Correlation of Two Colposcopic Indices for Predicting Premalignant Lesions of Cervix

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Cervical cancer is the second most common malignancy among women in India, mainly affecting the females of Peri-Menopausal age group. Colposcopy has been very useful for diagnosing cervical cancer to guide the biopsy. Reids and Scalzi proposed the Reids Colposcopic Index (RCI) to make colposcopic diagnosis less subjective, which is currently the most accepted scoring system. Recognizing the correlation of size of the lesion with likelihood of harbouring high grade disease, a new scoring system, the Swede score, has been devised by Strander et al in 2005. In present study we compared the Reids colposcopic index with Swede score. From the present study it is evident that Swede score of 8 or more has 100% specificity and can be used for performing direct excisional procedure as a "see-and-treat" method at this cut-off. This may be the preferred method for the treatment of high-grade CIN because it reduces the number of visits to the clinic and failure to receive treatment.

Keywords: Correlation coefficient, Reid's score, Swede's score

INTRODUCTION

rervical cancer continues to be an important public health problem in India. Cervical cancer is the second most common malignancy among women in India, mainly affecting the females of perimenopausal age group.^[1] It has a long precancerous stage during which early diagnosis can be made by various screening modalities.^[2] This fact has helped in making screening for cervical cancer successful. In developed countries, implementation of screening programs has decreased the mortality by 70%; however, in the developing world, it is still very high. Cervical cancer has a long precancerous phase and can therefore be prevented by screening and early detection using various procedures such as Pap smear, visual inspection with acetic acid, visual inspection with Lugol's iodine, and HPV DNA testing. Colposcopy has been very useful for this purpose to guide the biopsy. It was invented by Dr. Hans Hinselmann in Altona, Germany, in 1925.^[3,4] Reid and Scalzi proposed the Reid's Colposcopic Index (RCI) to make colposcopic diagnosis less subjective, which is currently the most accepted scoring system. The sensitivity of RCI with the threshold for any lesion detected was 89%, but fell to

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56% when the threshold was raised to high-grade lesion. The specificity for low-grade lesions was lower at 57.5% which increased to 92.9% for high-grade lesion.^[5,6]

Recognizing the correlation of size of the lesion with likelihood of harboring high-grade disease, a new scoring system, the Swede score, has been devised by Strander *et al.* in 2005.^[7] In addition to the various parameters of RCI, it also incorporates lesion size as a variable. In the initial study by Strander, the specificity was reported to be as high as 95% in detecting cervical intraepithelial neoplasia (CIN)2+ lesions. In the present study, we compared the RCI with Swede score in females coming to our hospital from August 1, 2015 to July 31, 2016.

METHODOLOGY

The study protocol was approved by the Institute Ethics Committee. All subjects were included in the study after an informed written consent. Participation in the

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study was voluntary. It was a cross-sectional study done at Department of Obstetrics and Gynaecology, Gandhi Memorial Hospital, associated with Shyam Shah Medical College, Rewa (Madhya Pradesh). Of 10,000 women who attended the outpatient department of Department of Obstetrics and Gynaecology from August 1, 2015 to July 31, 2016, 110 women between 30 and 59 years fulfilling the inclusion criteria were enrolled in the study. Thirty women were excluded from the study: 25 women had inadequate/incomplete colposcopy, three had visible cervical growth, and two had a history of procedures on cervix. Thus, eighty subjects were finally recruited in the study. All of them underwent colposcopy and biopsy. If any of the exclusion criteria were found to be applicable, the woman was excluded from the study.

- 1. Inclusion criteria: Pap smear showing ASCUS or worse, VIA or VILI positive, persistent inflammatory smears, unhealthy looking cervix, persistent discharge per vaginum, postcoital bleeding
- 2. Exclusion criteria: Obvious growth, previous procedure on cervix, for example, excision biopsy, cryotherapy, and conization, pregnant women, severe debilitating disease, and unsatisfactory colposcopy.

Detailed history was taken; complete general physical examination and pelvic examination were done. If any

of the exclusion criteria were found to be applicable, the woman was excluded from the study. The pro forma, including detailed demographic and reproductive history, was completed; thereafter, she was taken up for colposcopy.

Procedure

The woman was placed in the lithotomy position with the buttocks slightly over the end of the examining table. First, a naked eve examination of cervix was done to look for any obvious findings such as ectropion, polyp, nabothian follicles, congenital transformation zone, atrophy, inflammation and infection, leukoplakia (hyperkeratosis), condylomata, ulcer, growth or any obvious lesions in the vaginal fornices. Note was made of any abnormal discharge. Following this, excess mucus was removed gently from the cervix with saline-soaked cotton swabs. Adequate colposcopy was defined as all four quadrants of cervix visible.[8] Distal and proximal borders of the transformation zone were identified. Thereafter, visualization of cervix was done under magnification of $\times 5$ to $\times 16$ and findings were noted. The margins of the atypical cervical epithelium were graded according to a number of features, including sharpness, conformation, and thickness of the border and the presence of internal margins in a lesion.

	Box 1: The modified Reid	ls Colposcopic Index		
Colposcopic signs	Zero point	One point	Two point	
Color	Low-intensity acetowhitening (not completely opaque); indistinct acetowhitening. transparent or translucent acetowhitening. Acetowhitening beyond the margin of the transformation zone. Pure snow-white color with intense surface shine (rare)	Intermediate shade - gray/ white color and shiny surface (most lesions should be scored in this category)	Dull, opaque, oyster white; gray	
surface configuration co Fo ja	Microcondylomatous or micropapillary contour flat lesions with indistinct margins	Regular-shaped, symmetrical lesions with	Rolled, peeling edges internal demarcations between areas	
	Feathered or finely scalloped margins angular, jagged lesions 3 satellite lesions beyond the margin of the transformation zone	smooth, straight outlines	of differing colposcopic appearance - a central area of high-grade change and periphera area of low-grade change	
Vessels	Fine/uniform caliber vessels closely and uniformly placed. Poorly formed patterns of fine punctation and/or mosaic. Vessels beyond the margin of the transformation zone. Fine vessels within microcondylomatous or micropapillary lesions	Absent vessels	Well-defined coarse punctation or coarse mosaic	
Iodine staining	Positive iodine uptake giving mahogany brown color, negative uptake of insignificant lesion, i.e., yellow staining by a lesion scoring three points or less on the first three criteria areas beyond the margin of the transformation zone, conspicuous on colposcopy, evident as iodine-negative areas (such areas are frequently due to parakeratosis)	Partial iodine uptake - variegated, speckled appearance	Negative iodine uptake of significant lesion, i.e., yellow staining by a lesion already scoring four points or more on the first three criteria	

RCI: Reids Colposcopic Index, CIN: Cervical intraepithelial neoplasia. RCI (overall score) histology: 0-2: Likely to be CIN1, 3-4: Overlapping lesion - likely to be CIN1 or CIN2, 5-8: Likely to be CIN 2-3

Box 2: Swede score					
Characteristics		Score			
	0	1	2		
Acetouptake	0 or transparent	Cloudy, milky	Distinct, opaque white		
Margins and surface	0 or diffuse	Sharp but irregular, jagged, geographical satellites	Sharp and even, difference in surface level including "cuffing"		
Vessels	Fine, regular	Absent	Coarse or atypical vessels		
Lesion size	<5 mm	5-15 mm or 2 quadrants	>15 mm or 3-4 quadrants or endocervicall undefined		
Iodine staining	Brown	Faintly or patchy yellow	Distinct yellow		

Finally, the lesion was assessed after iodine staining. Scoring of all the findings based on Reid's score and Swede score was done as per Boxes 1 (Source: IARC 2011. Sellors JW, Sankaranarayanan R. Colposcopy and Treatment on Cervical Intraepithelial Neoplasia: A Beginners' Manual. Lyon, France: IARC Press; 2003.) and 2 (Source: Strander *et al.*^[7]) and composite score determined. Colposcopy-directed biopsy from abnormal areas was using a Tischler forceps irrespective of the final score, in case no such areas were delineated, then four-quadrant biopsy was taken from cervix and sent for histopathological examination.

Statistical analysis

The findings were reported using International Federation of Cervical Pathology and Colposcopy Terminology, 2011. The data were entered into Microsoft Excel spread sheet and analyzed using Statistical Product Service Solutions software IBM Version 19.0. Descriptive statistics such as mean, standard deviation, and range values were calculated for continuous variables. Frequency and present values were computed for qualitative variables. Mean values were compared using analysis of variance. Frequency distributions were compared using Chi-square/Fisher's exact test as appropriate. Sensitivity and specificity analyses were done between scores and histology. Spearman's correlation coefficient was computed between Reid's score and Swede score and kappa statistics was computed. A probability value of P < 0.05 was considered for statistical significance.

RESULTS

Total eighty sexually active women aged 30–59 years satisfying inclusion and exclusion criteria were included in the study. The majority (56.25%) of subjects were in the age group 30–39 years. Most of the subjects were multiparous, 20 (25%) subjects had two children. Around 50% females belonged to upper lower class, most (76.25%) were homemakers and one-third subjects were not using any type of contraceptive method. Majority were nonsmokers.

The main indication for colposcopy was abnormal Pap smear; 65 (81.25%) had abnormal Pap smear report

Table 1: Indications for colposcopy (n=80)		
Indication n		
Abnormal Pap smear	65 (81.25)	
Persistent discharge	6 (7.5)	
Postcoital bleeding	2 (2.5)	
Unhealthy cervix	7 (8.75)	

(\geq ASCUS). Persistent discharge, postcoital bleeding, and unhealthy cervix were some other indications in 6 (7.5%), 2 (2.5%), and 7 (8.75%), respectively [Table 1]. Findings of colposcopic examination were scored according to the modified RCI. Of the eighty patients, 65 (81.25%) had positive findings. Based on the RCI score, it was anticipated that 28/80 (35%) of cases could have some grade of CIN, while at least (Reid's score 5 or more) 21/80 (26.25%) would have high-grade CIN. Whereas from Swede score, it was predicted that 22/80 (27.5%) of cases (Swede's score 8 or more) would have high-grade CIN [Tables 2 and 3]. There was an excellent correlation between the Reid's score and Swede score; the correlation coefficient (R^2) was 0.924 [Figure 1].

On final histology, 40 (50%) subjects had chronic cervicitis, 22 (27.5%) subjects had CIN1 whereas 18 (22.5%) subjects had CIN2+ lesions [Table 4] which correlates well with predictions made by both the scores.

The additional parameter of lesion size incorporated in the Swede score was also compared with histopathology. Table 5 shows the association of lesion size with histopathology. Lesion size >15 mm involving >3 quadrants was present in 14 subjects. On histopathology, CIN2+ lesions were seen in 19 subjects, out of whom 8 (42.1%) had lesion size of 15 mm or more. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 42.10%, 86.9%, 57.14%, and 78.43%, respectively. The association between lesion size and CIN2+ histopathology was statistically significant (P < 0.05).

DISCUSSION

The sociodemographic parameters and patient profile of the present study were very similar to that of other studies, except the study by Kärrberg *et al.*^[9] which had included pregnant women. In the present study, we included women aged 30–59 years. The mean age was 40.05 \pm 7.84 which is comparable to other studies.^[7,10-12] About half of the subjects with CIN2+ lesions were >40 years although it was not statistically significant (*P* = 0.38).

Table 2: Distribution of subjects at different values of Reid's Colposcopic Index score (n=80)		
n (%)		
3 (3.75)		
13 (16.25)		
21 (26.25)		
6 (7.5)		
1 (1.25)		
10 (12.5)		
8 (10.0)		
1 (1.25)		
2 (2.50)		

RCI: Reids Colposcopic Index

 Table 3: Distribution of subjects according to the Swede score (n=80)

Swede score	n (%)	
0	1 (1.53)	
1	13 (20.0)	
2	4 (6.15)	
3	17 (26.15)	
4	8 (12.30)	
5	2 (3.07)	
6	7 (10.76)	
7	6 (9.23)	
8	4 (6.15)	
9	2 (3.07)	
10	1 (1.53)	

Table 4: Distribution according to histopathology reports (n=80)		
Histopathology	n (%)	
Chronic cervicitis	40 (50.0)	
CIN1	22 (27.5)	
CIN2	6 (7.5)	
CIN3	9 (11.25)	
ICC	3 (3.75)	
CIN: Cervical intraenithelial neonlasi	a ICC: Invasive cervicel	

CIN: Cervical intraepithelial neoplasia, ICC: Invasive cervical cancer

In the present study, subjects referred for colposcopy on the basis of an abnormal screening test were included in the study. In a study from Belgaum by Durdi et al.,^[12] discharge per vaginum and postcoital bleeding were the predominant complaints which was same in the present study. The present study evaluated 80 women referred to the colposcopy clinic in view of various indications, of which 65 (81.25%) subjects were referred because of abnormal Pap smear. Recurrent discharge, postcoital bleeding, and unhealthy cervix were other indications. The study by Mousavi et al.[11] had similar indications. In the studies by Strander et al.^[7] and Kärrberg et al.^[9] all subjects had abnormal cytology (100%). However, Pimple et al.^[13] population-based study used VIA as the screening test and referred all VIA positive patients for colposcopy and similarly a study by Ashrafunnessa in Bangladesh.^[10] In low-resource countries, VIA serves as a better screening method than cytology, as see and treat method can be implicated during the same visit. As shown in study by Singla et al. (2012) in which single visit approach was followed using visual screening methods followed by a combination of ablative and excisional therapy in the same sitting to improve compliance with treatment.^[14]

In the present study, CIN of any grade was detected in 50% of cases. In studies using abnormal cytology as

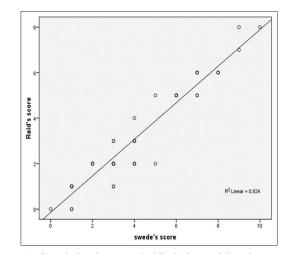


Figure 1: Correlation between Reid's index and Swede score. The two-way Scatter plot (jitter) showing the trendline between Reid's score and Swede score (the correlation coefficient $[R^2]$ is 0.924 which signifies an excellent correlation between the two scores)

Table 5: Association of lesion size with histopathology						
Score (lesion size)	Histopathology					
	Chronic cervicitis (%)	CIN1 (%)	CIN2 (%)	CIN3 (%)	ICC (%)	Total (%)
0 (<5 mm)	12 (66.67)	6 (33.3)	0	0	0	18 (100)
1 (5-15 mm)	8 (24.2)	14 (42.4)	6 (18.2)	5 (15.2)	0	33 (100)
2 (>15 mm)	4 (28.6)	2 (14.3)	0	5 (35.7)	3 (21.4)	14 (100)
Total	24 (36.9)	22 (33.8)	6 (9.2)	10 (15.4)	3 (4.6)	65 (100)

CIN: Cervical intraepithelial neoplasia, ICC: Invasive cervical cancer

the criterion for colposcopy referral, the CIN rate varied from 34.1% (Durdi *et al.*) to 88.4% (Bowring *et al.*). However, the studies using VIA as the criterion reported lower level of occurrence CIN, i.e., 24.2%–24.4%.^[12,13] High-grade CIN was detected in 22.5% in the present study, varying from 10.5% to 45% in other studies with abnormal cytology and 7%–18.4% in studies with VIA positive case.

Lesion size can be used as a predictor of high-grade lesion. Kierkegaard *et al.*^[15] showed in their study that lesion size larger than 50% (2 or more quadrants) of the visible cervix had an odds ratio of 3.6 (95% confidence interval: 2.1–6.3). In the present study, it was evident that as the lesion size increased, risk of high-grade lesion and depth increased. Lesion involving three quadrants had CIN3+ lesions in 11 subjects, including all cases of invasive cervical cancer. These patients should be referred for LEEP or other excisional procedures in all cases.

Performance of Reid's score

The performance of Reid's score as assessed by the present study was comparable with previous studies. Table 6 shows comparison of performance of Reid's score in various studies.

The Reid's score has been reported to correlate with histology, but there is an overlap between Reid's score 3-4 usually correlates with CIN1 to CIN2 and RCI score 5-8 which correlates with CIN 2-3.^[11,12,16] As a score of 3-4 suggests CIN1 to CIN2 lesion, but management of these two grades of lesion is very different. In the present study, standard cutoff is 5, but when using cutoff as 4,

Table 6: Comparison of performance of Reids score in						
various studies						
Sensitivity (%)	Specificity (%)	PPV	NPV			
74	90.7	92	70.5			
85.2	99.6	95.8	98.3			
91.3	92.9	93.6	90.3			
74.5	92.2	42.9	96			
94.44	91.48	80.95	97.73			
	various str Sensitivity (%) 74 85.2 91.3 74.5 94.44	various studiesSensitivity (%)Specificity (%)7490.785.299.691.392.974.592.294.4491.48	various studiesSensitivity (%)Specificity (%)PPV7490.79285.299.695.891.392.993.674.592.242.9			

PPV: Positive predictive value, NPV: Negative predictive value

sensitivity increased to 100% and specificity was 88.37% which becomes equivalent to Swede score at cutoff of 5. At the standard cutoff of 5, the Reid's score performed slightly worse than Swede score, but the difference was not statistically significant. Perhaps, a larger sample size may resolve this position. Singla *et al.* also found similar results with Reid's score cutoff as 4. Sensitivity and specificity was 78.3% and 90.5% to detect low-grade lesions, respectively, and for detecting high-grade lesions, sensitivity improved to 92.9% and specificity was 86.5%.^[14]

Performance of Swede score

Table 7 shows comparison of performance of Swede score in various studies. In all previous studies of Swede score, the cutoff for any excisional procedure for Swede score has been taken as 8 or more. Strander *et al.*^[7] showed that the specificity for a total score of 8 or higher was 90% and that no lesion of CIN2 or worse resulted when the score was <5. They also found that 70% of larger lesions scoring the maximum two points had CIN2 at least on histological diagnosis. In the present study, 8 subjects (42.1%) of CIN2+ were scoring more than 2 score for lesion size. Bowring et al.[17] found that a score of 8 or higher had a specificity of 95% for CIN2 or worse with a sensitivity of 38%, whereas lowering the cutoff to 6 improved the sensitivity at the expense of specificity (sensitivity = 65%; specificity = 82%). Lower scores showed high negative predictive values; a score of 3 or less resulted in a negative predictive value of 90%.

In the present study, specificity for Swede score at a score of 8 or more was 100% (92.32–100) and sensitivity was 36.84% for CIN2+ lesions, which was better than the results reported by Bowring *et al.* lowering the cutoff to 5 increased the sensitivity to 100%, while the specificity became 91.30%, which was better than the results reported by Strander *et al.*^[7]

Comparison between Reid's score and Swede score

The present study compared the performance (sensitivity, specificity, PPV, NPV) of Swede score with Reid's score. A good and graded agreement between colposcopic

Table 7: Comparison of performance of Swede score in various studies						
Study, year	Cut-off score	Sensitivity (%)	Specificity (%)	PPV	NPV	
Strander, 2005 ^[7]	≥5	79.0	95.0	-	-	
	≥ 8	-	90.0	-	-	
Kärrberg, 2012 ^[9]	≥ 8	76.0	70.0	-	-	
Bowring, 2010 ^[17]	≥ 8	38.0	95.0	83.0	70.0	
Nessa, 2014 ^[10]	≥ 5	83.3	24.2	88.0	16.7	
	≥ 8	40.0	87.9	89.0	37.5	
Present study	≥ 5	100	91.30	82.60	100	
2	≥ 8	36.84	100	100	79.31	

PPV: Positive predictive value, NPV: Negative predictive value

assessment using both Reid's score and Swede score with histopathology was documented. There was an excellent correlation between the Reid's score and Swede score, the correlation coefficient (R^2) was 0.924.

CONCLUSION

Thus, it was concluded that both the scores performed well in this hospital-based study on a selected population referred to the colposcopy clinic. From the present study, it is evident that Swede score of 8 or more has 100% specificity and can be used for performing direct excisional procedure as a "see and treat" method at this cutoff. This may be the preferred method for the treatment of high-grade CIN because it reduces the number of visits to the clinic and failure to receive treatment. The main strength of the present study is that biopsies were performed in all subjects irrespective of the presence or absence of a lesion on colposcopy, eliminating the verification bias. A larger study may help determine the most appropriate cutoff for use in population-based screening programs.

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Conflicts of interest

There are no conflicts of interest.

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