



Original Article

Clinicopathological correlation of ocular pigmented lesions

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ABSTRACT

Background: Ocular pigmented lesions, ranging from benign nevi to malignant melanomas, present a diagnostic challenge due to their varied clinical appearance. This study aimed to establish a definitive diagnosis correlating epidemiological, clinical, and histomorphological features of these lesions.

Materials and Methods: A hospital-based cross-sectional study was conducted from September 2021 to February 2023, over 18 months at Universal College of Medical Sciences and Teaching Hospital. After ethical clearance (Reference number: UCMS/IRC/108/21), 42 cases of ocular pigmented lesions received in the Department of Pathology were evaluated histologically using Hematoxylin and Eosin-stained sections. Statistical analysis of the data was performed using Statistical Package of the Social Sciences version 25.

Results: Of 42 patients (25 females, 17 males; mean age 26.36 ± 18.15 years), the vast majority, 40 (95.2%), were diagnosed as benign nevi, with only two cases (4.8%) of malignant melanoma. The most common lesion was compound nevus 20 (47.6%), followed by subepithelial nevus 14 (33.3%). Bulbar conjunctiva 19 (45.2%) and eyelid 18 (42.8%) were the predominant sites. Most lesions presented as a nodular 24 (57.1%), light-brown 22 (52.4%) mass or spot. Clinical diagnosis of nevus showed 100% concordance with histopathology, whereas clinical suspicion of melanoma had a low concordance (33.3%), with many such cases turning out to be nevi on histology.

Conclusions: Histopathological examination remains the gold standard for accurate diagnosis of ocular pigmented lesions. While benign nevi are far more common and typically affect a younger demographic, clinical features alone can be misleading, especially in suspected melanoma cases. High index of suspicion and routine biopsy are imperative for correct diagnosis and management.

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INTRODUCTION

Pigmented ocular and peri-ocular lesions arise in the eyelid, conjunctiva, sclera, iris, ciliary body, choroid, or retina. They range from benign nevi to highly malignant melanomas and represent an important diagnostic challenge in ophthalmic pathology. Among these, conjunctival melanocytic lesions are most common, accounting for about half of all conjunctival neoplasms.¹ Choroidal melanocytic proliferations constitute the most frequent primary intraocular tumors, whereas eyelid lesions include both benign and malignant entities; basal cell and squamous

cell carcinomas together form roughly one-third of eyelid tumors, while malignant melanoma represents only about one percent.²

Ocular melanoma (OM), though rare, is an aggressive malignancy responsible for approximately 3–5% of all melanomas and predominantly involves the uveal tract (\approx 85 % of ocular cases).^{3,4} Reported risk factors include fair skin, ultraviolet radiation exposure, increasing age, viral infection, smoking, and chemical exposure.⁵ Eyelid melanomas that extend to the conjunctiva are noted to behave more invasively than those limited to the eyelid skin.⁵ In contrast, ocular nevi are common benign melanocytic proliferations, particularly of the conjunctiva, caruncle, and choroid. They are usually flat or slightly raised and occur mostly in children and young adults.^{6–8} Although typically benign, a small proportion may undergo malignant transformation, especially lesions thicker than 2 mm, symptomatic lesions, or those located near the optic disc.⁹ The reported lifetime risk of malignant transformation of choroidal nevus to melanoma is about one in 8,800 in white populations.¹⁰

Because many pigmented ocular lesions display overlapping clinical features, histopathological examination (HPE) remains the gold standard for confirming diagnosis and assessing dysplasia, invasion, and malignant potential.¹¹ Early recognition of malignant transformation is crucial for appropriate management and improved prognosis. Despite their clinical significance, comprehensive studies correlating the clinical and histopathological features of all ocular pigmented lesions from a single population are scarce. This study aimed to bridge this gap by analyzing the epidemiological, clinical, and histomorphological spectrum of ocular pigmented lesions to establish an accurate diagnosis and highlight the importance of clinicopathological correlation.

MATERIALS AND METHODS

This hospital-based cross-sectional study was conducted in the Department of Pathology and Department of Ophthalmology at Universal College of Medical Sciences and Teaching Hospital (UCMS-TH), Bhairahawa, Nepal, from September 2021 to February 2023, taking ethical approval from the Institutional Review Committee (Ref.: UCMS/IRC/108/21). Participants were informed about the study objectives, and confidentiality of their data was assured. No interventions were performed, and the study posed no risk to participants. A total of 42 participants who underwent biopsy of the lesion in the eye, undergoing excision and incisions, were included in the study based on inclusion and exclusion criteria using a convenience sampling technique. All biopsy-proven cases of ocular pigmented lesions received in the department were included. Improperly labeled specimens, autolyzed tissues, inadequate biopsies, previously treated cases, and patients unwilling to provide consent were excluded from the study. Written informed consent was obtained from all participants prior to enrollment.

Sample size was calculated based on Cochran's formula at 95% level of significance and allowable error at 10%. The calculated sample size was 41.72, rounded up to a minimum of 42 participants.

Demographic details (age, sex, occupation), clinical features (mass, dark spots, diminution or loss of vision, ocular pain, and duration of symptoms), laterality, and site of lesion were recorded in a structured proforma. Clinical diagnoses were retrieved from ophthalmology case records.

Biopsyspecimens were fixed in 10% neutral buffered formalin, grossed, and processed routinely by an automated tissue processor (Leica TP1020). Paraffin blocks were prepared, and 4 μ m-thick sections were cut using a Leica RM2255 rotary microtome. Slides were stained with hematoxylin and eosin (H&E) according to standard protocols and mounted in DPX. All slides were independently examined under an Olympus BX-53 microscope by two pathologists, and representative photomicrographs were taken.

Histopathological evaluation included assessment of epithelial changes (erosion, ulceration, dysplasia), cellular features (pigmented cells, mitotic figures, necrosis, pleomorphism), and invasion. Standard definitions were applied for parameters such as ulceration, dysplasia, and neoplastic infiltration as per the WHO classification of ocular tumors (5th Edition). Clinicopathological correlation was noted when clinical and histopathological diagnoses matched.

Data were entered, cleaned, and coded in Microsoft Excel and analyzed using Statistical Package of the Social Sciences version 25. Results were expressed as frequency, percentage, mean, and standard deviation. Associations between variables were tested using the chi-square test as advised by the statistician. A p-value < 0.05 was considered statistically significant. Diagnostic accuracy was calculated by comparing clinical diagnosis with histopathological findings, considering histopathology as the gold standard.

RESULTS

A total of 2,202 biopsies were received at the Department of Pathology, UCMS-TH over 18 months from September 2021 to February 2023. Among those, 161 (5%) were ocular lesions and 42 (2%) were ocular pigmented lesions, which served as the basis for this study. The age of 42 patients ranged from 4 to 75 years (mean 26.36 ± 18.15 years); nearly half, 19 (45.2%), were aged \leq 20 years, followed by 21–30 years, 11 (26.2%), and 31–40 years, 6 (14.3%). Females, 25 (59.5%), outnumbered males, 17 (40.5%), with a male: female ratio of 0.6:1. Most patients were indoor workers, 34 (81%), and of the Hindu religion, 33 (78.6%). Only 3 (7%) patients reported a history of medication use.

Clinically, the commonest presenting symptom was a dark spot, 21 (50%), followed by a mass, 18 (42.9%);

diminution or loss of vision and ocular pain each accounted for one (2.4%) case. Duration of symptoms was greater than 12 months in 17 (40.5%) patients, less than 6 months in 16 (38.1%), and 6 to 12 months in 9 (21.4%) patients. The left eye was involved in 24 (57.1%) cases, the right eye in 17 (40.5%) cases, and both eyes in 1 (2.4%) case. Regarding anatomical location, bulbar conjunctiva (nasal quadrant) was the most common site, 12 (28.5%), followed by bulbar conjunctiva (temporal), 7 (16.7%), upper eyelid, 10 (23.8%), and lower eyelid, 8 (19%). Less common sites included medial canthus, 2 (4.8%), caruncle, 1 (2.4%),

limbus, 1 (2.4%), and choroid, 1 (2.4%). On clinical appearance, lesions were nodular in 24 (57.1%), flat in 9 (21.4%), papilliform in 8 (19.0%), and diffuse in 1 (2.4%). Clinically, the lesions most frequently appeared light brown, 22 (52.4%), then dark brown, 12 (28.6%), black, 6 (14.3%), and greyish-white, 2 (4.8%). Gross size was 0–10 mm in 39 (92.8%), 11–20 mm in 2 (4.8%), and > 20 mm in 1 (2.4%). Regarding origin, 27 (64.3%) lesions were acquired, and 15 (35.7%) were congenital. Histopathologically, 40 (95.2%) lesions were benign and 2 (4.8%) malignant.

Table 1: Cross-tabulation between the site of lesion and presenting symptoms

Site of lesion	Presenting Symptoms					Total
	Mass n (%)	Dark Spot n (%)	Diminution of vision n (%)	Vision Loss n (%)	Ocular Pain n (%)	
Conjunctiva	3 (15.8%)	14 (73.7%)	1 (5.3%)	0 (0.0%)	1 (5.3%)	19 (45.2%)
Eyelid	13 (72.2%)	5 (27.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	18 (42.8%)
Canthus	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.8%)
Limbus	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)
Uvea	0 (0.0%)	0 (0.0%)	0 (0.0%)	1(100.0%)	0 (0.0%)	1 (2.4%)
Caruncle	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)
Total	18 (42.8%)	21(50.0%)	1 (2.4%)	1 (2.4%)	1 (2.4%)	42 (100.0%)

Table 2: Clinical appearance, color, and size of lesions

Variable	Frequency (n)	Percentage (%)
Clinical appearance		
Nodular	24	57.1
Flat	9	21.4
Papilliform	8	19.0
Diffuse	1	2.4
Clinical color		
Light brown	22	52.4
Dark brown	12	28.6
Black	6	14.3
Greyish-white	2	4.8
Gross size		
0–10 mm	39	92.8
11–20 mm	2	4.8
> 20 mm	1	2.4

Statistical analysis revealed no significant association between age group and site of lesion ($p = 0.59$), nor between age group and nature of lesion (benign vs malignant, $p = 0.98$). There was also no significant association between the site of lesion and the nature of the lesion ($p = 0.143$). However, a statistically significant association was found between occupation (indoor vs outdoor) and nature of lesion (Benign and Malignant) ($p = 0.008$) and between religion and nature of lesion ($p = 0.011$). The majority of patients were Hindu, and all 33 (100%) lesions were benign. Out of the other 9 Muslim patients, 7 (77.8%) lesions were benign.

Site of lesion and clinical appearance were significantly associated ($p = 0.007$), as lesions in the eyelid were more frequently nodular/papilliform and those in the conjunctiva more frequently flat/nodular. In histopathological features, dysplasia was significantly associated with lesion site ($p = 0.005$), and invasion was significantly associated with histopathological diagnosis (malignant melanomas, $p = 0.013$).

Table 3: Histopathological diagnosis of ocular pigmented lesions (n = 42)

Histopathological subtype	Frequency (n)	Percentage (%)
Compound nevus	20	47.6
Subepithelial nevus	14	33.3
Junctional nevus	4	9.5
Dysplastic nevus	1	2.4
IJCN	1	2.4
Malignant melanoma	2	4.8
Total	42	100%

DISCUSSION

The present study shows that ocular pigmented lesions are predominantly benign and most commonly involve the conjunctiva, a pattern consistently reported across diverse populations. Studies by Shields et al. and García et al. similarly identified the conjunctiva as the principal site of melanocytic lesions, supporting the view that this ocular surface is particularly susceptible to melanocytic proliferation.^{13,14} The predominance of benign nevi in our

series aligns with international reports, where malignant melanoma represents only a small proportion of ocular pigmented lesions.^{15,16}

The younger age distribution observed in this study parallels findings from Alkatan et al. and Shields et al., who noted that conjunctival nevi are more frequently diagnosed in children and young adults.^{17,18} This trend likely reflects earlier clinical detection due to cosmetic visibility rather than biological aggressiveness. The female predominance observed in our cohort has also been documented by Lin et al. and Grossniklaus et al., and may be influenced by health-seeking behavior rather than true sex predilection.^{19,20}

Occupational exposure emerged as a relevant contextual factor when interpreted alongside existing literature. Although most lesions occurred in indoor workers, malignant lesions were restricted to outdoor workers, a finding that supports epidemiological studies linking ultraviolet exposure with ocular melanoma risk.^{21,22} Vajdic et al. also demonstrated increased melanoma risk among individuals with prolonged sunlight exposure, reinforcing the potential role of UV radiation in malignant transformation of ocular melanocytic lesions.²³

Clinically, the presenting features of pigmented spots or mass lesions are in agreement with descriptions by Shields et al. and Urban et al.^{18,24} However, as highlighted in previous studies, clinical appearance alone is insufficient to reliably distinguish benign from malignant lesions.²⁵ This limitation was evident in our series, where a proportion of clinically suspected melanomas were not confirmed histologically. Similar diagnostic discordance has been emphasized by Shields et al., underscoring the indispensable role of histopathological evaluation.¹⁸

Histologically, the predominance of compound and subepithelial nevi mirrors findings from Alkatan et al., Grossniklaus et al., and Negretti et al.^{17,20,26} Lesions were mostly nodular or flat and light brown in color, similar to reports by Bogdanici et al. and Sayyad et al.^{27,28} Junctional and dysplastic nevi were infrequent, consistent with their reported rarity in ocular tissues compared with cutaneous sites. Malignant melanoma in our study showed histological features traditionally associated with aggressive behavior, including invasion and necrosis, findings comparable to those described by Kaliki et al. and other series.^{16,29} The occasional presence of tumor-infiltrating lymphocytes may reflect host immune response, as suggested in earlier studies, and may have prognostic relevance, although its significance in ocular melanoma requires further clarification.³⁰

The preferential involvement of the bulbar conjunctiva, particularly the nasal quadrant, has been attributed in prior studies to patterns of sunlight exposure.²² This anatomical distribution has also been reported in studies from Japan and Denmark, suggesting that environmental factors may exert similar effects across different geographic regions.^{31,32} The

significant association between dysplasia and conjunctival location observed in this study is consistent with findings by Fattahi et al. and further supports the need for close surveillance of conjunctival pigmented lesions.³³

Overall, the findings of this study are in concordance with existing literature, reinforcing that most ocular pigmented lesions are benign and clinically indolent. Nevertheless, the overlap in clinical features between benign and malignant lesions highlights the importance of histopathological confirmation. While malignant melanoma was uncommon, its association with outdoor occupation and aggressive histological features emphasizes the need for early biopsy and vigilant follow-up. Future large-scale, multicentric studies are required to better delineate environmental and demographic risk factors, particularly the contribution of UV exposure in the Nepalese population.

This study has several limitations, including its cross-sectional design and limited time frame. Further treatment and outcome of the case were not followed. The relatively small sample size and single-center study may not reflect the whole population. Accurate diagnosis of the lesion was limited by the immunohistochemistry facilities.

CONCLUSIONS

This study demonstrated a strong clinicopathological correlation in ocular pigmented lesions, with most cases being benign nevi, particularly compound type, predominantly involving the bulbar conjunctiva. Malignant melanoma was rare and occurred in older patients with larger, extrabulbar lesions. Histopathological examination proved essential for confirming diagnosis, evaluating dysplasia, and distinguishing benign from malignant lesions, especially in clinically ambiguous cases. Clinical diagnosis showed high accuracy for benign lesions but tended to overestimate malignancy in a few cases. Overall, the pattern and distribution of lesions in this study were comparable to global findings.

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