential in pheochromocytoma and paraganglioma. PLoS One. 2017;12(11):e0187398.
[10] Amar L, Bertherat J, Baudin E, Ajzenberg C, Bressac-de Paillerets B, Chabre O, et al. Genetic testing in pheochromocytoma or functional paraganglioma. J Clin Oncol. 2005;23(34):8812-18.
[11] Gill AJ, Benn DE, Chou A, Clarkson A, Muljono A, Meyer-Rochow GY, et al. Immunohistochemistry for SDHB triages genetic testing of SDHB, SDHC and SDHD in paraganglioma–pheochromocytoma syndromes. Hum Pathol. 2010;41(6):805-14.
[12] Cho YY, Kwak MK, Lee SE, Ahn SH, Kim H, Park DJ, et al. A clinical score to predict metastatic potential of pheochromocytomas and paragangliomas. J Clin Endocrinol Metab. 2016;101(12):4794-802.
[13] Liu T, Brown TC, Juhlin CC, Stenman A, Stålberg P, Åkerström G, et al. Histopathological predictors of malignant pheochromocytomas: A systematic review and meta-analysis. Endocr Pathol. 2018;29(6):459-68.
[14] Fassnacht M, Arlt W, Bancos I, Dralle H, Newell-Price J, Sahdev A, et al. Management of adrenal incidentalomas: European Society of Endocrinology Clinical Practice Guideline. Eur J Endocrinol. 2016;175(2):G1-G34.
[15] Neumann HP, Bausch B, McWhinney SR, Bender BU, Gimm O, Franke G, et al. Germline mutations in nonsyndromic pheochromocytoma. N Engl J Med. 2002;346(19):1459-66.
[16] Walther MM, Reiter R, Keiser HR, Choyke PL, Venzon D, Hurley K, et al. Clinical and genetic characterization of pheochromocytoma in von Hippel–Lindau families: Comparison with sporadic pheochromocytoma gives insight into natural history. J Urol. 1999;162(3 Pt 1):659-64.
[17] Van Leeuwaarde RS, Ahmad S, Links TP, Giles RH. Von Hippel–Lindau Syndrome. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018.
[18] Eisenhofer G, Walther MM, Huynh TT, Li ST, Bornstein SR, Vortmeyer A, et al. Pheochromocytomas in von Hippel–Lindau syndrome and multiple endocrine neoplasia type 2 display distinct biochemical and clinical phenotypes. J Clin Endocrinol Metab. 2001;86(5):1999-2008.

PARTICULARS OF CONTRIBUTORS:
1. Consultant Pathologist, Department of Pathology, Satribari Christian Hospital, Guwahati, Assam, India.
2. Professor, Department of General Pathology, Christian Medical College and Hospital, Vellore, Tamil Nadu, India.
3. Associate Professor, Department of General Pathology, Christian Medical College and Hospital, Vellore, Tamil Nadu, India.
4. Professor, Department of General Pathology, Christian Medical College and Hospital, Vellore, Tamil Nadu, India.
5. Associate Professor, Department of Endocrine Surgery, Christian Medical College and Hospital, Vellore, Tamil Nadu, India.
6. Professor, Department of Endocrine Surgery, Christian Medical College and Hospital, Vellore, Tamil Nadu, India.
7. Professor, Department of Endocrine Surgery, Christian Medical College and Hospital, Vellore, Tamil Nadu, India.
8. Professor, Department of Endocrine Surgery, American Mission Hospital, Manama, Kingdom of Bahrain, Manama, Bahrain.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Elanthenral Sigmani,
Fourth Floor, ASHA Building, CMC Hospital, Vellore-632002, Tamil Nadu, India.
E-mail: sethenral@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jun 09, 2025
- Manual Googling: Oct 09, 2025
- iThenticate Software: Oct 11, 2025 (10%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? No
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **May 27, 2025**
Date of Peer Review: **Aug 01, 2025**
Date of Acceptance: **Oct 14, 2025**
Date of Publishing: **Feb 01, 2026**