RESEARCH ARTICLE

Cervical Cytological Screening Results of 8,495 Cases in Turkey - Common Inflammation but Infrequent Epithelial Cell Abnormalities?

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Abstract

Background: Cervical cancer is the ninth most common cancer among females in Turkey. Cervical smear is a routine screening test used for the detection of cervical abnormalities and also it detects certain infections of the cervix. Objective: To analyze cervical smear results of our clinic in order to determine most frequent pathology of the women in North Eastern Anatolia Region of Turkey. Materials and Methods: In a retrospective study design, 8,495 cervical cytology cases diagnosed at the Pathology Department of the Regional Education and Research Hospital in Erzurum over the last one and half years extending from August 2012 to December 2013 were investigated. Results: The most common diagnosis was found to be inflammation, 65.5 % (5,566 out of 8,495), and the least was squamous epithelial abnormalities 0.2% (13 out of 8,495). There was some variation among the three pathologists regarding diagnosis but findings for the latter. Conclusions: Regular cervical smear tests are one of the most important strategies in early diagnosis of cervical cancer but there are conflicting data regarding the prevalence of epithelial cell abnormalities in Turkey, and the reasons of this should be investigated.

Keywords: Cervical cancer - cervical cytology - incidence data

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Introduction

Cervical cancer is the second most common cancer among women worldwide, with approximately 500,000 new cases and 274,000 deaths each year (World Health Organization, 2008). About 88% of the cases are in developing countries, accounting for 13% of all female cancers. The highest rates are found in South and Central America, sub-Saharan Africa and South and Southeast Asia. (Ferlay et al., 2010). In Turkey, it is the ninth leading female cancer and thirteenth leading cause of cancer related deaths with an incidence of 4.2/100.000 (Eser et al., 2010). Although the effectiveness of the Papanicolaou (Pap) Test in reducing cervical cancer incidence and mortality has already been demonstrated in many developed countries there is a wide disparity in rates of screening for cervical cancer in developing countries with the average screening coverage rate in developed countries at 63% compared to 19% in developing countries (Anttila et al., 1999; Gakidou et al., 2008).

Pap Smear Test is a simple, quick, and painless procedure performed on cells from the uterine cervix and used as a screening test for the prevention of the cancer of uterine cervix (Michalas et al., 2000). Altough the Pap Smear was origanally designed to detect malignant cervical lesions, when reporting the results of cervical Pap Smear Tests usually a remark is made on the possible presence of infection based on cytological criteria (Bertolino et al., 1992). Cervical cancer is one of the most preventable cancer in the World (Whynes et al., 2007). American Cancer Society declares that sexually active women older than 19 years old should take the Pap Smear Test once a year for early diagnosis (Stekler and Joann, 2000). In Turkey Turkish Ministry of Health reported that the cervical cancer ranked third among genital cancers, with 763 cases and an incidence rate of 2.2 for the year 2008. (Ministry of Health, 2008). In Turkey Early Cancer Diagnosis and Screening Centers (KETEM) are established in many cities (Karabulutlu.; 2013). According to the screening programme in Turkey, women aged between 35 and 40 are supposed to have cervical cancer screening at least once and the Pap Smear Test would be repeated in five-year intervals and screening would be finalized for 65 years old women whose last two tests are negative (Ministry of Health, 2009). In Turkey there were different results reported about the rate of the Pap testing of women. While Akyuz et al were reporting the rate as 51.2%, it was 16, 2% according to Karaca and

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was 30.4% in the study of Gurel et al. (Akyuz et al., 2006; Gurel et al., 2009; Karaca et al., 2009).

The aim of the current study was to determine the distribution of the diagnosis of the smears which were reported before and compare the data with those from other countries.

Materials and Methods

Cervical smear samples received and reported by three pathologists at the pathology department of Education and Research Hospital in Erzurum between August 2012-December 2013 were included in this study. The evaluation was made using the Bethesda 2001 citeria for cervical epithelial abnormalities and specific cervicovaginal infections. And also the adequacy of the specimen and the presence or absence of the endocervical cells are noted. The groups of the diagnosis are determined as negative for intraepithelial lesion or malignancy (NILM), inflammation, atrophy, fungal organisms morphologically consistent with candida, bacteria morphologically consistent with actinomyces, shift in flora suggestive of bacterial vaginosis, squamous epithelial abnormalities and no diagnosis because of unsatisfactory samples.

SPSS 20.0 was used for statistical calculations. Pearson's chi-square was used to compare categorical variables. P values <0.05 were accepted as statistically significant.

Results

A total of 8495 smears were included in this study in which patients were diagnosed at the Pathology Department of Education and Research Hospital in Erzurum, between 1 August 2012 and 31 December 2013. Patients were presented with the mean age 39.74±11.24. The youngest woman was 15 years old and the eldest one was 91 years old. When we compared the mean ages of the groups we saw that the youngest group was fungal organisms morphologically consistent with candida group; with the mean age 36.31±8.78 and the eldest one was atrophy group with the mean age 55.5±10.55 (Table 1).

The frequency of the diagnosis in different preparation types as conventional Pap smears (CPS) and liquid based preparations (LBP) were analyzed. In both of the groups the most frequent diagnosis was inflammation (5249 of 7886 and 317 of 604) and the least was squamous epithelial abnormalities (12 of 7886 and 1 of 604). Relationship between the preparation type and the diagnosis of the patients was analyzed and the difference was statistically significant (p=0.000) (Table 2). When all the smears were analyzed together, again the most frequent diagnosis was inflammation with a total of 5566 cases (65.5%), the second most common one was NILM with a total of 1480 cases (17.4%), and the least was squamous epithelial abnormalities with a total of 13 cases (0.15%) (Figure 1). The adequacy of the smears were analyzed and we noticed that 8004 of all smears were noted as satisfactory, 121 of them were noted as unsatisfactory and 366 of them had no data about the adequacy status on the pathology reports. When we compared the relationship between the preparation type and the specimen adequacy the difference was statistically significant (p=0.000) (Table 3). The status of endocervical cells were changing according to the

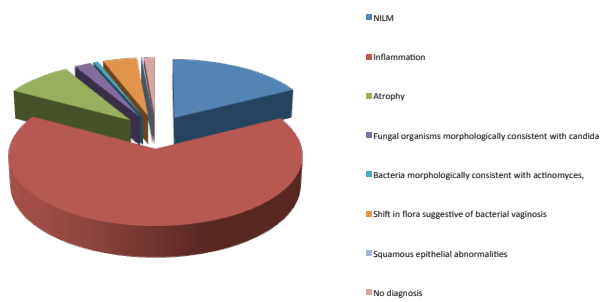

Figure 1. Distribution of the Diagnosis of Cervical Cytology (n=8495)

Table 1. The Mean Ages of the Subjects according to Different Groups of Diagnosis

Diagnosis	Mean age	Minimum	Maximum
NILM	39.20	16	76
Inflammation	38.03	15	81
Atrophy	55.54	19	91
Candida	36.31	18	71
Actinomyces	38.79	21	57
Bacterial vaginosis	39.57	17	72
Squamous epithelial abnormalities	37.61	24	52
No diagnosis	37.55	16	66

Table 2. The Number and Percentage of the Diagnosis According to the Preparation Type*

Diagnosis	Conventional		Liquid based		Total	
	No.	%	No.	%	No.	%
NILM	1334	16.9	146	24.2	1480	17.4
Inflammation	5249	66.6	317	52.6	5566	65.5
Atrophy	678	8.6	40	6.6	718	8.5
Candida	141	1.8	42	6.7	183	2.2
Actinomyces	39	0.5	14	2.3	53	0.6
Bacterial vaginosis	319	4.0	44	7.4	363	4.3
Squamous epithelial abnormalities	12	0.2	1	0.2	13	0.2
No diagnosis	114	1.4	0	0	114	1.3
Total	7886	100	604	100	8490	100

*Conventional Pap Smear; n=7886 and Liquid Based Preparation; n=604

Table 3. The Number and Percentage of the Cases According to the Specimen Adequacy Both for Conventional and Liquid Based Preparations

Preparation type	Satisfactory		Unsatisfactory		Not noted satisfactory or Not	
	No.	%	No.	%	No.	%
Conventional	7440	94.3	123	1.6	326	4.1
Liquid based	564	93.2	1	0.2	40	6.6
Total	804	94.2	124	1.5	366	4.3

Table 4. The Relationship between Presence of Endocervical Cells with the Preparation Type

Preparation type	Present		Absent		Not noted if present or absent	
	No.	%	No.	%	No.	%
Conventional	2820	35.8	4566	57.9	501	6.4
Liquid based	106	17.8	428	70.9	70	11.6
Total	2926	34.8	4994	58.7	571	6.5

Table 5. The Relationship between the Frequency of the Diagnosis with the Pathologist who Reports the Cases

Diagnosis	Pathologist 1 (n=1058)		Pathologist 2 (n=4880)		Pathologist 3 (n=2553)	
	No.	%	No.	%	No.	%
NILM	183	17.3	795	16.3	502	19.6
Inflammation	614	58.0	3222	66.0	1730	67.7
Atrophy	112	10.6	378	7.7	228	8.9
Candida	62	5.8	110	2.3	11	0.4
Actinomyces	15	1.4	29	0.6	9	0.3
Bacterial vaginosis	70	6.6	261	5.3	32	1.3
Squamous epithelial abnormalities	2	0.3	10	0.3	1	0.2
No diagnosis	0	0	75	1.5	40	1.6
Total	1058	100	4880	100	2553	100

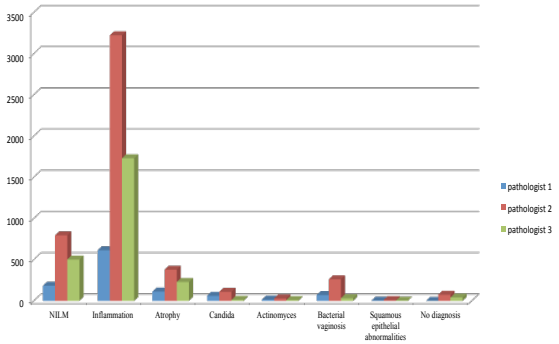

Figure 2. Distribution of the Cases which were Reported by Different Pathologists

specimen type (p= 0.000) (Table 4). When we compared the diagnosis with the pathologists who were reporting the cases again there were some differences about the frequency of the diagnosis (p= 0.000) (Table 5, Figure 2) And also we saw some differences when we compared the presence of endoservical cells, with the pathologists who were the reporter (p=0.000).

Discussion

Cervical cancer is the second most common gynaecological cancer type worldwide and the first in developing countries and it has a very high rate of mortality unless it is diagnosed in the early stage (Tezcan and Sahincioglu, 2008). CPS is a routine screening test used for the detection of cervical abnormalities and precancerous dysplastic changes of the uterine cervix (Papanicolaou, 1942). It also detects certain viral, bacterial, and fungal infections of the cervix and vagina (Avwioro, 2002). LBP is an alternative technique for transferring the cellular material collected from the transformation zone of the uterine cervix. In contrast to CPS, the cells are not directly spread on a slide, but rather into a vial containing fixative liquid (Arbyn et al., 2008).

Recent study represents the results of 8495 cervical cytology specimens which includes 7886 CPS and 604 LBC. According to our results patients were presented with the mean age 39.74±11.24. The mean age was 31.92 in Sogukpınar's study and was 35. 7 years in Kulkarni's study. (Kulkarni et al., 2013; Sogukpınar et al., 2013). The mean ages were comparable and the differences may be because of the social behaviours. In most regions of Turkey, since individuals begin active sex life generally with marriage, the rate of having obstetric or gynaecological examination increases with the increase in marriage duration. Our region is not one of the regions which has declining age of first sexual intercourse. This may be the reason of elder mean age in our results. And also the mean ages were changing between the different diagnosis groups. It was 36.31±8.78 in candida group and 55.5±10.55 in atrophy. In the study of Takei candida was reported most frequent between the ages of 11 and 20 (Takei et al., 2006). But the mean age of atrophy group in our results was predictable because atrophy is a normal aging phenomenon with a wide spectrum of cellular changes and variable amounts of inflammation (Solomon and Ritu, 2004).

It is known that the LBP is rapidly replacing the CPS. Because the LBP of cervical specimens are characterized by excellent fixation, homogeneous thin-layer dispersal of cellular material, crisp cellular detail, and a clean background (Takei et al., 2006). In our clinic we have just started to use this LBP technology but the most frequent diagnosis and the least were not changing according to the groups. According to the study of Veena K the majority of the smears were similarly the inflamatuar smears with the ratio of 46% (Veena, Suresh, 2011). In our study the most frequent diagnosis was inflammation with a total of 5566 cases (65.5%). The least one was squamous epithelial abnormalities with a total of 13 cases (0.15%). When we compared the number of squamous epithelial abnormalities with the literature we saw that our results were not similar. As we know the main focus of cervical screening is the detection of cervical abnormalities, we saw that we have to question why our epithelial cell abnormalities were lesser than the other studies from many countries. Veena K reported the ratio of squamous epithelial abnormalities as 3% and Kulkarni PR reported it as 12% (Veena, Suresh, 2011; Kulkarni et al., 2013). According to Almobarak A the ratio was 3.4% (Almobarak et al., 2013) In Turkey the prevalence of abnormal smear was reported as 1.8% (Turkish Cervical Cancer and Cervical Cytology Research Group, 2009) and it was 2.8% in a study by Atılgan (Atilgan et al., 2012). A study from Mardin reported the prevalence of abnormal smear as 6.3% and it was higher than in other regions of Turkey (Barıs, Karakaya, 2013) When we compared these results with ours' it was clear that our results were not consistent with other studies around the world. Our results were presenting the incidence of abnormal smear, lesser than in many regions of Turkey and in many other countries. Some regional differences may be acceptable because it is known that cervical cancer is closely related with many factors such as life style, cultural differences, fertility behaviors, etc. Many epidemiologic studies reported that many factors such as starting to have intercourse at an early age, getting married before 18, giving birth at an early age, giving birth to more than three babies, smoking cigarettes, lack of fruit/vegetable intake in a diet, poor genital hygiene, risky sexual behavior, refractory reproductive tract infection caused by Human Papilloma Virus (HPV), are cervical cancer risk factors (Juneja et al., 2003; Reiter et al., 2009). According to a study reported from Thailand; smoking status and sexually transmitted infection history

were found to be in association with abnormal smears (Prompakay et al., 2013). As a result of all these studies we can say that sociocultural factors, traditional lifestyle, religious beliefs and the low prevalence of HPV may be the possible reasons of low abnormal smear incidence in this current study or maybe the pathologists in this study were missing the abnormal cells.

Although it is not the main focus of cervical screening, reporting the presence of microorganisms is essential for a complete diagnostic evaluation of cervicovaginal specimens. In the 2001 Bethesda system under the category of "Organisms," 5 microorganisms (Trichomonas vaginalis, Candida species, bacterial species, Actinomyces species, and Herpes simplex virus) should be reported as part of the "nonneoplastic findings," if present (Solomo, Ritu, 2004). Infections of the uterine cervix are closely related with age, marital status, socioeconomic status, malnutrition and genital hygiene (Veena, Suresh, 2011). In our study there were 363 bacterial vaginosis cases, 183 candida cases and 53 actinomyces cases and no other microorganisms were found in significant numbers. In Kulkarni P R's study the most common microorganism was trichomonas (1.94%) followed by candida (0.39%) (Kulkarni et al., 2013). Robry had reported a high incidence of Gardnerella Vaginalis (Robry et al., 2002). And Takei had noted the most common one as bacterial vaginosis; shift in bacterial flora (34.8%) (Takei, 2006).

Most comparison studies of LBP and CP have documented that LBP offers an increased rate of detection of squamous intraepithelial lesions (SILs) and improvement of specimen adequacy, particularly in reducing obscuring factors such as background flora and debris (Baker, 2002; Abulafia, 2003). According to our results the diagnosis as NILM, candida, actinomyces, bacterial vaginosis were reported more often with LBP than with CPS. But the diagnosis as inflammation and atrophy were less frequent with LBP than with CPS. The squamous epithelial abnormalities were similar. Takei H et al reported in their study that trichomonas and a shift in bacterial flora were detected more often with CP than with LBP (13.4% *vs* 8.3% and 38.7% *vs* 30.2%, respectively). In contrast, candidiasis was detected more frequently with LBP than with CP (13.7% *vs* 7.7%) (Takei, 2006).

When we compared the specimen adequacy with the preparation type we saw that the ratio of unsatisfactory cases was 1.6% with CP and 0.2% with LBP. But the ratio of cases which had no knowledge about the adequacy status on the reports were much more in LBP (6.6% *vs* 4.1%) Maybe the reason is that the LBP is a new technique for our pathologists.

One of the objectives of the Bethesda System was to provide a uniform terminology for reporting cytologic diagnosis and to develop specific criteria for each diagnostic category (Solomon, Ritu, 2004). In recent study our pathologists didn't evaluate the same cases. But when we analyzed the results we had seen some differences in the ratio of the diagnosis. The ratio of NILM, inflammation and atrophy were similar but the ratio of microorganisms were changing from one pathologist to another (p= 0.000). But this was not an interobserver variability study, so we had just noted the situation.

In conclusion, although in our results there were not so many cases with squamous epithelial abnormalities, we still know that cervical cancer is one of the most preventable cancer in the world and cervical screening test is very important in early diagnosis. As in all developed countries cervical smear should be performed as part of the pelvic examination. And also the awareness about the importance of the cervical smear could be increased by giving more knowledge to the women who are admitted for gynaecological examination.

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