ISSN: 2536-7153 SJMLS

Sokoto Journal of Medical Laboratory Science 2024; 9(3): 81 - 92

SJMLS - 9(3) - 008

Concordance between PAP Smears and P53 Expression in Women with Cervical Abnormalities in Osogbo, Southwest, Nigeria

Oyenike Musiliu Adewale*[1], Avwioro Godwin Ovie[2], Iyare Godfrey Innocent[3] Omosigho Omoruyi Pius[3], Olatunbosun Luman O.[4], Olawuyi Abduahi[5], Jimoh Abdullah Abiodun,[1] Tijani Busira Adesina[6], Lasisi Adewale Ismaila[7], Ojo Timothy Ayodele[8], Suleiman Ibrahim Eleha[9].

Department of Medical Laboratory Science, College of Health Sciences Lautech Ogbomoso, Oyo State [1], Department of Medical Laboratory Science, Delta State University, Abraka, Nigeria [2], Department of Medical Laboratory Science, Edo State University Uzaire, Edo State [3], Department of Medical Laboratory Science, Al-Hikmah University Ilorin, Kwara State [4], Department of Medical Laboratory Science, Federal University of Health Sciences, Ila, Orangun, Osun State [5], Department of Haematology and Blood Transfusion, University of Osun State University Teaching Hospital (Uniosunth) , Osogbo Osun State [6], Lasisi Adewale Ismaila, Osun state Poly-technique, Iree Osun State [7], Department of Morbid, University of Osun State University Teaching Hospital (Uniosunth), Osogbo Osun State [8], Department of Chemical Pathology and Immunology, University of Ilorin Teaching Hospital [9].

Author for Correspondence*: oyenikem@gmail.com/https://dx.doi.org/10.4314/sokjmls.v9i3.8

Abstract

Cervical cancer screening, involving Papanicolaou (PAP) smear and assessment of p53 expression, is crucial for early detection and prevention of cervical cancer. The aim is to evaluate the concordance between Papanicolaou (PAP) smears and P53 expression in detecting cervical abnormalities in Osogbo women southwest, Nigeria. This cross-sectional study involved 221 women aged 18-65 attending Uniosun teaching hospital for cervical screening between January 2023 and December 2023. Cervical cytology was performed using PAP smears, and P53 expression was assessed through immunohistochemistry the smear samples. The agreement between cytology, PAP smear results and P53 expression were analyzed. Of the 221women, 86 (38.9%) had abnormal Pap smear results, categorized as ASC-US, LSIL, or HSIL. P53 overexpression was observed in 86 (38.9%) cases. A statistically significant association was found between age group and Pap smear results, with a higher proportion of abnormal results among the 30-39 age groups. Additionally, a significant association was observed between miscarriage history and Pap smear results, with a higher proportion of abnormal results among those with more than 2 miscarriages. The relationship between PAP smear results and p53 expression revealed a statistically significant association (p=0.047), with a higher proportion of normal PAP smear results having negative p53 expression (99.3%) compared to abnormal PAP smear results (100% negative p53 expression. The concordance rate between Pap smear findings and P53 expression, indicating that there is no substantial agreement. The highest concordance was observed in normal cases (95.6%).This study suggests that p53 expression can be used as a complementary negative marker to Pap smear in cervical cancer screening although there was no concordance substantial between PAP smears and P53 expression in detecting cervical abnormalities. This could help in enhancing the accuracy of cervical cancer screening or for monitoring of the disease but not for diagnosis.

Keywords: PAP smear, P53, cervical abnormalities, cervical cancer, immunohistochemistry

Introduction

Cervical cancer remains a significant public health concern globally, with an estimated 604,000 new cases and 342,000 deaths in 2020 (Sung *et al.,* 2021). Early detection and treatment of precancerous cervical lesions are crucial for reducing cervical cancer incidence and mortality. The Papanicolaou (Pap) smear has been the cornerstone of cervical cancer screening for decades, enabling the identification of

abnormal cervical cells but the sensitivity varies (Sawaya, *et al.*, 1995). However, the interpretation of Pap smears can be subjective, leading to potential discrepancies in diagnosis (Mocellin *et al*., 2022). Cervical abnormalities, the abnormalities in the cells of the cervix that range from precancerous lesions to invasive cervical cancer (Bruni, *et al*, 2019) and can be typically detected through cervical cancer screening methods, such as the Papanicolaou (Pap) test or HPV testing. Precancerous cervical lesions, also known as cervical intraepithelial neoplasia (CIN) under Cytological Examination, PAP smears are classified into three grades according to the Bethesda System as:- Normal, - Atypical squamous cells of undetermined significance (ASC-US)- Low-grade squamous intraepithelial lesion (LSIL)- High-grade squamous intraepithelial lesion (HSIL).

1. CIN 1 (low-grade lesion): Mild dysplasia, representing early precancerous changes in the cervical cells
2. CIN 2 (moderate-grade lesion): Moderate dysplasia, indicating more advanced precancerous changes.
3. CIN 3 (high-grade lesion or carcinoma in situ): Severe dysplasia or carcinoma in situ, which is considered a precursor to invasive cervical cancer if left untreated (Bruni, *et al*, 2019).

The outcomes of cervical abnormalities can vary depending on the severity of the lesion and the management approach taken, particularly low-grade lesions (CIN 1), may regress spontaneously without treatment, especially in younger women (Giorgi, 2017). The Precancerous lesions that do not regress may persist and require close monitoring or treatment to prevent progression to invasive cancer (Pourhoseingholi *et al.,* 2013). If precancerous lesions are left undetected or untreated, they may progress to invasive cervical cancer, which can metastasize to other parts of the body and lead to significant morbidity and mortality (Kavatkar *et al.,* 2008). The Untreated high-grade precancerous lesions (CIN 2 and CIN 3) have a higher risk of progressing to invasive cervical cancer over time.

The appropriate management approach for cervical abnormalities depends on the severity of the lesion, age, reproductive status, and other factors (Nayar & Wilbur, 2015). The prevalence and distribution of these cytological categories, along with associated risk factors, are reported in the study population.

Complementary biomarkers, such as the expression of the p53 tumor suppressor gene, have been explored to improve the accuracy of cervical cancer screening and triage. The p53 gene plays a critical role in regulating cell cycle progression, apoptosis, and genomic stability. Mutations or dysregulation of p53 have been implicated in various cancers, including cervical cancer (Mirza *et al.,* 2022). P53 is one of the most extensively studied biomarkers in cancer research. While numerous studies have shown p53's prognostic value, there is still debate around establishing standardized cutoffs to definitively categorize samples as p53-positive or p53-negative (Mirza *et al.,* 2002). Most research uses immunohistochemistry to evaluate p53, with nuclear staining indicating p53 protein overexpression. However, the optimal percentage of stained nuclei considered positive varies across studies from >1% to >25% (Harris and Hollstein, 1993).

The overexpression or aberrant localization of p53 in cervical cells has been associated with the presence of precancerous lesions and cervical cancer (Gao *et al.,* 2023). By combining cytological evaluation with molecular biomarkers such as p53, healthcare providers may be better equipped to identify women at higher risk for cervical cancer progression, facilitating appropriate management and follow-up strategies (Srivastava *et al.,* 2023). A high degree of concordance between abnormal Pap smear results and elevated p53 expression could reinforce the cytological diagnosis and aid in identifying women at higher risk for cervical cancer progression (Goel *et al.,* 2019). It is important to note that the evaluation of p53 expression in cervical tissues can be influenced by various factors, including the specific antibodies used for detection, the immunohistochemical staining protocols, and the scoring criteria employed (Tan *et al*., 2021). Furthermore, the interpretation of p53 immunohistochemistry results can be subjective, highlighting the need for standardized protocols

and rigorous quality control measures. Despite the potential utility of p53 as a biomarker for cervical cancer screening and risk stratification, the concordance between Pap smear findings and p53 expression has been inconsistent across different studies. Some investigations have reported a strong correlation between abnormal Pap smear results and elevated p53 expression, particularly in high-grade cervical lesions and invasive cervical cancer (Dimitrakakis *et al.,* 2020). However, other studies have found discordant results, with some cases exhibiting abnormal Pap smears but no detectable p53 overexpression or vice versa (Ghasemi *et al.,* 2019). These discrepancies may arise from various factors, including differences in study populations, sampling techniques, and methodological approaches for p53 assessment.

This tumor suppressor protein P53, that often altered in cervical carcinogenesis (Roensbo *et al.,* 2020), may provide additional diagnostic value. This study aims to assess the concordance between PAP smears and P53 expression in women with cervical abnormalities in Osogbo Southwest Nigeria. By combining cytological evaluation and molecular biomarkers, healthcare providers may be better equipped to identify women at higher risk for cervical cancer progression, facilitating appropriate management and follow-up (Gao *et al.,* 2023).

Materials and Methods

Study Design and Population

This cross-sectional study was conducted at Uniosun Teaching Hospital, including 221 women aged 18-65 who underwent cervical screening from January 2023 to December 2023. Women with previous cervical cancer treatment were excluded.

Ethical Clearance

The Clearance for this study was approved by Ethics and Research Committee of Uniosun Teaching Hospital, Osogbo, Osun State with reference number UTH/REC/23/01/20/747.

Study Design and Population

This study was conducted at Osun State University Teaching Hospital (Uniosunth), Osogbo, Osun state, analyzed data from January 2020 to December 2022. The study included women aged 18-50 who underwent cervical screening via Pap smear.

Sample Size determination

The sample size (N) was determined using the formula $N= Z^2 P (1-p) / d2$ (Pourhoseingholi *et al*., 2013) with prevalence rate of (14.7%), confidence interval of (1.96) and desired level of significance taken as 0.05. This calculation resulted at 198 women sample which happened to be the minimum samples (Pourhoseingholi *et al*., 2013).

Samples and Data Collection:

Demographic and clinical data were recorded. Cervical samples for Papanicolaou (Pap) smears were collected and characterized according to the Bethesda System. Parts of the cervical smear samples were taken from women and screened for cervical abnormalities using Papanicolaou (Pap) techniques. The PAP results were examined for P53 immunocytochemically. Cervical smear sample of about 221 were collected using a previously described method of Kavatkar *et al*. (2008) in which a cytobrush was inserted into the endocervical canal at vagina wall with sterile speculum, rotated clock wisely withdrawn and inserted into fixative, liquid base cytology. The fixed smear samples were allowed to stand for 30 minutes or more, labelled accordingly and spun at 1500rpm for 60 seconds, decanted and diluted with cellular solution. About 50ul part of the diluted mixture was used to prepare smear on dried clean sides with the use of cytobrush as applicator while the remaining was stored in refrigerator for further analysis (Darragh *et al,* 2012).

Data were extracted (analyzed) from the research records, including demographic information (age, marital status, occupation and socioeconomic status from questionnaires), clinical contraceptive use, history age at first sexual intercourse, number of sexual partners, and liquid base cytology results.

Cytological Examination

PAP smears were classified as: - Normal- Atypical squamous cells of undetermined significance (ASC-US)- Low-grade squamous intraepithelial lesion (LSIL),- High-grade squamous intraepithelial lesion (HSIL).

Atypical squamous cells of undetermined significance (ASC-US) indicate the presence of squamous cells with atypical features. They are undetermined in terms of their potential to represent a precancerous lesion. It is a borderline category that requires further evaluation or follow-up (Daragh *et al.*, 2012).

Low-grade squamous intraepithelial lesion (LSIL) group represents mild dysplasia or cervical intraepithelial neoplasia grade 1 (CIN 1) that is characterized by cellular changes steady with productive human papillomavirus (HPV) infection. This includes nuclear abnormalities such as enlargement, hyperchromasia, and irregular nuclear membranes (Daragh *et al.*, 2012).

High-grade squamous intraepithelial lesions (HSIL) are those that are moderate and severe dysplasia, corresponding to cervical intraepithelial neoplasia grades 2 and 3 (CIN 2 and CIN 3). HSIL is characterized by more significant cellular abnormalities, including marked nuclear atypical, increased nuclear-to-cytoplasmic ratio, and the presence of mitotic figures (Daragh *et al.*, 2012).

P53 Immunocytochemistry Analysis

Cervical smear slides were fixed and subjected to immunohistochemical analysis for p53 expression. P53 expression was assessed in smear samples using standard immunocytochemical techniques and overexpression was defined as strong nuclear staining in >10% of epithelial cells.

The staining protocol involved permeabilization, blocking, incubation with primary and secondary antibodies, nuclear counterstaining, and mounting. Slides were observed under a fluorescence microscope, and the presence and localization of p53 expression were assessed

Statistical Analysis

Data were analyzed using SPSS 19 software. Bivariate analysis was performed to determine prevalence rates, and statistical tests, including chi-square and logistic regression, were employed to identify associations between risk factors and the presence of cervical abnormalities. The concordance between Papanicolaou (Pap) smear results and P53 expressions were analyzed using the kappa statistic. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for P53 expression relative to Papanicolaou (Pap) smear findings. The level of significance was set at $p < 0.05$.

Results

Demographic and Clinical Characteristics

The study participants' demographic and clinical characteristics are summarized in Table 1. The majority were in the 40-49 age group (40.3%), followed by the 30-39 age group (29.9%). Most participants were married (93.2%) and skilled workers (67.9%). All participants were of Yoruba ethnicity. A significant proportion reported a history of miscarriage (39.8% had 1-2 miscarriages) and child abuse (81.9%). Only 4.1% of the participants had received a pre-vaccine.

Table 1: Showing Socio-demographic Characteristics of the study participants

	Variables	Frequency	Percentage
	Subjects Recruited	***n=221***	
A	**AGE**		
	20-29	36	16.8
	30-39	66	29.9
	40-49	89	40.3
	50-59	30	13.6
	Mean ± SD (Range)		(21 – 59)
B	**MARITAL STATUS**		
	Divorced	1	0.5
	Married	206	93.2
	Singe	11	5.0
	Window	3	1 54
C	**OCCUPATION**		
	Skilled	150	67.9
	Self employed	36	16.3
	Tertiary	58	48.3
D	**MISCARRIAGE**		
	None	113	51.1
	1-2	88	39.8
	Less than 2	20	9.1
E	**PRE-VACCINE**		
	Nil	212	95.9
	Yes	9	4.1
F	**CHILD ABUSE**		
	None	40	18.1
	Yes	181	81.9
G	**ETHNICITY**		
	Yoruba	221	100

PAP smear Results

The Pap smear results are presented in Table 2. Among the 221 women recovered, the majority of the samples, 135(61.1%) had normal squamous epithelial cells, negative PAP result which carried the highest percentage in the population. Out of a significant proportion 86 (38.9%) that showed abnormal cytological characteristics, women with Low- grade Squamous intraepithelial lesion (LSIL) had 39 (17.65%), followed by High- grade Squamous intraepithelial lesion (HSIL) with 28 (12.67%) and Atypical Squamous cells of Undetermined significance (ASC-US) women that had 19 (8.60).

Table 2: Showing Pap smear Cytological changes of Epithelia cell abnormalities distributions among the participants in Osogbo

	Cervical Cytological	Frequency	Percentage
	Subjects Recruited	*n=221*	
	Category		
A	Negative or Normal for intraepithelial lesion	135	61.1
B	Atypical Squamous cells of Undetermined significance (ASC-US)	19	8.60
C	Low- grade Squamous intraepithelial lesion (LSIL)	39	17.65
B	High- grade S quamous intraepithelial lesion (HSIL)	28	12.67
	Total	***221***	**100**

Association between Pap smear Results and Demographic Factors

Table 3 shows the distribution Cytology abnormalities that occurred of within women ages groups and examined the relationship between Pap smear results (normal vs. abnormal) and various demographic factors. Out of 221 women participated, 39(LSIL), 28(HSIL) and 19(ASCUS) respectively A statistically significant association was found between age group and Pap smear results (p=0.035), with a higher proportion of abnormal results among the 30-39 age group. Additionally, a significant association was observed between Occupation history and Pap smear results (p=0.023) with a higher proportion of abnormal results among those with Skilled. No significant associations were found between Pap smear results and marital status or religion.

Table 3; Showing association between Pap Smear Results and Demographic Factors

Variable	**Pap Smear**					**p-value**
Age group	**ASC-US (%)**	**HSIL (%)**	**LISL (%)**	**NEG (%)**	**Total of abnormal (%)**	
20-29yrs	6(31.6)	3(10.7)	7(17.9)	20(14.8)	16(18.6)	0.035*
30-39yrs	5(26.3)	9(32.1)	19(45.7)	33(24.4)	33(38.4)	
40-49yrs	4(21.1)	14(50.0)	9(23.1)	62(46.0)	27(31.4)	
≥50yrs	4(21.1)	2(7.1)	4(10.3)	20(14.8)	30(34.9)	
Total	19	28	39	135	86(100)	
Occupation						
Self employed	6(31.6)	3(10.7)	7(17.9)	20(14.8)	16(18.6)	
Skilled	6(31.6)	19(67.9)	27(69.2)	98(72.6)	52(60.5)	0.023*
Unemployed	7(36.8)	6(21.4)	5(12.8)	17(12.6)	18(20.9)	
Total	**19**	**28**	**39**	**135**	**86(100)**	

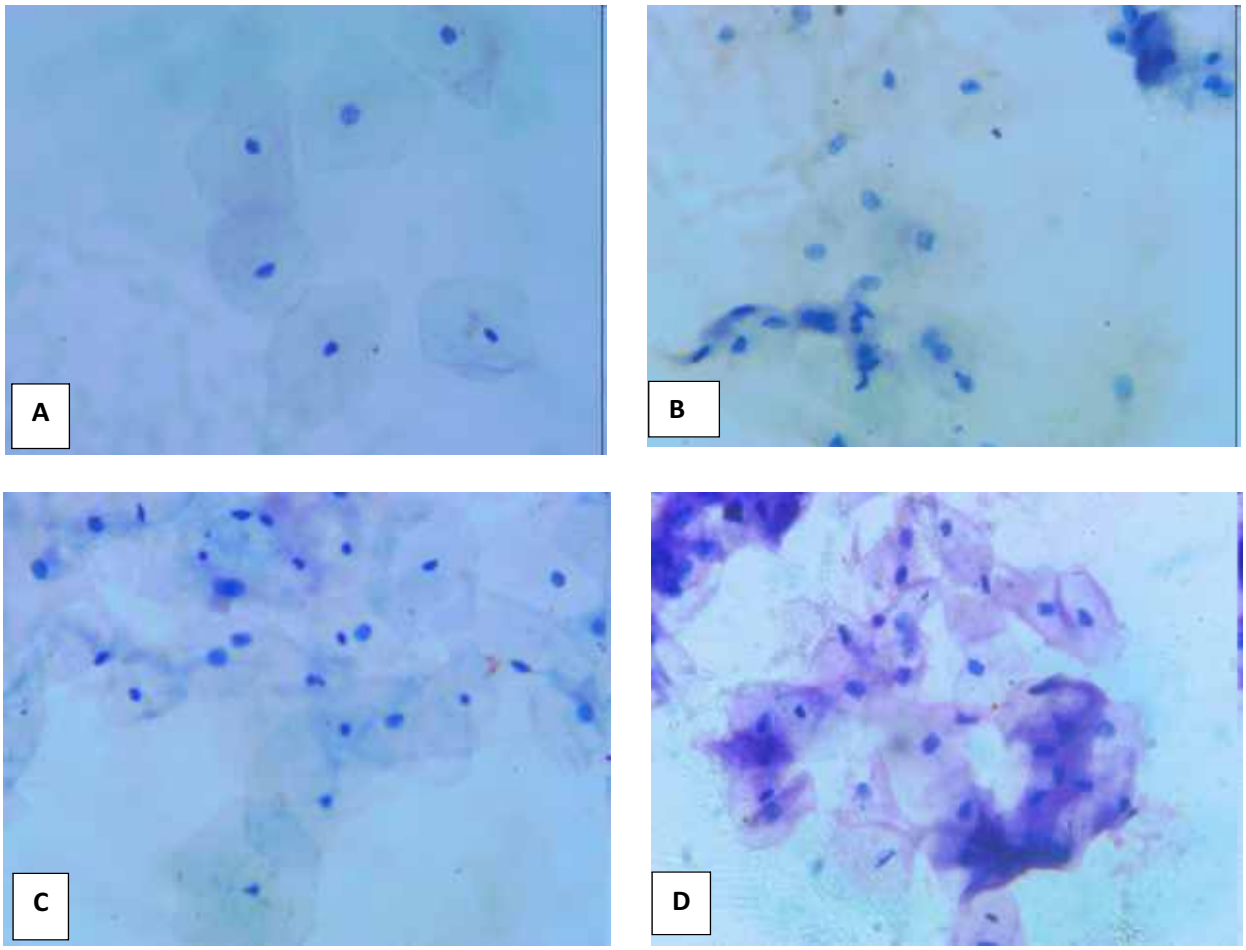


Plate A; The photomicrograph features suggestive of Normal (no abnormity) cervical cell.
Plate B; The photomicrograph features suggestive of ASC-US." which shows several" Squamous cells with slightly enlarged nuclei; mildly irregular membranes; minimal hyperchromasia.
Plate C; "This photomicrograph demonstrates several squamous cells typical of LSIL. Squamous cells with 3-4 times the size of normal; irregular membranes; granular chromatin; kilobytes present.
Plate D; the photomicrograph reveals some partially cluster cells characteristic of HSIL. The nuclei are enlarged and darker than the size of normal when compared Nucleus /Cytoplasm ratios with highly irregular membranes; hyperchromatic.

P53 Expression and P53 overexpression observed

Table 4; the relationship between Pap smear results (normal vs. abnormal) and p53 expression among women Osogbo, Osun State

Variables	Pap	Normal	Abnormal	X^2	p- value
P53	NEG	134(99.3)	86(100)	0.640	0.424
	POS	1(0.7)	0		
P53	EXPRESS	6(4.4)	0	3.929	0.047
	UNEXPRES	129(95.6)	86(100)		

Concordance Analysis

The overall concordance rate between PAP smears and P53 expression was 38.9%, Indicating substantial agreement. Expression of p53 was observed in 6 cases (4.4%), all within the Negative Pap smear group. - All abnormal Pap smears showed unexpressed p53. The expression of p53 was exclusively in Negative Pap smears, while counterintuitive, might suggest that p53 is responding to early cellular changes not yet visible in cytology. The complete absence of p53 expression in abnormal smears is striking. This could indicate that p53 function is lost or altered in these lesions, which is consistent with the role of p53 as a tumor suppressor. Based on this data, there is a very low concordance between p53 expression and abnormal Pap smears. In fact, they appear to be mutually exclusive in the sample. The sensitivity of p53 for detecting abnormal Pap smears would be 0% (since no abnormal smears showed p53 expression). - The specificity would be high (95.6% if considering unexpressed p53 as "negative"), but this is mainly due to the low overall prevalence of p53 expression

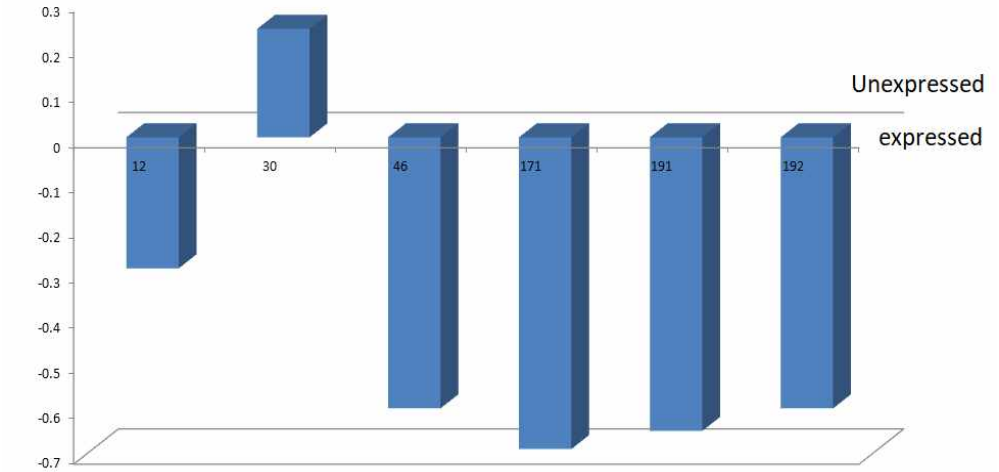
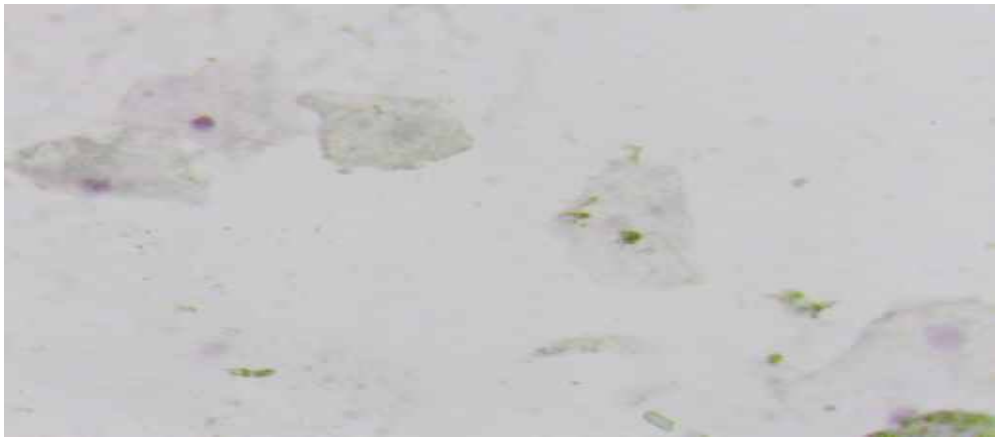


Figure 1: P53 Expression and P53 overexpression within the observed PAP Smeared.

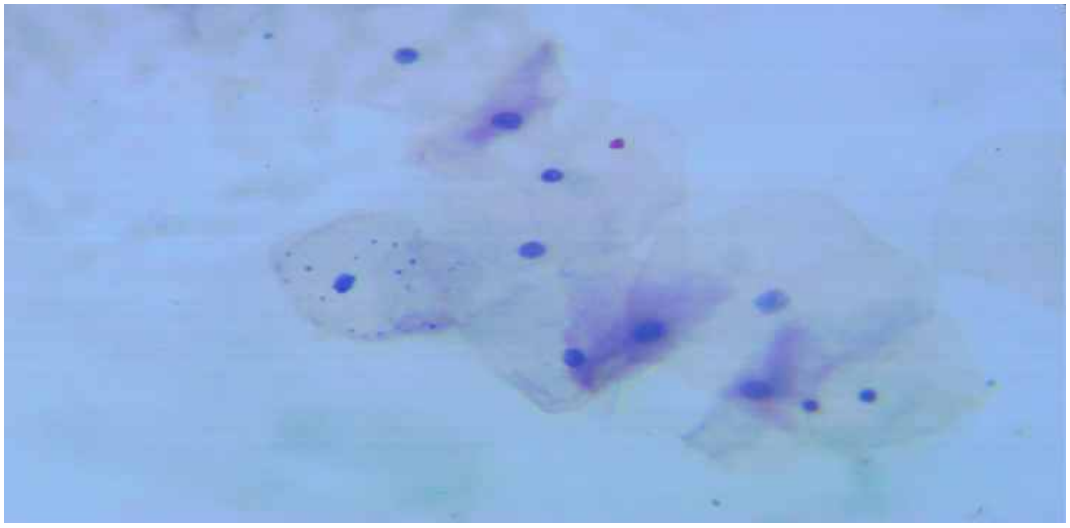
Immunocytochemistry Analysis

1. Immunocytochemistry of positive stained showed P53 antibody for the target antigen as evidenced by the distinct and localized staining pattern observed under the microscope. The positive signal appeared as distinct brown, indicating the presence of the antigen of interest. The staining pattern has been nuclear bound on the target antigen's localization within the cells. The lack of staining on other samples could suggest that the antigen was not expressed or present at detectable levels in these particular samples.



Pate 1: Photomicrograph Showing Negative Papanicolaou staining of cervical smear, with normal *moderate nuclear ratio cytoplasm.*

Figure 1. Immunocytochemical staining for p53 protein. (A) Photomicrograph showing positive staining for p53 protein (brown staining) in a subset of cells. (B) Negative control sample with no p53 staining. Scale bar: 50 μm."



Pate 2: Photomicrograph showing positive Pap staining for cervical smear, with normal *moderate nuclear ratio cytoplasm enlargement Suggestive of ASC-US.*

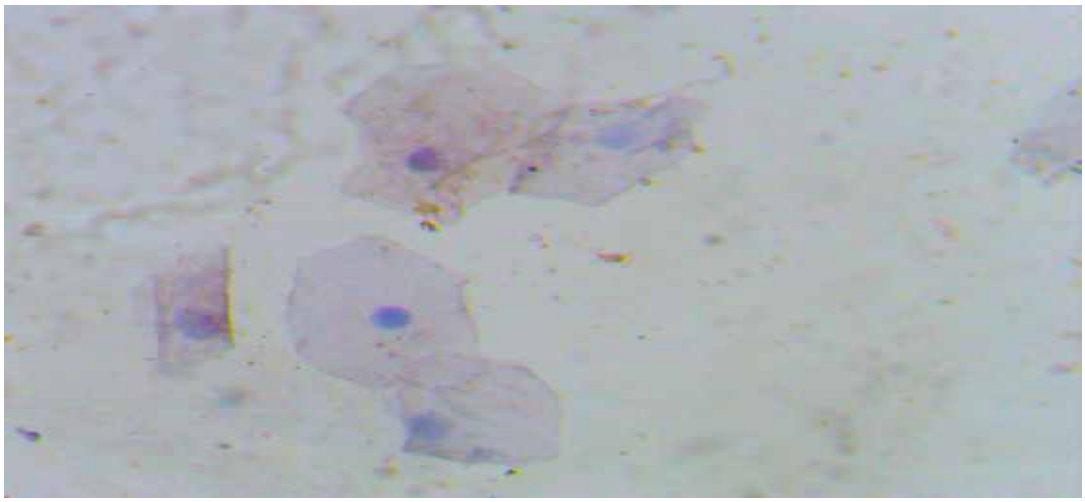
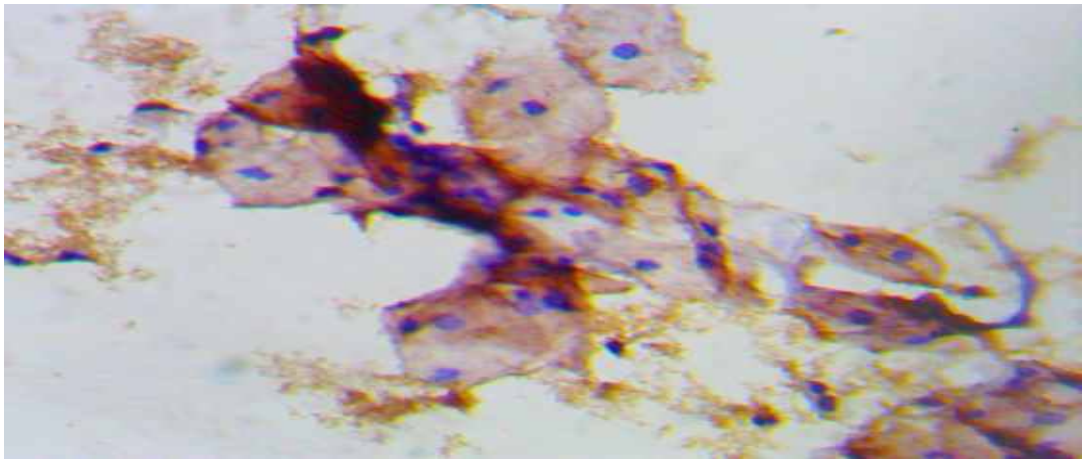


Plate 3: Showing Immunocytochemistry staining of P53 Inflammatory cell, with *moderate nuclear enlargement Suggestive of* Immunocytochemistry positive.



Pate 4: Showing Immunocytochemistry Positive staining of P53 with *dense cytoplasm, irregular nuclear, Control*

Discussion

This finding showed that women aged 30-39 had a higher proportion of abnormal Pap results aligns with prior research by Kim *et al.* (2018) and Duggan *et al.* (2021), which showed cervical dysplasia risk peaks in the late 20s and 30s. This lends support to the idea that increased HPV exposure over time, as suggested by Kuguyo *et al.* (2017), may contribute to this elevated risk in this age group. However, the association between skilled worker occupation and higher abnormal Pap rates contrasts with some previous studies. While Ekechi *et al.* (2014) and Sankaranarayanan *et al.* (2016) linked certain occupational exposures to cervical cancer risk; more specificity is needed on the particular occupational factors increasing risk for the skilled workers in this Nigerian population.

The lack of association between Pap abnormalities and marital status contradicts research by Benard *et al*. (2017) which found a potential link between marital status and cervical cancer risk. This discrepancy may be due to differences in the study populations or other confounding factors not accounted for. Additionally, the finding that religion did not influence Pap abnormality rates suggests cultural or religious influences may play a lesser role in this particular context.

Regarding p53 expression, the observation that abnormal Pap results exhibited higher p53 positivity supports the established role of p53 in cervical carcinogenesis, as described by Jain *et al.* (2019) and Pahel *et al.* (2020). The lack of association between p53 expression levels and Pap abnormalities, however, contradicts some previous research suggesting quantitative p53 levels may be informative biomarkers (Tornesello *et al.,* 2020).

The authors' proposal to integrate p53 analysis with Pap screening aligns with recommendations from Pahel *et al.* (2020) and Tornesello *et al.* (2020) regarding the value of using p53 and other biomarkers in conjunction with cytology for improved cervical cancer detection and risk stratification.

Overall, while some findings support prior research, this study also contradicts certain previous associations reported in the literature. This highlights the need for more extensive research in diverse populations to fully elucidate the complex relationships between demographic, occupational, and molecular factors in cervical cancer risk and screening.

Conclusion

This study could not demonstrate substantial concordance between PAP smears and P53 expression in detecting cervical abnormalities. The study's findings on the potential role of p53 expression in cervical abnormalities diverge from some previous research, underscoring the need for further investigation into the interplay between molecular markers and cervical cancer pathogenesis, particularly in diverse populations and screening strategies.

Recommendations

1. Cervical cancer screening programs in Southwest Nigeria should incorporate cytological evaluation, HPV and immunocytochemistry testing to enhance early detection and improve disease management.
2. Reproductive health history, including miscarriage history, should be considered in the management and prevention of cervical abnormalities.
3. Further research is needed to investigate the interplay between p53 expression, and cervical cancer pathogenesis in diverse populations and screening strategies.
4. The development of age-specific screening strategies should be considered to address the elevated risk of cervical abnormalities in middle-aged women.
5. Investigating the regional and population-specific factors influencing screening outcomes and disease progression would inform the development of more effective, evidence-based cervical cancer prevention and control strategies in Southwest Nigeria.

Acknowledgments

We acknowledge the support of my supervisors, the contributions of the Pathology Department, and the women who participated in the study.

Reference

Benard, V. B., Thomas, C. C., King, J., Massetti, G. M., Doria-Rose, V. P., & Saraiya, M. (2017). Vital signs: Cervical cancer incidence, mortality, and screening - United States, 2007-2012. *MMWR*. Morbidity and Mortality Weekly Report; **66(32)**:848–853. https://doi.org/10.15585/mmwr.mm6632a.

Bruni, L, Albero G, Serrano B, (2019). Human Papillomavirus and Related Diseases in the World. Summary Report ICO/IARC *Information Centre on HPV and Cancer* (HPV Information Centre).

Darragh, T. M., Colgan, T. J., Cox, J. T., Heller, D. S., Henry, M. R., Luff, R. D. Wilkinson, E. J. (2012). The Lower Anogenital Squamous Terminology Standardization Project for HPV-Associated Lesions: Background and consensus recommendations from the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology. *Archives of Pathology & Laboratory Medicine*; **136(10)**: 1266-1297. https://doi.org/10.5858/arpa.LGT200570.

Dimitrakakis, C., Kymioni, M., Bilirakis, E., Loutradis, D., Rodolakis, A., Michalas, S., & Antsaklis, A. (2020). Increased expression of p53 in cervical dysplasia—relationship to human papillomavirus infection. *European Journal of Gynaecological Oncology;* **41(1)**: 54-58. https://www.ejgo.net/index.php/jog/article/view/2020.5.

Duggan, C., Coronado, G. D., Becker, T.M., Moye, V.A., Jimbo, M., Buren, D., ... & Kinney, A.Y. (2021). Cervical cancer screening and adherence to follow-up among women with abnormal Pap smears: A retrospective cohort study. *Cancer Causes & Control;* **32(7)**: 709-719. .

Ekechi, C., Nwaufa, P., & Nwokeji, C. (2014). Cervical dysplasia and occupation: A case control study among private sector health workers in Onitsha, South East Nigeria. *Journal of Community Medicine and Primary Health Care;* **26(2)**: 98-106. https://www.ajol.info/index.php/jcmphc/article/view/113876.

Gao, Y., Guo, H., Zhang, Y., Qi, Y., Li, J., & Yang, R. (2023). P53 expression in cervical intraepithelial neoplasia and cervical cancer: A systematic review and meta-analysis. *Frontiers in Oncology;* **13**: Article 1043473. https://doi.org/10.3389/fonc.2023.104347.

Ghasemi, F., Shafiee, M., Izadian, T., Hosseini, Z. H., Khosravi, A., Mohebbi, E., & Baruni, M. (2019). Evaluation of the concordance between p53 protein overexpression in cervical tissue and Pap smear results in Iranian patients. *Middle East Journal of Cancer;* **10(4)**: 331-337.

Giorgi Rossi, P., Fortunato, C., Barbarino, P., Boveri, S., Caroli, S., Del Mistro, A & Ronco, G. (2017). Cervical cancer screening in immigrants living in Italy. *International Journal of Public Health;* **62(6)**: 727-733. https://doi.org/10.1007/s00038-017-0957-7.

Goel, M. M., Kumari, V., Batra, M., Paul, S., Kapil, U., & Sunesh, K. (2019). Correlation of p53 expression with cervical cancer and its role as a risk factor: A systematic review and meta-analysis. *Asian Pacific Journal of Cancer Prevention;* **20(12)**: 3581-3587. https://doi.org/10.31557/APJCP.2019.20.12.3581.

Jain, V., Singh, M., Mehrotra, S., Mehrotra, S., Bhuani, D., Garg, B., & Kushwaha, V. (2019). Clinical utility of p53 and CK17 in cervical cancer screening and early detection. *Annals of Diagnostic Pathology;* **42**: 40-44. https://doi.org/10.1016/j.anndiagpath.2019.06.008.

Kavatkar, A. N., Nagwanshi, C. A., & Dabak, S. M. (2008). Study of a manual method for rapid screening of lung cancer cases using tumor markers. *Journal of Cancer Research and Therapeutics;* **4(1)**: 1-4. https://doi.org/10.4103/0973-1482.39583.

Kavatkar, A. N., Sahasrabuddhe, V. V., & Gajanan, G. (2008). Cytological screening for cervical cancer. *Journal of Cytology / Indian Academy of Cytologists;* **25(2)**: 47–55.

Kim, J. H., Cho, H. S., Lee, J. I., Lee, S. W., & Kim, J. H. (2018). Prevalence of abnormal cervical cytology according to age and residence: A nationwide population-based study in Korea. *Obstetrics & Gynecology Science*; **61(5)**: 610-616. https://doi.org/10.5468/ogs.2018.61.5.610.

Kuguyo, O., Matimba, A., Tsikai, N., Simbini, T., Manicaland-Mutsaka, S., Masocha, M., & Katsidzira, A. (2017). Cervical cancer in Zimbabwe: a situation analysis. *Pan African Medical Journal;* **27**: 215. https://doi.org/10.11604/pamj.2017.27.215.12994.

Massad, L. S., Einstein, M. H., Huh, W. K., Katki, H. A., Kinney, W. K., Schiffman, M. (2013). ASCCP Consensus Guidelines Conference. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer

precursors. *Obstetrics and Gynecology;* **121(4)**: 829-846. https://doi.org/10.1097/AOG.0b013e3182883a34.

Mirza, A., Jalil, B., & Mirza, N. (2022). Oncogenic role of p53 mutation in cervical cancer. *Journal of Cancer Research and Clinical Oncology*; **148(10)**: 2527-2540. https://doi.org/10.1007/s00432-022-04221-y.

Mocellin, S., Meuti, A., Vianello, F., Bonanni, L., & Pillotti, M. (2022). Concordance in reporting cervical cytology: A systematic review and meta-analysis. *Cytopathology;* **33(2)**: 184-196. https://doi.org/10.1111/cyt.13068.

Nayar, R., & Wilbur, D. C. (2015). The Bethesda System for reporting cervical cytology: historical perspective. *Acta Cytologica;* **59(4)**: 359-372. https://doi.org/10.1159/000439091.

Pahel, G., Kumar, V., & Srivastava, A. N. (2020). Biomarkers in cervical cancer screening. In Cancer Biomarkers (pp. 99-114). *Academic Press:*.

Pourhoseingholi, M. A., Vahedi, M., & Rahimzadeh, M. (2013). Sample size calculation in medical studies. *Gastroenterology and Hepatology from Bed to Bench;* **6(1)**: 14–17.

Roensbo, M. T., Hoeffding, H. C., Jakobsen, K. K., Bertelsen, B. I., Kruse, A. J., Engel, U. H., & Balslev, E. (2020). P53 expression as a potential diagnostic supplement to cytology in cervical cancer screening. *Journal of Molecular Diagnostics;* **22(8)**: 953-962. https://doi.org/10.1016/j.jmoldx.2020.05.006.

Sankaranarayanan, R., Nene, B. M., Shastri, S. S., Jayant, K., Muwonge, R., Budukh, A. M., & Malvi, S. G. (2015). HPV screening for cervical cancer in rural India. *New England Journal of Medicine;* **372(17)**: 1615-1623. https://doi.org/10.1056/NEJMoa1408545.

Sawaya, G. F., Jacobsen, V., Fry, A. M., Mitchell, S., Ryan, N., Winder, S., & Silverberg, M. J. (2019). Cervical cancer screening intervals based on human papillomavirus test performance and local cervical cancer risk. *The Journal of the American Medical Association;* **321(24)**: 2414-2426. https://doi.org/10.1001/jama.2019.7983.

Srivastava, S., Fatima, N., Mishra, R. K., Mittal, V., & Mishra, R. (2023). Biomarkers for cervical cancer screening: Challenges and future prospects. *Frontiers in Oncology*; **13**: Article 1016328. https://doi.org/10.3389/fonc.2023.1016328.

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: *A Cancer Journal for Clinicians;* **71(3)**: 209-249. https://doi.org/10.3322/caac.21660.

Tan, H. P., Tan, W. J., Mei, D., Anantharaman, D., Low, J., Cornain, S., & Lim, A. Y. H. (2021). Immunohistochemical assessment of p53 protein overexpression in invasive cervical cancer: A tissue microarray study. *Pathology;* **53(2)**: 231-238. https://doi.org/10.1016/j.pathol.2020.10.008.

Tornesello, M. L., Buonaguro, L., Buonaguro, F. M., & Stellato, G. (2020). Molecular markers for cervical cancer screening: New prospective biomarkers? *Journal of Oncology;* **2020**: 254763. https://doi.org/10.1155/2020/2547863

Conflicts of Interest

The authors declare no conflicts of interest related to this study.

Author Contributions

[Oyenike Musiliu Adewale]: Conceptualization and manuscript writing., 0000000221601433, oyenikem@gmai.com,
[Iyare G.]: Review, 0009000728912932
[Avwioro O. G]: Review, 000000290186042, avwiorio@gmail.com
[Omosigho O.P.]: Review 0000-000284313033, omoruyi@gmail.com
[Olatunbosun L. O,]: Data data analysis, deluy@gmail.com
[Olawuyi A.]: Computation of results, olawuyiabdul@gmail.com
[Jimoh A.A.]: Editing. 0000-90005303395861, Muhammadbabatunde6843@gmail.com
[Tijani B. A]: Methodology, 0000000214190867. busiratijani@gmail.com
[Lasisi A. I]: Editing, 000900007376144. muhammedadigun @gmail.com
[Ojo Timothy Ayodele]: Data analysis, timothyojo04@gmail.com

Citation: Concordance between PAP Smears and P53 Expression in Women with Cervical Abnormalities in Osogbo, Southwest, Nigeria. Oyenike Musiliu Adewale, Avwioro Godwin Ovie, Iyare Godfrey Innocent Omosigho Omoruyi Pius, Olatunbosun Luman O., Olawuyi Abduahi, Jimoh Abdullah Abiodun, Tijani Busira Adesina, Lasisi Adewale Ismaila, Ojo Timothy Ayodele, Suleiman Ibrahim Eleha. ***Sokoto Journal of Medical Laboratory Science*; 9(3): 81 – 92.** https://dx.doi.org/10.4314/sokjmls.v9i3.8