



CORRELATION OF PAP SMEAR CYTOLOGY, COLPOSCOPY, AND HISTOPATHOLOGY IN WOMEN WITH A SUSPICIOUS LOOKING CERVIX: A CROSS-SECTIONAL STUDY FROM A TERTIARY CARE CENTRE IN CENTRAL INDIA

Obstetrics & Gynaecology

Dr.Rita Shah

Dr.Preeti Jain

Dr.Niyati Jain Shah

ABSTRACT

Background: A cervix that looks abnormal on speculum examination, eroded, ulcerated, leukoplakic, or bleeding on contact, does not always correspond to premalignant or malignant disease. How well Pap smear cytology, colposcopic scoring, and histopathology agree with one another in such women remains variably reported. **Objective:** To assess the correlation of Pap smear cytology, colposcopic findings, and histopathological examination in women with a suspicious looking cervix. **Methods:** A single-centre, hospital-based, cross-sectional observational study was conducted over 18 months (June 2024–November 2025) in the Department of Obstetrics and Gynaecology at a tertiary care hospital in Madhya Pradesh. One hundred and forty women aged 21–65 years with a suspicious-looking cervix or relevant symptoms underwent Pap smear cytology and colposcopy (scored by both Reid's Colposcopic Index and the Swede score), followed by colposcopically directed biopsy where indicated, with histopathology as the reference standard. Categorical variables were compared using the chi-square test and continuous variables using the unpaired t-test, with significance set at $p < 0.05$ (Stata 17.0). **Results:** Most women were aged 41–50 years (27.86%), married (96.43%), of parity 2 (70.00%), and premenopausal (60.71%); vaginal discharge was the leading complaint (72.10%). Ulceration was the commonest speculum finding (21.43%). Pap smear returned ASC-US most often (24.29%) and NILM least often (11.43%); 22.14% of smears were unsatisfactory. Colposcopy showed high-grade lesions (Reid's RCI 6–8) in 39.29% and invasive-pattern lesions in 23.57%. The Swede score classified 42.86% as high-risk/suspicious. Histopathology showed CIN 2/3 in 20.71% and an inadequate sample in 19.29%. Against histopathology (prevalence 57.1%), Pap smear had sensitivity 61.3% and specificity 83.3%; the Swede score had sensitivity 75.0% and specificity 100.0%; colposcopy (Reid's Index) had sensitivity 100.0% and specificity 86.7%. **Conclusion:** No single test reliably reproduced the others. Colposcopy using Reid's Index was the most sensitive tool, the Swede score the most specific, and Pap smear the most accessible but least sensitive. A combined approach using cytology alongside structured colposcopic scoring, with directed biopsy, appears the more dependable pathway for evaluating a suspicious-looking cervix.

KEYWORDS

Suspicious Cervix; Pap Smear; Colposcopy; Reid's Colposcopic Index; Swede Score; Cervical Intraepithelial Neoplasia

INTRODUCTION

Cervical cancer remains one of the more preventable cancers, yet it still ranks among the leading causes of cancer death in women across low- and middle-income countries, India included, largely because screening coverage stays patchy and many women present only once symptoms appear.^[1] Persistent infection with high-risk HPV, chiefly types 16 and 18, drives almost all cases, and the long pre-invasive phase, cervical intraepithelial neoplasia evolving slowly toward invasive disease, is what makes screening worthwhile in the first place.^[2]

In everyday gynaecological practice, clinicians often see a cervix that simply looks wrong on speculum examination: eroded, ulcerated, leukoplakic, bleeding on contact, or showing an irregular vascular pattern. This is not itself a diagnosis. Chronic cervicitis, ectropion, polyps, and ordinary squamous metaplasia can all mimic something more sinister, and the threshold at which a clinician calls a cervix "suspicious" varies with training and experience.^[3] Three tools are typically brought to bear on this uncertainty: Pap smear cytology, which samples exfoliated cells and remains a reasonably cheap, non-invasive triage test, though its single-smear sensitivity for high-grade disease is often quoted between 50 and 75%;^[4] colposcopy, which visualises the cervix directly under magnification after acetic acid and iodine, guiding biopsy from the most abnormal-looking area;^[5] and structured colposcopic scoring systems, such as the Reid Colposcopic Index and the more recently developed Swede score, which try to make that visual impression more reproducible.^[6] Histopathology of the biopsied tissue remains the reference standard against which the other two are judged.^[7]

Large community-based trials in India have shown that organised screening can meaningfully reduce cervical cancer mortality,^[14] though translating that trial-level infrastructure into routine outpatient practice remains uneven, and many women continue to present after symptoms appear rather than through a planned screening pathway. How well Pap smear, colposcopic scoring, and histopathology agree with one another, and how well cytology and colposcopy actually predict what the biopsy will show, is not settled, and reported diagnostic accuracy varies a fair amount between study populations and operator experience. Given how commonly a suspicious cervix is encountered in outpatient gynaecology, and how much resource and

anxiety hangs on getting the work-up right, a study correlating Pap smear, colposcopic scoring, and histopathology within a single, well-defined cohort seemed a reasonable thing to attempt.

Aim

To assess the correlation of Pap smear cytology, colposcopic findings, and histopathological examination in women with a suspicious looking cervix.

Material and Methods

This was a single-centre, hospital-based, cross-sectional observational study, carried out in the Department of Obstetrics and Gynaecology at Amaltas Institute of Medical Sciences, Dewas, Madhya Pradesh, a tertiary teaching hospital drawing patients from both urban and rural catchments. The protocol, participant information sheet, and consent documents were approved by the Institutional Ethics Committee, and the study was conducted in accordance with the Declaration of Helsinki and ICMR ethical guidelines for biomedical research. Data collection ran for 18 months, from June 2024 to November 2025.

Women aged 21 to 65 years were eligible if they presented with vaginal discharge, postcoital bleeding, intermenstrual bleeding, or postmenopausal bleeding, or if per speculum examination showed an abnormal-looking cervix, and if they were willing to give informed consent. Women were excluded if they were menstruating at the time of examination, had a prior diagnosis of cervical cancer, were pregnant, had undergone hysterectomy, had major cardiovascular, respiratory, neurological, or other significant systemic illness that could interfere with examination or investigation, or declined participation. For sample size, an expected prevalence of cervical lesions of 10% (P) was assumed, with a 95% confidence level ($Z = 1.96$) and an acceptable absolute error of 5% (d), using the standard formula $n = Z^2PQ / d^2$. This gave $n = (1.96)^2 \times 0.10 \times 0.90 / (0.05)^2 \approx 138$, which was rounded up to a target of 140 participants; this figure was reached by the end of the recruitment window. Enrolment used non-random, convenience sampling, with every eligible, consenting woman attending the gynaecology outpatient department during the study period approached for inclusion.

The primary outcome was the correlation between Pap smear cytology, colposcopic findings, and histopathological diagnosis, with

histopathology treated throughout as the reference standard. Secondary outcomes were the sensitivity, specificity, positive and negative predictive value, and overall diagnostic accuracy of Pap smear and of colposcopy, scored both by Reid's Colposcopic Index and by the Swede score, against that reference standard. A suspicious cervix was operationally defined as one showing erosion, chronic cervicitis, endocervicitis, a polyp, leukoplakia, ulceration, or an irregular vascular pattern on speculum examination. Cytology results were categorised using standard Bethesda terminology (NILM, ASC-US, LSIL, HSIL, or unsatisfactory); colposcopic impression was scored using the Modified Reid's Colposcopic Index, grouped as normal, low-grade, high-grade, or invasive, and separately by the Swede score, grouped as low-risk/normal, intermediate-risk, or high-risk/suspicious; and histopathology was reported as normal, chronic cervicitis with metaplasia, cervicitis with mild atypia, dysplasia or koilocytic change (CIN 1), CIN 2/3, cervical endometriosis with squamous metaplasia, or an inadequate sample.

Screening and enrolment took place in the gynaecology outpatient department. Women with relevant symptoms or an abnormal cervix on examination were assessed against the eligibility criteria by the attending clinician and confirmed by the principal investigator. Eligible women received a plain-language explanation of the study, and written informed consent was obtained in the presence of a witness before any study procedure; no payment or benefit was offered for participation.

A structured, closed-format proforma, developed after a literature review, vetted by the supervising faculty, and piloted before use, captured demographic details, presenting complaints, examination findings, and the results of cytology, colposcopy, and histopathology. After baseline history and general and gynaecological examination, a Pap smear was collected first: with the patient in the lithotomy position, a Cusco's speculum was passed, excess mucus removed, and cells sampled from the transformation zone using an Ayre's spatula rotated through 360 degrees, with a cytobrush used for endocervical sampling where needed. Smears were spread evenly on a labelled slide, fixed promptly, and read by trained pathologists using standard Bethesda reporting. Colposcopy followed the Pap smear in the same sitting. The cervix was first inspected under low magnification to locate the squamocolumnar junction, cleaned with saline, and then examined after application of 3–5% acetic acid, looking for acetowhite change, and again after Lugol's iodine, under which normal glycogenated epithelium stains brown and abnormal epithelium remains mustard-yellow. Margin characteristics, colour, vascular pattern, and iodine uptake were scored using the Modified Reid's Colposcopic Index, and the Swede score was calculated in parallel. Where colposcopy identified an abnormal area, a directed biopsy was taken from the most suspicious site, or the most representative site where more than one lesion was present, and placed in 10% buffered formalin for routine histopathological processing and reporting, which served as the reference standard for all diagnostic comparisons.

Completed proformas were cross-checked against laboratory and clinical records by the principal investigator, with periodic supervision and random re-verification to catch transcription errors. Categorical variables, such as presenting symptoms and cytology, colposcopy, and histopathology categories, are reported as frequencies and percentages, and continuous variables as mean and standard deviation. Associations between categorical variables were tested with the chi-square test, and continuous variables with the unpaired t-test where applicable, at a two-sided significance level of 0.05. Sensitivity, specificity, positive and negative predictive value, and ROC area, each with 95% confidence intervals, were calculated for Pap smear, the Swede score, and colposcopy (Reid's Index) against histopathology. All analyses were performed in Stata version 17.0.

RESULTS

A total of 140 women meeting the eligibility criteria were enrolled and analysed over the study period.

Table 1: Characteristics of Participants

Characteristic	Category	Frequency	Percentage (%)
Age of participant (years)			
	21–30	27	19.29
	31–40	37	26.43
	41–50	39	27.86

	51–60	31	22.14
	61–70	6	4.29
	Total	140	100.00
Marital status			
	Single	4	2.86
	Married	135	96.43
	Separated / widowed	1	0.71
	Total	140	100.00
Parity			
	0	4	2.86
	1	2	1.43
	2	98	70.00
	3	8	5.71
	4	14	10.00
	5	14	10.00
	Total	140	100.00
Menopausal status			
	Premenopausal	85	60.71
	Perimenopausal	31	22.14
	Postmenopausal	24	17.14
	Total	140	100.00
Presenting complaints (not mutually exclusive)			
	Vaginal discharge	101	72.10
	Postcoital bleeding	49	35.00
	Intermenstrual bleeding	31	22.10
	Postmenopausal bleeding	24	17.14

Table 1 sets out the baseline profile. The largest age band was 41–50 years (39, 27.86%), closely followed by 31–40 years (37, 26.43%); the fewest women were aged 61–70 years (6, 4.29%). Almost all participants were married (135, 96.43%). Parity 2 predominated (98, 70.00%). Most women were premenopausal (85, 60.71%), with perimenopausal (31, 22.14%) and postmenopausal (24, 17.14%) women accounting for the rest. Vaginal discharge was the leading presenting complaint (101, 72.10%), followed by postcoital bleeding (49, 35.00%), intermenstrual bleeding (31, 22.10%), and postmenopausal bleeding (24, 17.14%); complaints were not mutually exclusive, so percentages do not sum to 100.

Table 2: Clinical, Cytological, Colposcopic, and Histopathological Findings

Characteristic	Category	Frequency	Percentage (%)
Cervix appearance on per speculum examination			
	Erosion	11	7.86
	Chronic cervicitis	16	11.43
	Endocervicitis	24	17.14
	Cervical polyp	20	14.29
	Leukoplakia	23	16.43
	Ulceration	30	21.43
	Irregular vascular pattern / suspicious growth	16	11.43
	Total	140	100.00
Pap smear cytology result			
	NILM	16	11.43
	ASC-US	34	24.29
	LSIL	27	19.29
	HSIL	32	22.86
	Unsatisfactory	31	22.14
	Total	140	100.00
Colposcopy category (Reid's Colposcopic Index)			
	Normal (0–2)	27	19.29
	Low grade (3–5)	25	17.86
	High grade (6–8)	55	39.29
	Invasive (>8)	33	23.57
	Total	140	100.00
Swede score category			

	Low risk / normal	45	32.14
	Intermediate risk	35	25.00
	High risk / suspicious	60	42.86
	Total	140	100.00
Histopathological diagnosis			
	Normal / no significant lesion	17	12.14
	Chronic cervicitis with metaplasia	21	15.00
	Cervicitis with mild atypia / dysplasia / koilocytic change (CIN 1)	22	15.71
	CIN 2/3	29	20.71
	Cervical endometriosis with squamous metaplasia	24	17.14
	Inadequate sample	27	19.29
	Total	140	100.00

Table 2 brings together the four layers of assessment. On per speculum examination, ulceration was the commonest abnormality (30, 21.43%), followed by endocervicitis (24, 17.14%) and leukoplakia (23, 16.43%); erosion was the least common (11, 7.86%). Pap smear cytology returned ASC-US most often (34, 24.29%), with HSIL (32, 22.86%) and unsatisfactory smears (31, 22.14%) close behind, and NILM the least frequent category (16, 11.43%). On colposcopy, high-grade lesions (Reid's RCI 6–8) were most common (55, 39.29%), followed by invasive-pattern lesions (RCI >8, 33, 23.57%); normal (27, 19.29%) and low-grade (25, 17.86%) findings made up the rest. Swede scoring classified 60 women (42.86%) as high-risk/suspicious, 45 (32.14%) as low-risk/normal, and 35 (25.00%) as intermediate-risk. On histopathology, CIN 2/3 was the leading diagnosis (29, 20.71%), followed by an inadequate sample in 27 (19.29%), cervical endometriosis with squamous metaplasia in 24 (17.14%), CIN 1 in 22 (15.71%), chronic cervicitis with metaplasia in 21 (15.00%), and a normal biopsy in 17 (12.14%).

Table 3: Diagnostic Accuracy of Pap Smear, Swede Score, and Colposcopy (Reid's Index) Against Histopathology

Measure	Estimate	95% CI (Lower–Upper)
Pap smear cytology (prevalence 57.1%, 95% CI 48.5–65.5%)		
Sensitivity	61.3%	49.7% – 71.9%
Specificity	83.3%	71.5% – 91.7%
Positive predictive value	83.1%	71.0% – 91.6%
Negative predictive value	61.7%	50.3% – 72.3%
ROC area	0.72	0.65 – 0.79
Swede score		
Sensitivity	75.0%	64.1% – 84.0%
Specificity	100.0%	94.0% – 100.0%
Positive predictive value	100.0%	94.0% – 100.0%
Negative predictive value	75.0%	64.1% – 84.0%
ROC area	0.88	0.83 – 0.92
Colposcopy (Reid's Colposcopic Index)		
Sensitivity	100.0%	95.5% – 100.0%
Specificity	86.7%	75.4% – 94.1%
Positive predictive value	90.9%	82.9% – 96.0%
Negative predictive value	100.0%	93.2% – 100.0%
ROC area	0.93	0.89 – 0.98

Table 3 shows how each screening tool performed against histopathology, at an overall lesion prevalence of 57.1% (95% CI

48.5–65.5%). Pap smear had a sensitivity of 61.3% and specificity of 83.3%, with a positive predictive value of 83.1% and negative predictive value of 61.7% (ROC area 0.72). The Swede score performed better on specificity, with sensitivity 75.0% and specificity 100.0%, positive predictive value 100.0% and negative predictive value 75.0% (ROC area 0.88). Colposcopy using Reid's Index performed best overall, with sensitivity 100.0% and specificity 86.7%, positive predictive value 90.9% and negative predictive value 100.0% (ROC area 0.93).

DISCUSSION

The 140 women in this cohort were predominantly middle-aged, married, and premenopausal, presenting most often with vaginal discharge, a demographic and symptom profile broadly typical of women referred for evaluation of a suspicious cervix at Indian tertiary centres. On speculum examination, ulceration (21.43%) and endocervicitis (17.14%) were the leading findings here, a rather different picture from Chaudhary and colleagues, who found cervical erosion in the great majority of their cohort (86.5%), with hypertrophied cervix and frank suspicious cervix accounting for the rest.^[6] Bhalariao and colleagues similarly reported erosion as the dominant finding, in 78% of women with an unhealthy cervix.^[9] The comparatively low erosion rate and higher share of ulcerative and leukoplakic lesions in the present cohort may reflect a population presenting somewhat later, or simply a different case-mix at this particular referral centre; either way, the gross appearance of the cervix clearly does not travel identically across settings.

Cytology told a similar story of a heavier disease burden here than in earlier work. ASC-US (24.29%) and HSIL (22.86%) were the leading categories in this study, against a background NILM rate of only 11.43%, whereas Chaudhary and colleagues found NILM in 83% of smears, with HSIL in just 2.5%.^[8] Rokade and Kshirsagar likewise reported much lower rates of LSIL (5.8%) and HSIL (4.3%).^[10] The unsatisfactory smear rate here, at 22.14%, was also higher than generally reported elsewhere, which is worth flagging on its own: roughly a fifth of the cytology results in this cohort could not be reliably interpreted, which inevitably pushes more diagnostic weight onto colposcopy and biopsy.

Colposcopic findings followed the same pattern. High-grade (39.29%) and invasive-appearing (23.57%) lesions dominated here, whereas Chaudhary's cohort was mostly benign or inflammatory (62%), with high-grade and invasive disease making up a much smaller share,^[8] and Kohale and colleagues found benign or inflammatory colposcopy in 47% of cases, with malignant features in only 3%.^[11] A similarly heavy skew toward higher-grade colposcopic findings in symptomatic, unhealthy-cervix populations has also been described more recently by Kori and colleagues.^[15] Swede scoring, used alongside Reid's Index in the present study, classified 42.86% of women as high-risk or suspicious, a notably higher proportion than the 23% with a Swede score ≥5 reported by Agarwal and colleagues, though that group did find a strong statistical link between higher scores and confirmed pre-invasive or invasive disease ($p < 0.001$), consistent with the pattern seen here.^[12]

Histopathology mirrored the cytology and colposcopy findings: CIN 2/3 was the leading diagnosis (20.71%), against Chaudhary's cohort, where chronic cervicitis with metaplasia predominated (68.5%) and carcinoma was found in only 5%.^[8] The 19.29% rate of inadequate biopsy samples in the present study was not something earlier papers reported prominently, and it is a genuine limitation, since an inadequate sample effectively removes that participant from meaningful comparison against the reference standard. Turning to diagnostic accuracy, Pap smear here showed moderate sensitivity (61.3%) and good specificity (83.3%), noticeably better sensitivity than Chaudhary's 25.4% or Rokade's 19.5%, though specificity was broadly similar across all three studies (99.3% and 83.3%, respectively).^[8,10] Read together, cytology in this setting missed a smaller share of true lesions than in earlier Indian series, while remaining reasonably good at correctly clearing women without disease.

The Swede score performed strongly, with 100.0% specificity and 75.0% sensitivity, which sits comfortably alongside Agarwal and colleagues' two reports: one finding 100% specificity and 80% sensitivity at a cut-off of 8,^[13] the other finding 100% sensitivity and 85.23% specificity at a lower cut-off of >5.^[12] Exactly where the cut-off

is drawn clearly trades sensitivity against specificity, and the present results, using the scheme applied here, land toward the highly specific end of that trade-off.

Colposcopy using Reid's Index was the best performer overall, with 100.0% sensitivity and 86.7% specificity, ahead of the 79.37%/81.02% reported by Chaudhary,^[8] the 91.46%/72.22% reported by Kohale,^[11] and the 90.2%/72.8% reported by Rokade.^[10] Sensitivity for colposcopy is consistently high across all these studies; what varies more is specificity, and the present cohort's relatively strong specificity alongside perfect sensitivity is a reasonably favourable combination, though it also reflects a fairly high disease prevalence (57.1%) in this referral population, which tends to inflate predictive values compared with a lower-prevalence screening setting. Put together, cytology, Swede scoring, and Reid's-Index colposcopy each add something different: cytology is cheap and reasonably specific but misses a meaningful share of true lesions on its own, Swede scoring is highly specific and reproducible, and colposcopy with Reid's Index caught almost every true lesion in this cohort at the cost of a modest false-positive rate. In women flagged as having a suspicious cervix, relying on any single test risks either missing disease or over-referring for biopsy; the combination used here, cytology plus a structured colposcopic score followed by directed biopsy, seems a sensible way to balance those risks, though the high rate of unsatisfactory cytology and inadequate histopathology samples in this cohort is a reminder that specimen quality matters as much as the choice of test.

CONCLUSION

In this cohort of 140 women with a clinically suspicious cervix, histopathology confirmed CIN 2/3 or worse in a substantial minority, and each screening tool added something useful: Pap smear was moderately sensitive and reasonably specific, the Swede score was highly specific, and colposcopy using Reid's Index was the most sensitive of the three. No single test reliably stood in for the others. A combined approach, cytology alongside a structured colposcopic score with directed biopsy where indicated, appears the more dependable pathway for evaluating a suspicious-looking cervix in this setting, though the sizeable share of unsatisfactory or inadequate specimens warrants attention.

Funding

This study received no external funding; all costs were met by the institute and the principal investigator.

Conflict of Interest

The authors declare no conflict of interest.

REFERENCES

- Berman T, Smith JA. Cervical Cancer. In: O'Connell MB, Smith JA, Borgelt LM, editors. *Women's Health Across the Lifespan*, 3rd ed. New York: McGraw Hill Education; 2024.
- Hoffman BL, Schorge JO, Halvorson LM, Hamid CA, Corton MM, Schaffer JI. Cervical Cancer. In: *Williams Gynecology*, 4th ed. New York: McGraw-Hill Education; 2020.
- Milingos DS, Harry VN, Cruickshank ME. The Clinically Suspicious Cervix—How Often Is It Cancer? *J Low Genit Tract Dis*. 2010;14(3).
- Knowlton CA, Mackay MK. Papanicolaou Smear. In: *Encyclopedia of Radiation Oncology*. StatPearls Publishing; 2013. p.610.
- Basu DP, Sankaranarayanan R. *Colposcopy Digital Atlas*. Scr Publications; 2017.
- Bist R, Mohi MK, Garg R. Colposcopic findings to study cervical changes in reproductive age group women using various contraceptives. *Arch Gynecol Obstet*. 2024;309(6):2799–809.
- Nistha V, Rani Gandhi S, Satish Vishwekar P. A Study on Correlation of Pap Smear, Colposcopy and Colposcopic Directed Biopsy in Women With Unhealthy Cervix. *J Evol Med Dent Sci*. 2017;6(07):515–8.
- Chaudhary R, Inamdar S, Hariharan C. Correlation of diagnostic efficacy of unhealthy cervix by cytology, colposcopy and histopathology in women of rural areas. *Int J Reprod Contracept Obstet Gynecol*. 2014;3(1):213–8.
- Bhalerao A, Kulkarni S, Ghike S, Kawthalkar A, Joshi S. Correlation of Pap Smear, Colposcopy and Histopathology in Women with Unhealthy Cervix. *J SAFOG with DVD*. 2012;4:97–8.
- Rokade A, Kshirsagar N. PAP Smear versus Colposcopy in Symptomatic Women and Women with Suspicious-Looking Cervix. *J Nat Sci Biol Med*. 2020;9(May):14–8.
- Kohale MG, Dhobale AV, Hatgoankar K, Bahadure S, Salgar AH, Bandre GR. Comparison of Colposcopy and Histopathology in Abnormal Cervix. *Cureus*. 2024;16(2):e54274.
- Agarwal N, Gupta M, Agrawal A, Tekta K. Evaluation of colposcopy in screening of suspicious-looking cervix using swede score and its correlation with the histopathological findings. *Santosh Univ J Health Sci*. 2022;8(1):20–5.
- Agarwal N, Gupta M, Agrawal A. Colposcopic Evaluation Using Swede Score as a Tool to Screen Suspicious-looking Cervix and its Correlation to Histopathological Findings. *J South Asian Fed Obstet Gynaecol*. 2023;15(2):188–92.
- Sankaranarayanan R, Nene BM, Shastri SS, Jayant K, Muwonge R, Budukh AM, et al. HPV Screening for Cervical Cancer in Rural India. *N Engl J Med*. 2009;360(14):1385–94.
- Kori A, Ahirwar M, Meravi J, Sirpurkar M, Kumar A. Colposcopic evaluation of unhealthy cervix in gynecology patients: A prospective observational study. *Bioinformation*. 2025;21(7):2001–5.