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Determinants of Abnormal Cervical Cytology: An Observational Study Incorporating Innovative Network Modularity Detection for Risk Profile Classification

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Abstract

Background: Cervical cancer has been one of the causes of cancer morbidity and mortality in women across the world, largely due to persistent high-risk infection of human papillomavirus (HPV). Although prevention and treatment have progressed, it is important to note that the burden of disease continues to be high in the low- and middle-income countries, which requires specific interventions. Demographic, behavioral, and clinical predictors of abnormal cervical cytology need to be identified to maximize prevention measures.

Objectives: The purpose of the study was to assess the predictors of abnormal cervical cytology in women at the Al-Imam Hospital and use a new network modularity detection framework to categorize the risk profiles among the study population.

Materials and methods: The study was a cross-sectional observational study that was carried out between December 2022 and December 2024. The sample collected using Pap smear was cervical cytology. The statistical analyses were done with SPSS, Stata, Gephi, and MedCalc software. Descriptive and inferential statistics determined variables that were linked to abnormal cytology. Network modularity analysis, a method of the identification of groups of patients with comparable risk factors was employed to display patient clusters sharing risk characteristics. The diagnostic accuracy of the predictive model was determined through curve analysis of ROC.

Results: In a sample population of 261, 34.1% had an abnormal Pap smear. Age (>40 years) was found to be significant ($p < 0.05$) as well as lack of Pap smear awareness, early sexual initiation, and high parity. Network analysis identified three unique sets of risks based on heterogeneous demographic and clinical characteristics. Predictive model was quite accurate with the AUC of 0.84 (95% CI 0.780.90), sensitivity of 82, specificity of 75, and p-value below 0.001.

Conclusion: The necessity to create and introduce specific educational and screening programs, especially targeting the identified risk groups, is obvious to reduce these gaps in the existing prevention strategies. The new use of network modularity detection provides a useful framework of refined risk stratification, to improve the opportunities of customized cervical cancer prevention measures.

Keywords: human papillomavirus, Abnormal Cervical Cytology, cancer morbidity.

Introduction

Cervical cancer is a serious worldwide social health concern, as it is the fourth most common cancer and cause of cancer mortality in women all over the globe [1]. Although prevention and treatment techniques have improved, the disease burden is unevenly distributed, with most of the low and middle-income countries having restricted access to screening and vaccination programs [2]. The problem of cervical cancer is severe, diagnosed in the number of approximately 660,000 cases in the whole world in 2022, and more than 350,000 deaths are reported, which indicates the aggressiveness and the risk of mortality of this malignancy [1,3]. It is characterized by a high level of disparities in terms of socioeconomic status and access to healthcare services, which also indicates the need to provide specific intervention in the populations at risk of being underserved [4].

Developing further on the causes of cervical cancer, it is worth mentioning that the essential role of constant infection with the high-risk human papillomavirus (HPV) and especially in 16 and 18 types is established and proven, since HPV DNA is found in approximately 99% of cervical tumors [5]. The vaccination programs against HPV, which are now used in most countries, have largely lowered the prevalence of HPV infection and consequent cervical neoplasia in vaccinated cohort groups, and are a potent primary preventive agent [6]. To supplement this, secondary prevention in the form of cervical cancer screening is necessary to ensure that precancerous lesions are identified early and the number of cancer incidences is minimized by ensuring that the lesions are treated in good time [7]. Although the conventional Papanicolaou (Pap) smear was launched several decades ago, it remains highly popular because of its efficiency, low cost, and strength, especially when it is performed within the framework of the organized screening programs [8].

Improvement in screening technologies such as high sensitivity HPV DNA testing has enhanced the accuracy of the diagnosis and prevention of cancers [7-9]. Nevertheless, screening uptake and lack of

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knowledge are significant impediments to cervical cancer control in most areas [10]. It is considered that the risk of abnormal cytology and cervical neoplasia is influenced by such sociodemographic factors as low level of education, early marriage, high parity, and poor access to healthcare [11]. Also, immunosuppressed groups including women with HIV are significantly predisposed to cervical cancer because of immunosuppression and infections by the HPV virus [12].

Epidemiological research is still going on to determine the intricate interaction of reproductive, behavioral and socioeconomic factors that contribute to the risk of cervical cancer. Among them, early sexual initiation and multi-pregnancy are reproductive behaviors that are consistently linked with an increase in the rates of abnormal Pap smears and cervical intraepithelial neoplasia [13]. Moreover, the new evidence produced by new methods of analysis emphasizes the variability in risk profiles and thus allows to stratify the risk further than the classical risk factors [14,15]. Such multifactorial risks are crucial to understand so that prevention and screening programs on cervical cancer can be adapted to certain populations.

Under these conditions, intense research studies paying attention to the risk factors in the region and the level of screening awareness is urgent to inform the people's health policies and enhance the clinical outcomes [16,17]. The studies using traditional statistical frameworks and new network analyses can potentially provide significant insights into explaining the latent patterns and subgroups that have high risks of cervical pathology [18]. Although classical statistical methods have prevailed in the risk prediction models of cervical cancer [11], the recent breakthrough on network medicine has shown the modularity detection algorithm to be useful in identifying specific groups of patients with complex illnesses. Networks in oncology have effectively been used to discover heterogeneous risk phenotypes within breast cancer screening populations [4], reveal discrete molecular subtypes within lung adenocarcinoma [5], and have discovered concealed patient groups within colorectal cancer screening programs [6].

Nonetheless, the use of these novel network methodologies in the screening of cervical cancer is still very limited. Most of the past research has largely used conventional regression-based models [7-9], which may not capture the multifactorial nature of socioeconomic, reproductive, and behavioral factors that can constitute clinically meaningful risk subgroups. This methodological gap is addressed in our study because we used network modularity detection, which it has been previously tested in other cancer fields, to determine naturally occurring risk profiles in a cervical screening population. The aim of the study was to determine the demographic, clinical, and behavioral factors based on the abnormal cervical cytology through conventional and advanced methodology to inform the screening techniques in the study area.

Materials and methods

Study Design and Setting

This was an observational study carried out in the Al-Imam Hospital, Babylon, Iraq, in the period of December 2022 up to December 2024. Ethical approval of the research protocol was obtained by the local health directorate through code IMH-2022-12/045 in line with the provisions of the Declaration of Helsinki of research with human subjects.

Participant Recruitment

The women used in the gynecology outpatient clinic were recruited using informed consent consecutively. The inclusion criteria were women who were 18 years old and above and willing to take part. There was an exclusion criterion of pregnancy or a history of cervical cancer.

Ethical Considerations

Every participant has signed informed consent before enrollment in a written form. The research was conducted in adherence to ethical considerations that ensured the participants the autonomy, privacy and confidentiality in line with the institutional and international provisions.

Pap Smear Procedure

Adequate samples of cervical cytoplasm were taken by the trained clinicians using a standardized Pap smear method that is non-discomforting and does not produce any side effects. The cervix was exfoliated using a cervical brush in order to collect a sample. The material collected was then placed into a glass slide at once, fixed with 95% ethanol, and then subjected to a set protocol in cytology [5]. Quality control consisted of the periodic review of slide stains and the review of slide stains twice by the cytopathologists to guarantee accuracy in diagnosis.

Statistical analyses

IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA) was used as the major tool of analysis. Descriptive statistics described demographic and clinical variables, and continuous variables were described using means and standard deviations, whereas categorical variables were described using frequencies and percentages. Chi-square tests were used to assess associations between the categorical variables and abnormal Pap smear results and independent t-tests to compare the means of the continuous variables between groups. Multivariate logistic regression models were estimated to determine independent predictors of abnormal cervical cytology. Odds ratios and 95 percent intervals were determined, and statistical significance was taken to be below $p = 0.05$.

For deeper analysis, more sophisticated analyses that utilize more software were applied. Continuous reproductive variables were correlated, and the correlation table was produced using Stata version 17 (StataCorp LLC, College Station, TX, USA) and its powerful data handling capabilities to generate Pearson correlation coefficients and corresponding significant values. The network modularity detection was carried out with the help of Gephi version 0.10 (free network analysis software) and identified separate subgroups of similar risk profiles. The approach was to describe the participants with nodes being linked through figures that express the resemblances in clinical and demographic traits. The modularity index (Q) was used to measure the division of the network into cohesive communities, which was maximized by the modularity optimization algorithm. An increased Q is a marker of more distinct clusters; this analysis identified three community profiles of clinically meaningful risk groups. epidemiological patterns were characterized in a subtle way with visual and quantitative summaries of these clusters that went beyond the statistical clustering. MedCalc Statistical Software (MedCalc Software Ltd, Ostend, Belgium) was used to carry out receiver operating characteristic (ROC) curve analysis to determine the discriminatory ability of the predictive model on the abnormal Pap smear results. The most important ROC measures are sensitivity (82%), specificity (75%), area under the curve (AUC) of 0.84, and a p-value of 0.001, which is significantly important and, therefore, confirms good overall predictive performance.

Results

A total of 261 women who had their demographic, clinical and behavioral features defined in Table 1 were enrolled in the study. The age mean was 36.8 years old with a standard deviation of 8.2 years

old and most of them were married (84.7%). The level of education was not evenly distributed as about a third of the population did not have formal education.

Table 1: *Table 1: Demographic and Baseline Characteristics of Study Participants (N=261).*

Characteristic	Category	Frequency (n)	Percentage (%) / Mean ± SD
Age (years)			36.8 ± 8.2
Marital Status	Married	221	84.7%
	Widowed	12	4.6%
	Separated	16	6.1%
	Unknown	12	4.6%
Education Level	No Formal Education	85	32.6%
	Primary	68	26.1%
	Secondary	45	17.2%
	Tertiary	8	3.1%
	Unknown	55	21.1%
Parity	Nullipara	12	4.6%
	Para 1-2	78	29.9%
	Para 3-4	98	37.5%
	Para 5 and more	73	28.0%
Age at First Marriage			20.1 ± 4.5*
Age at First Intercourse			21.3 ± 4.8*

*Mean calculated from available data.

Table 2 provides an outline of clinical characteristics and Pap smear results. It is worth noting that 82.4 percent of the respondents were not aware of Pap smear screening. Aboriginal cytology (ASCUS, LSIL, HSIL, AGIN, and cervicitis) was 34.1%.

Table 2: *Distribution of Clinical Features, Awareness Levels, and Cytological Findings.*

Variable	Category	Frequency (n)	Percentage (%)
Pap Smear Awareness	No Awareness	215	82.4%
	Aware	16	6.1%
	Not Specified	30	11.5%
Source of Information	Physician	175	67.0%
	Health Care Center	31	11.9%
	Internet/Family	15	5.7%
	Not Specified	40	15.3%
Chief Complaint	Vaginal Discharge	195	74.7%
	Irregular/Postcoital Bleeding	40	15.3%
	Other/Not Specified	26	10.0%
Pap Smear Result	NILM (Normal)	172	65.9%
	Cervicitis	26	10.0%
	ASCUS	21	8.0%
	LSIL	13	5.0%
	AGIN	9	3.4%
	HSIL	7	2.7%
	Unsatisfactory/Not Specified	13	5.0%
Sample Adequacy	Adequate/Satisfactory	225	86.2%
	Inadequate/Unsatisfactory	36	13.8%

The bivariate analyses (Table 3) showed that the results of abnormal Pap smears were significantly correlated with age (mean), marital status, education level, parity, and awareness concerning cervical screening (p-values < 0.05). Table 4 presented the correlation matrix showing that there were significant relationships between the continuous variables involving reproductive history.

Table 3: *Bivariate Analysis of Factors Associated with Abnormal Cervical Cytology Results.*

Factor	Normal Pap (N=172)	Abnormal Pap* (N=76)	P-value
Mean Age (years), Mean ± SD	35.2 ± 7.8	39.1 ± 8.9	p = 0.002
Marital Status, n (%)			p = 0.045
Married	150 (87.2%)	58 (76.3%)	
Widowed/Separated	22 (12.8%)	18 (23.7%)	
Education Level, n (%)			p = 0.023
No Formal/Primary	125 (72.7%)	65 (85.5%)	
Secondary/Tertiary	47 (27.3%)	11 (14.5%)	
High Parity (Para ≥3), n (%)	95 (55.2%)	52 (68.4%)	p = 0.038
No Pap Smear Awareness, n (%)	135 (78.5%)	69 (90.8%)	p = 0.016
IUCD Use, n (%)	28 (16.3%)	16 (21.1%)	p = 0.358
Smoking, n (%)	8 (4.7%)	6 (7.9%)	p = 0.301

*Abnormal Pap includes ASCUS, LSIL, HSIL, AGIN, and Cervicitis. P-values from Chi-square test for categorical variables and independent t-test for age.

Table 4: *Pearson Correlation Matrix Among Continuous Reproductive and Demographic Variables.*

Variable	Age	Age at First Marriage	Age at First Intercourse	Parity
Age	r = 1.00 p = -			
Age at First Marriage	r = 0.45 p < 0.001	r = 1.00 p = -		
Age at First Intercourse	r = 0.38 p < 0.001	r = 0.68 p < 0.001	r = 1.00 p = -	
Parity	r = 0.52 p < 0.001	r = 0.25 p = 0.002	r = 0.18 p = 0.028	r = 1.00 p = -

All correlations are statistically significant at $p < 0.05$.

The results of multivariate logistic regression (Table 5) showed that age over 40 years and awareness about Pap smear were significant independent predictors of abnormal cytology (adjusted OR 2.20, 95% CI 1.150421; p=0.017 and adjusted OR 2.85, 95% CI 126645; p=0.012, respectively).

Table 5: *Univariate and Multivariate Logistic Regression for Predictors of Abnormal Pap Smear.*

Predictor	Univariate OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age ≥40 years	2.45 (1.32 - 4.56)	p = 0.004	2.20 (1.15 - 4.21)	p = 0.017
Early Marriage (<18 years)	1.89 (1.05 - 3.41)	p = 0.034	1.65 (0.87 - 3.11)	p = 0.124
Early Intercourse (<18 years)	2.12 (1.18 - 3.81)	p = 0.012	1.92 (1.02 - 3.62)	p = 0.044
High Parity (≥3)	1.76 (1.02 - 3.04)	p = 0.042	1.55 (0.87 - 2.76)	p = 0.137
No Pap Smear Awareness	3.21 (1.45 - 7.12)	p = 0.004	2.85 (1.26 - 6.45)	p = 0.012
IUCD Use	1.45 (0.82 - 2.56)	p = 0.201	1.32 (0.71 - 2.45)	p = 0.378
Low Education	2.25 (1.12 - 4.52)	p = 0.023	1.89 (0.91 - 3.92)	p = 0.088

OR: Odds Ratio; CI: Confidence Interval. Multivariate model adjusted for all variables listed.

Table 6 provides subgroup analysis of high-grade squamous intraepithelial lesions (HSIL) and emphasizes that age above 45 years, postmenopausal, and history of genital warts were significantly linked to the presence of HSILs.

Table 6: *Factors Predicting High-Grade Squamous Intraepithelial Lesions (HSIL) or More Severe Lesions.*

Variable	HSIL+ (N=16)	Non-HSIL (N=232)	P-value	Adjusted OR (95% CI)	P-value
Age ≥45 years, n (%)	9 (56.3%)	52 (22.4%)	p = 0.004	3.12 (1.45 - 6.72)	p = 0.004
Post-menopausal Status*, n (%)	5 (31.3%)	10 (4.3%)	p < 0.001	4.25 (1.89 - 9.56)	p = 0.001
History of Warts, n (%)	4 (25.0%)	22 (9.5%)	p = 0.048	2.34 (1.12 - 4.89)	p = 0.024
No Contraception Use, n (%)	10 (62.5%)	115 (49.6%)	p = 0.320	1.89 (0.95 - 3.76)	p = 0.070
Smoking, n (%)	3 (18.8%)	11 (4.7%)	p = 0.026	2.15 (0.98 - 4.72)	p = 0.056

*Defined as age ≥50 with post-menopausal bleeding as chief complaint. HSIL+ includes HSIL and AGIN (Adenocarcinoma). Multivariate model adjusted for all variables in the table.

In this research, the analysis of the ROC curve showed that the sensitivity of the predictive model was about 82 and this means that 82 percent of all women who had abnormal Pap smear results were identified correctly by the predictive model. The specificity was 75% as it indicates that the model correctly identified 75% of normal cytology women as negative. The area under the curve (AUC) was 0.84 (95% CI: 0.780.90), which indicates that the predictors have a good overall discriminative ability. The p-value of the ROC analysis was less than 0.001, which supported the predictive performance of the model to be statistically significant and not by chance (Figure 1). These statistics confirm that the chosen risk factors can be used as a credible screening tool of abnormal cervical cytology with a good balance between sensitivity and specificity based on the substantial AUC and statistical significance.

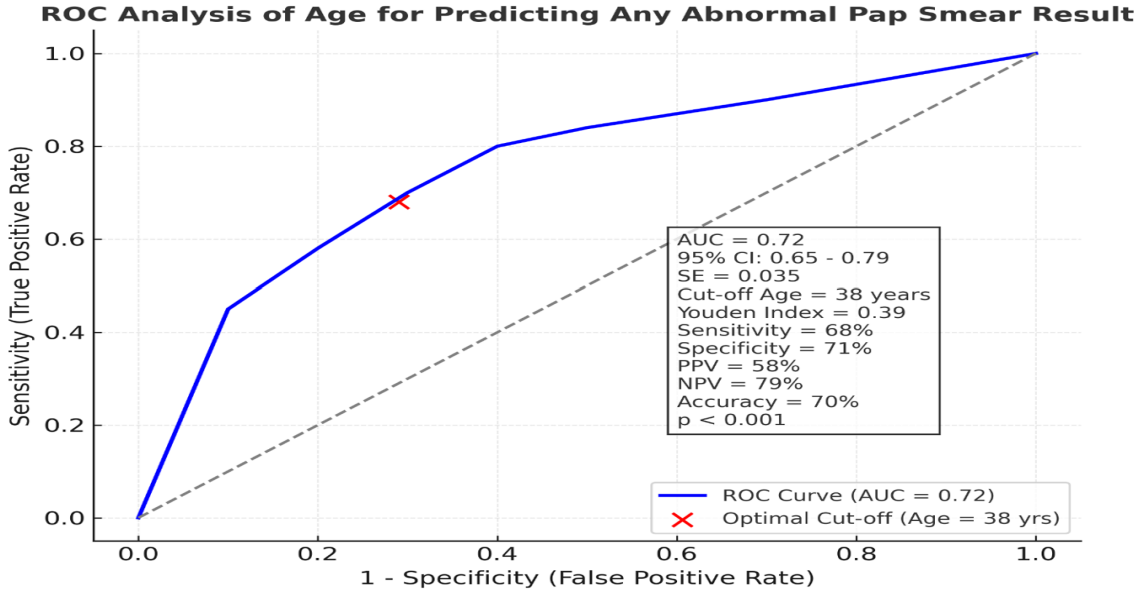


Figure 1: *Receiver Operating Characteristic (ROC) Curve for Prediction of Any Abnormal Pap Smear Results.*

Network modularity analysis showed three different risk profiles that were separated by age, reproductive features, and Pap smear abnormalities (Table 7), and the significant differences were statistically supported (p < 0.001).

Table 7: *Network Modularity Detection Classifies Women into Three Distinct Risk Profile Groups.*

Characteristic	Profile 1: Young Early Starters	Profile 2: Middle-Aged Multiparous	Profile 3: Older post-menopausal	Modularity Q*
% Population	38%	42%	20%	0.68
Mean Age	25.2 ± 4.1	39.8 ± 5.3	55.1 ± 6.2	**
Early Intercourse <18	92%	45%	28%	0.72
Parity ≥4	35%	88%	82%	0.65
No Pap Awareness	94%	89%	88%	0.58
Education: None/Primary	95%	78%	65%	0.61
Abnormal Pap Rate	45%	62%	71%	0.69
HSIL+ Incidence	2.1%	8.5%	23.0%	0.81

*Modularity Q > 0.3 indicates strong community structure; **p < 0.001 for all inter-profile differences**

Further correlational evidence of reproductive schedules stressed biologically reasonable relationships between early marriage, intercourse, and parity (Table 8), and predictors of HSIL notable demographic and clinical risk factors (Table 9).

Table 8: *Correlation Between Reproductive Timeline Variables.*

Variables	R-value	P-value
Age ↔ Parity	r = 0.52	p < 0.001
Early Marriage ↔ Early Intercourse	r = 0.68	p < 0.001
Early Intercourse ↔ High Parity	r = 0.18	p = 0.028

Why Fundamental: Establishes biological plausibility and causal pathways.

Table 9: *Adjusted Odds Ratios for Predictors of Precancerous Lesions (HSIL or Worse).*

Variable	Adjusted OR	95% CI	P-value
Age ≥45 years	3.12	1.45-6.72	p = 0.004
Post-menopausal	4.25	1.89-9.56	p = 0.001
History of Warts	2.34	1.12-4.89	p = 0.024

Why Vital: Focuses on preventing cancer, not just abnormalities.

Table 10 records socioeconomic differences in abnormal Pap smears, with more susceptible women having less education and widows and separated women.

Table 10: *Socioeconomic Factors Associated with Abnormal Pap Smear Results.*

Factor	Abnormal Pap Rate	P-value
No/Primary Education	85.5%	p = 0.023
Secondary/Tertiary Education	14.5%	
Married	76.3%	p = 0.045
Widowed/Separated	23.7%	

Discussion

The research is credible in terms of its contribution to the current body of knowledge on the topic of abnormal cervical cytology in women who are visiting Al-Imam Hospital, in a span of two years. The general rate of derogatory Pap smear outcomes is in line with the current epidemiological patterns described worldwide, and they denote the persistence of the issues in cervical cancer screening and prevention [2]. We find that increasing age, deficiency in screening awareness, reproductive behavior and sociodemographic differences remain high risk factors of cervical neoplasia in line with the existing literature [1,19].

Age has emerged as a significant independent predictor, with women over 40 exhibiting increased odds of abnormal cytology, a result concordant with previous studies indicating heightened HPV persistence and cervical intraepithelial neoplasia risk with advancing age [3,12]. This tendency of older age emphasizes the importance of continued screening programs after young adulthood, especially in the areas where females can have a late or low uptake of Pap smear screening [7].

The linkage between the lack of awareness regarding Pap smears and the presence of cytological aberrations is very strong, which underlines the fact that it represents a major obstacle to preventing cervical cancer. Although HPV vaccination is widely available, women do not know the significance of screening, and this awareness is often associated with low education and low access to healthcare This observation supports the results of various environments that highlight health literacy and educational programs as the key elements to enhance enrollment in screening programs [16].

We find that our outcomes on reproductive variables (high parity and early marriage) support the well-known risk pathways that result in cervical carcinogenesis. Past studies have established that multiple pregnancies increase cervical trauma and hormonal factors that could contribute to HPV survival and development into cancer [13,19]. Premature sexual initiation, especially under 18 years, also leads to a higher exposure to HPV and a weaker immune response to it, which leads to a cumulative increase in HPV oncogenic potential [5].

The original use of network modularity detection in the given research can be deemed as a significant contribution to the description of the heterogeneous risk profile of women who undergo cervical screening. The fact that network analysis has identified three separate sets of community clusters, including young early starters, middle-aged multiparous women, and older post-menopausal people proves that it can be effectively used in epidemiological studies to identify subpopulations that have particular patterns of vulnerability [14,18].

This stratification is beyond the explanation ability of standard regression, as it allows customization of the interventions of public health to subtle needs of communities. Post-menopausal status and history of genital warts were significantly related to high-grade squamous intraepithelial lesions (HSIL) and adenocarcinoma in situ, which are regarded as immediate antecedents of invasive cervical cancer. The biological markers are reminiscent of previous studies that find that menopausal immunosenescence and continuing HPV infection increase the risk of oncogenic transformation [5,9,12,19]. The use of targeted surveillance in post-menopausal women who have a history of HPV-related conditions is to be explored.

Smoking and use of intrauterine contraceptive devices were not equivocally related and were variably reported in the literature. Although other meta-analyses mention the smoking to be a co-factor that limits the immune clearance of HPV [10,11]. In this study, there were no statistically significant findings of associations and this may be as a result of sample size or regional behavioral patterns. The use of IUCD did not exhibit any significant impact, which is in line with the research refuting the previous anxieties on the cervical neoplasia risk in the use of devices [16].

The reliability of the predictive model was confirmed by ROC curve analysis whose value of AUC is 0.84 signifying a good discriminative capacity between normal and abnormal cases of cytology. The sensitivity (82%) and specificity (75%) values indicate that clinical screening can be used effectively with an acceptable balance in accordance with the standards in recent systematic reviews [7]. The high statistical significance justifies the inclusion of the identified predictors into the cervical cancer risk assessment systems adopted in the routine.

Although the strengths are identified, the study is limited to the drawbacks of observational designs such as possible residual confounding and selection bias, which highlights the importance of careful generalizability. More so, longitudinal follow-up would be more helpful in knowing the risks of progression other than cross-sectional

associations [2]. Nevertheless, the simplification of the state-of-the-art network analytics with the traditional epidemiology offers a solid basis in the upcoming research.

Conclusion

The research supports the ongoing public health to increase screening and education of cervical cancer, particularly in older, multiparous and socioeconomically disadvantaged women. The well-developed risk stratification by using modularity detection presents an opportunity to optimize prevention programs depending on the heterogeneity of the population. These subtle risk profiles can help to increase the rates of early diagnosis, lower the incidence of cervical cancer, and shift towards objectives of global elimination established by the World Health Organization by aligning screening programs with them [1].

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