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Original Research

Evaluation of Pap Smear Results of Women in the Turkish Population by Age Group

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Abstract

Background: Cervical cancer is one of the leading malignancies affecting women globally, particularly in developing nations. The Pap smear is a crucial diagnostic tool for early detection and prevention of cervical cancer. This study aimed to evaluate the Pap smear results of patients who visited the clinic over a two-year period. **Methods**: A total of 620 patients who visited the clinic between January 2015 and December 2016 were included in this retrospective cohort study. Patients with a history of gynecological malignancy or hysterectomy were excluded. The Pap smear results were evaluated using the Bethesda 2001 system. Descriptive statistics and analysis of variance (ANOVA) were employed for data analysis. **Results**: The majority of the 620 participants were young and middle-aged. Among the microscopic findings, superficial squamous cells, polymorphonuclear (PMN) leukocytes, lactobacilli, squamous metaplasia, mature squamous cells, immature squamous cells, and endocervical cells were observed. The presence of transformation components, other quality indicators, and non-neoplastic conditions varied significantly across different age groups. The incidence of bacteria in Pap smear results was higher in young female patients in Turkey compared to the literature. **Conclusions**: Pap smear tests may yield false results, warranting consideration of age and cultural differences, particularly among women from diverse populations. Although human papillomavirus (HPV) vaccination is cost-effective in preventing cervical precancerous lesions, the Pap smear remains a preferred and financially viable method, especially in underdeveloped and developing countries. The findings of this study contribute to the existing literature, and emphasize the importance of expanding cervical cancer screening programs and raising awareness among women. Large-scale multicenter studies are warranted to further validate these findings.

Keywords: Pap smear; cervical cancer; diagnosis; Bethesda system; age

1. Introduction

Varied populations and genders have different rates of cancer incidence and mortality. One of the top five malignancies affecting women is cervical cancer (CC), the second most prevalent cancer in developing nations, after breast cancer [1]. The World Health Organization reported that 2784 million women aged 15 years and older are at risk for CC, and approximately 570,000 new cases of CC are seen annually, of which 311,000 women die [2]. The incidence of CC is 14.0 per 100,000 people worldwide, and it has been reported that it is most commonly seen in Africa [3,4]. Among the types of cancer seen in women, CC ranks fourth in the world, after breast and colorectal cancers [5]. The mortality rate of CC worldwide is 6.8 per 100,000 people [2,4].

It is known that the risk factors for CC range widely [6]. These risk factors are: young age; overweight; a diet poor in vegetables and fruits; low socio-economic status; smoking and alcohol use; immunosuppression; multiple full-term pregnancies; family history of CC; sexual history due to having more than one sexual partner, or having a polygamous partner; history of sexually transmitted infection; not using condoms regularly; early marriage; early initiation of sexual activity; presence of human papillomavirus (HPV); and late diagnosis due lack of Pap smear [4]. The Pap smear is one of the most effective screening tests today [7]. However, as in every test, there is a margin of error for this test. It has been reported that the sensitivity and specificity of the test vary widely, especially when evaluating microorganisms [8]. Therefore, any information about the test results is necessary to consider and eliminate these margins of error.

In studies conducted on women from different countries, efforts should be made to increase the screening coverage among high-risk women, and ensure the quality of the CC screening program in order to reduce its risk [9]. In this context, screening approaches and communication should be adapted to the needs of different populations. Any information would help reach the unknown, as further work is needed to determine the causes of regional differences in CC risk [10].

Worldwide, gynecological cancers are seen as an important cause of morbidity and mortality. Therefore, early diagnosis and treatment methods for these cancers are fundamental today. The Pap smear is an essential diagnostic method in preventing and reduce death due to CC. More

Table 1. ANOVA results for macroscopic findings.

	Age	N	Mean ± SD	*p*	Source of difference
Macroscopic findings	<25	110	1.09 ± 0.29	0.032	<25 or >40
	26–30	112	1.06 ± 0.24		
	31–35	108	1.05 ± 0.21		
	36–40	92	1.08 ± 0.27		
	>40	173	1.01 ± 0.11		
	Total	595	1.05 ± 0.22		

ANOVA, analysis of variance; SD, standard deviation.

costly treatments can be avoided with the cheap and easy-to-apply Pap smear method. However, different findings are reported in different populations [11,12]. Therefore, as much data we are able to obtain from our Turkey cohort study, the more it will contribute to science and future studies. Therefore, in this study, we aimed to evaluate the Pap smear results of the patients admitted to our clinic over the course of two years.

2. Material and Methods

2.1 Study Design

In this cohort study, the Pap smear results of 620 patients admitted to our clinic between January 2015 and December 2016 were evaluated retrospectively. Inclusion criteria: age >18 years, no comorbid disease and no previous history of hysterectomy. The smear results of patients with a history of gynecological malignancy and hysterectomy were excluded from the study. The smear results obtained were evaluated according to the Bethesda 2001 system. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution, on 28 May 2015 with protocole number 771 and informed consent has been obtained from all participants. Females ≥18 years of age with nomalignities or situations preventing fertility were excluded.

Pap smear was applied to 586 of 620 patients, and liquid-based cytology was applied to 34 of them. Superficial squamous cells, polymorphonuclear (PMN) leukocytes, lactobacilli, squamous metaplasia, mature squamous, immature squamous, and endocervical cell parameters were examined via microscopic evaluation.

2.2 Statistics

To evaluate the findings obtained in the study, the SPSS program (Version 22.0, IBM Corp., Armonk, NY, USA) was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, frequency) and analysis of variance (ANOVA) were used for quantitative data. The results were evaluated at the 95% confidence level. A p-value of <0.05 has been considered statistically significant.

3. Results

The study was conducted between January 2015 and December 2016, on 620 patients aged between 16 and 77. Of the participants, 110 (17.7%) were younger than 25 years, 112 (18.1%) were between 26 and 30 years, 108 (17.4%) were between 31 and 35 years, 92 (14.8%) were between 36 and 40 years, and 173 (27.9%) were over 40 years. Among the participants, 25 (4%) did not specify their age. According to these findings, most participants were young and middle-aged.

According to the macroscopic findings, Pap smear samples were obtained from 586 (94.5%) participants and liquid-based cytology samples were obtained from 34 (5.5%) participants. When the microscopic findings of the participants were examined, 323 (52.1%) participants had superficial squamous cells, 323 (52.1%) had PMN leukocytes, 346 (55.8%) had lactobacilli, 557 (89%) had squamous metaplasia, 271 (43.7%) participants had mature squamous cells, 84 (13.5%) participants had immature squamous cells, and 31 (5%) participants had endocervical cells.

After microscopic sub-findings analysis, transformation components were found in 122 (19.7%) participants, while no transformation component was found in 498 (80.3%) participants. When the other quality indicators of the participants were examined, 536 (86.5%) participants had indicators partially covered with inflammation, 32 (5.2%) participants had indicators partially covered with blood "Profuse Bleeding", and 52 (8.4%) participants had indicators partially covered with blood and covered "Bleeding".

Next, general diagnoses were analyzed, 590 (95.2%) participants were found to be malignancy or intraepithelial lesion negative, and 30 (4.8%) participants were found to have epithelial cell abnormality. When the annotated diagnostic findings were analyzed, 23 (3.7%) participants had morphologic candida, 31 (5%) had coccobacilli, 172 (27.7%) had bacteria, 17 (2.7%) had torulopsis, 14 (2.3%) had leptorex, 48 (7.7%) participants had vaginalis, and 28 (4.5%) participants had trichomonas, while 265 (42.7%) participants had no organism in their annotated diagnosis.

Other non-neoplastic conditions were examined within the scope of annotated diagnosis, reactive changes were found in 546 (88.1%) participants, inflammation

Table 2. ANOVA results for microscopic findings.

Microscopic findings	Age	N	Mean	SS	*p*	Source of difference
Superficial squamous cells	<25	109	1.60	2.03	0.517	
	26–30	112	1.45	0.50		
	31–35	108	1.44	0.50		
	36–40	92	1.43	0.50		
	>40	172	1.58	0.50		
	Total	593	1.51	0.98		
PMN leukocyte	<25	110	1.41	0.49	0.046	<25 or >40
	26–30	112	1.46	0.50		
	31–35	108	1.44	0.50		
	36–40	92	1.45	0.50		
	>40	173	1.57	0.50		
	Total	595	1.48	0.50		
Lactobacilli	<25	110	1.41	0.49	0.961	
	26–30	112	1.44	0.50		
	31–35	108	1.44	0.50		
	36–40	92	1.43	0.50		
	>40	173	1.46	0.50		
	Total	595	1.44	0.50		
Squamous metaplasia	<25	110	1.11	0.31	0.384	
	26–30	112	1.09	0.29		
	31–35	108	1.15	0.36		
	36–40	92	1.10	0.30		
	>40	173	1.08	0.26		
	Total	595	1.10	0.30		
Mature squamous	<25	110	1.59	0.49	0.330	
	26–30	112	1.49	0.50		
	31–35	108	1.52	0.50		
	36–40	92	1.61	0.49		
	>40	173	1.58	0.49		
	Total	595	1.56	0.50		
Immature squamous	<25	110	1.85	0.35	0.517	
	26–30	112	1.90	0.30		
	31–35	108	1.89	0.32		
	36–40	92	1.83	0.38		
	>40	173	1.86	0.35		
	Total	595	1.87	0.34		
Endocervical cells	<25	110	1.99	0.10	0.356	
	26–30	112	1.95	0.23		
	31–35	108	1.94	0.23		
	36–40	92	1.96	0.21		
	>40	173	1.94	0.23		
	Total	595	1.95	0.21		

PMN, polymorphonuclear; SS, standard score.

(including typical repair) in 545 (87.9%) participants, and atrophic vaginitis in 59 (9.5%) participants. Macroscopic findings were analyzed using ANOVA and age was shown to have a statistical significant effect (p = 0.032). In this case, although the significant difference was between participants younger than 25 years and participants older than 40, liquid-based cytology examination was higher in participants younger than 25 years, and Pap smear examination was higher in participants older than 40 years (Table 1).

Macroscopic findings were analyzed using ANOVA, and age was shown to have a statistical significant effect only on PMN leukocytes (p = 0.046). In this case, the significant difference was between participants younger than

Table 3. ANOVA results for the presence of transformation component and other quality indicators.

	Age	N	Mean ± SD	*p*	Source of difference
Transformation component	<25	110	1.70 ± 0.46	0.021	<25 or >40
	26–30	112	1.79 ± 0.41		
	31–35	108	1.82 ± 0.38		
	36–40	92	1.78 ± 0.41		
	>40	173	1.86 ± 0.35		
	Total	595	1.80 ± 0.40		
Other quality indicators	<25	110	1.01 ± 0.10	0.000	>40 or <25 >40 or 26–30 >40 or 31–35 >40 or 36–40
	26–30	112	1.02 ± 0.13		
	31–35	108	1.00 ± 0.00		
	36–40	92	1.00 ± 0.00		
	>40	172	1.41 ± 0.49		
	Total	594	1.12 ± 0.33		

25 years and participants older than 40 years. However, the probability of finding PMN leukocyte was higher in participants younger than 25 years and lower, than in participants older than 40 years (Table 2). ANOVA revealed no significant difference between general diagnoses by age (p = 0.213).

There was a difference between the transformation component and other quality indicators by age (p = 0.021 and p = 0.000, respectively). In this case, although the significant difference was between participants younger than 25 and older than 40, the transformation component was more likely among the participants younger than 25. When the findings of the quality indicators were analyzed, the significant difference was between participants younger than 25 years, between 26 and 30 years, between 31 and 35 years, between 36 and 40 years, and participants older than 40 years. However, participants between 31 and 35, and 36 and 40 years of age were more likely to be partially covered with inflammation, whereas participants over 40 were more likely to be partially covered with blood and abundant bleeding (Table 3).

As a result of ANOVA, only atrophic vaginitis showed a significant difference according to age (p = 0.024). In this case, the significant difference was between participants aged between 26 and 30 years and participants older than 40 years, but participants older than 40 years were more likely to have atrophic vaginitis (Table 4).

4. Discussion

A Pap smear is a highly successful method for early CC diagnosis [7]. False-negative Pap smear findings pose a medical problem [13]. Inadequate smears are associated with a higher incidence of preinvasive, and invasive cervical lesions [14]. Due to these problems, the American Society for Colposcopy and Cervical Pathology, and the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology recommend repeat smears as soon as 1.5–4 months after an inadequate smear, in order to avoid this situation [15]. In this respect, more comprehensive data are needed to clarify why Pap smears are inadequate. Our study contributes to the literature in this respect, by evaluating Pap smear findings. In order to lower the rate of CC, it is essential to increase screening programs for the disease and educate women about it. CC is still a serious health issue, particularly in emerging and undeveloped nations, despite the fact that screening programs can lower the incidence and mortality of the disease [16].

Our study found statistically significant differences between age groups in regards to some CC findings. Hanlıoğlu and Süer [17] supported that CC progression is parallel with age, as epithelial cell abnormalities increase significantly with increasing age. Similarly, the importance of a Pap smear for early diagnosis was also demonstrated in this study. When age difference was analyzed, similar to the study conducted by Nazlıcan *et al.* [18], it was determined that the mean age of the participants was approximately 40 years. In addition, 48.7% of the cervical smears were found to be expected, and 13.3% were found to have bacterial vaginosis. In this case, we observed higher incidence of bacteria in our study compared to the literature. This finding could be supported by the fact that the study included patients who presented characteristics such as having unprotected intercourse at a young age, and having more than one partner.

Our study contributes to the existing literature on Pap smear results in the Turkish population. The findings highlight the importance of expanding CC screening programs and raising awareness among women about the significance of regular screenings. CC prevention strategies should be tailored to the specific needs and characteristics of diverse populations, considering age, cultural factors, and regional differences in risk factors [19].

Despite the valuable insights provided by our study, there are several limitations that should be acknowledged. First, our study was conducted at a single clinic, which may limit the generalizability of the findings to the entire Turkish population. Large-scale multicenter studies are warranted to validate our results and provide a more compre-

Table 4. One-Way ANOVA results for annotated diagnoses.

Annotated diagnosis	Age	N	Mean ± SD	*p*	Source of difference
Organisms	<25	108	5.55 ± 2.53	0.828	
	26–30	109	5.63 ± 2.60		
	31–35	101	5.39 ± 2.50		
	36–40	89	5.57 ± 2.42		
	>40	166	5.76 ± 2.46		
	Total	573	5.60 ± 2.50		
Reactive changes	<25	110	1.08 ± 0.28	0.088	
	26–30	112	1.09 ± 0.29		
	31–35	108	1.08 ± 0.28		
	36–40	92	1.14 ± 0.35		
	>40	173	1.17 ± 0.37		
	Total	595	1.12 ± 0.32		
Including typical repair of inflammation	<25	110	1.08 ± 0.28	0.101	
	26–30	112	1.09 ± 0.29		
	31–35	108	1.08 ± 0.28		
	36–40	92	1.15 ± 0.36		
	>40	173	1.16 ± 0.37		
	Total	595	1.12 ± 0.32		
Atrophic vaginitis	<25	110	1.91 ± 0.29	0.024	>40 or 6–30
	26–30	112	1.95 ± 0.23		
	31–35	108	1.94 ± 0.25		
	36–40	92	1.92 ± 0.27		
	>40	173	1.84 ± 0.36		
	Total	595	1.90 ± 0.29		

hensive understanding of Pap smear results across different regions of Turkey. Second, the retrospective nature of our study introduces inherent limitations, such as the potential for missing or incomplete data. Prospective studies with standardized protocols would be valuable in overcoming these limitations and obtaining more robust findings. In recent years, artificial intelligence has started to be used in Pap smear scans in order to avoid false results and to reduce errors that may occur with the human factor [10,20,21].

CC screening programs are extremely important to reduce the incidence and death rates of this cancer. The primary goal of screening for CC is the accurate detection and timely treatment of intraepithelial precursor lesions of the cervix, in order to prevent CC. With the Pap smear test, cells in the cancerous stage are detected in the endocervical canal, and cancer development can be prevented before the cells turn into cancer with cancer treatment at this stage. The Pap smear test, which is used in early diagnosis, is an easy-to-apply, low-cost, non-damaging, high-sensitivity test that also reduces the burden of treatment. Recent developments in the field of artificial intelligence have achieved serious success in the diagnosis of CC [19].

5. Conclusions

It should be noted that the Pap smear test may give false results, especially for women from different cultures. HPV vaccination may be more cost-effective in preventing cervical precancerous lesions and, thus CC. However, a Pap smear may be preferred as it is quite cost-effective, especially in underdeveloped and developing countries. Therefore, findings should be evaluated by considering age and cultural differences. Compared with the literature, the incidence of bacteria is higher in the Pap smear results of young female patients in Turkey. This finding is important for preventive medicine.

The findings emphasize the need for expanding CC screening programs, raising awareness among women, and considering age-specific interpretations of Pap smear results. The Pap smear remains a preferred and financially viable screening method, particularly in underdeveloped and developing countries. Further research is needed to explore the reasons behind the higher incidence of bacteria in Pap smear results among young Turkish women, and its potential implications for CC risk. By improving screening practices and implementing targeted prevention strategies, we can work towards reducing the burden of CC and improving women's health outcomes.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

FH contributed to the design, data collection, statistical analysis, interpretation, writing and revision processes, while EK contributed to the data collection and writing processes. Both authors contributed to editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Informed consent was obtained from the patients. The study was carried out with the permission of Tepecik Training and Research Hospital Clinical Ethics Committee (Date: 28.05.2015, Decision No: 771).

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Conflict of Interest

The authors declare no conflict of interest.

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