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Cytomorphological Evaluation and Clinical Correlation of Epithelial Cells Abnormalities in Gynaecology Pap Smears

Dr. Romali Deshmukh[1], Dr. Vaishali Anand[2], Dr. Hansa Goswami[3]

[1]Third Year Resident, Department of Pathology, B. J Medical College, Ahmedabad, India

[2]Assistant Professor, Department of Pathology, B. J Medical College, Ahmedabad, India

[3]Professor & Head of Department, Department of Pathology, B. J Medical College, Ahmedabad, India

Corresponding Author Email id: *deshmukh95romali[at]gmail.com*
Mobile no: 9429611135

Abstract: ***As per Globocon2020, Cervical cancer accounted for 9.4% of all cancers and 18.3% of new cases in 2020 in India. Cervical cancer was being 2nd leading cause of cancer-related deaths in women in India with crude mortality rate of 10.3% in 2020. Pap test (or cervical Pap smear) is the time tested screening method for cervical precancerous lesions. The aim of the present study was to evaluate women for precancerous cervical lesions, categories them according The 2014 Bethesda System for reporting cervical cytology and investigate the clinical correlation. Materials & Methods: A prospective study was carried out on all the PAP smears received during period of 8 months from January 2022 to August 2022. All PAP smears which were satisfactory for evaluation based on the 2014 Bethesda System for cervical cytology were included in the study. Patients who had repeat PAP smears and those which were unsatisfactory for evaluation were excluded. Result: Out of 292 smears received during study period, 12.67% (37) cases are found to be unsatisfactory for evaluation thus excluded. Among 255 Pap smears which were found to be satisfactory, 210 were reported as "Negative for intra-epithelial lesion or malignancy" (i.e. Non-neoplastic) and 45 were reported as having Epithelial cell abnormalities. Out of all abnormal pap smears, Atypical squamous cell with undetermined significance (ASC-US) was more common finding accounting for 55.55% followed by Low grade intra-epithelial lesion (LSIL) accounting for 17.77%. Glandular cell abnormalities are observed in 8.88 % cases of epithelial cell abnormalities. Most common age-group observed to be involved in study was 31-40 year. The mean age for non-neoplastic lesions was 36.05 years while that for suspected neoplastic lesions was 46.9 years. Discharge per vagina was found as most common presenting complaint accounting for 51.37% of all cases in study followed by Abdominal pain (17.25%). Regarding per speculum examination, Normal cervix was seen in 37.64 % of all cases followed by cervical erosion in 33.72 % of all cases. However, Epithelial cell abnormalities was seem to be more associated with Erosion of cervix which is seen in 44.44% of cases with abnormal pap smears. Conclusion: While reviewing all the results, it is concluded that premalignant and malignant lesions of cervix are not uncommon in our set up. Cervical cytology by Pap smear is a simple, safe and effective test to detect premalignant and malignant lesions of cervix at an early stage, and thus help the clinicians in early and more efficient management of the patients. The information obtained from this study could help the institution to know about the prevalence of various abnormal smears in this area and accordingly screening programs can be emphasized and can further be used for various other research purposes.***

Keywords: Bethesda, Pap smear, Epithelial cell abnormalities

1. Introduction

According to Globocan 2020, Estimated number of new cases of cervical cancer was 604, 100 in 2020, worldwide among females of all age group and number of deaths were attributed to this malignancy was 341, 831. In India, cervical cancer accounted for 9.4% of all cancers and 18.3% of new cases in 2020. Cervical cancer was being 2nd leading cause of cancer-related deaths in women in India with crude mortality rate of 10.3% in 2020. (1)The situation is more alarming in the rural areas where the majority of women are illiterate and ignorant about the hazards of cervical cancer as well as healthcare resources. The most effective prevention strategy for cervical cancer is the systematic screening of women along with treatment and follow-up of the screen-detected precursor lesions. (2)

Cervical cytology by Papanicolaou smears is the time tested screening method which forms a simple and effective means of screening for pre-malignant lesions of the cervix as well as identify reactive conditions and infections. Due to easy availability, cost effectiveness and reliability, cervical smears became a valuable tool in screening and diagnosing various pathologies of the cervix even at peripheral level in rural places.

The category of "Epithelial cell abnormality'' from The 2014 Bethesda System for reporting cervical cytologyincludes cytological abnormalities of Squamous cell and glandular cell. Squamous cell abnormalities encompasses a spectrum of squamous cell lesions starting from the precancerous lesions of low-grade dysplasia associated with transient human papilloma virus (HPV) infection to higher grade lesions, including cervical intraepithelial neoplasia 2 and 3 (CIN 2 and 3) and ultimately invasive squamous cell carcinomas. (3)While Glandular cell abnormalities includes subcategory of atypical glandular cell, Endocervical adenocarcinoma in situ and Adenocarcinoma. (3)

Aims

- To study the different cytomorphological abnormalities in epithelial cells evaluated on pap smear and categories them according to the 2014 Bethesda System for reporting cervical cytology.
- To study the Age wise incidence of non cancerous and precancerous cervical lesions.
- To correlate non cancerous and precancerous cervical lesions with clinical presentation and examination.

2. Materials & Methods

A prospective study was carried out on all the PAP smears received in the Department of Pathology, B J medical college, Ahmedabad during period of 8 months from January 2022 to August 2022. The patient details were obtained from the Clinical requisition forms and Report register from electronic data base of the department.

- Sampling Methods: Sampling was done using Ayre's spatula and fixed by keeping it Methanol for 10 minutes. All smears stained by using modified PAP stain and examined by the pathologist.
- Inclusion Criteria: All PAP smears which were satisfactory for evaluation based on the 2014 Bethesda System for cervical cytology were included in the study.
- Exclusion Criteria: Patients who had repeat PAP smears and those which were unsatisfactory for evaluation were excluded in the study.
- Reporting format: Reporting was done according to The 2014 Bethesda System for reporting cervical cytology. The findings were correlated with clinical details in cases of suspected epithelial abnormalities.

3. Results

A total of 292 pap smears were received due to various complaints during period of January 2022 to August 2022. Out of these 37 pap smear (12.67 %) excluded because of unsatisfactory smears for evaluation, majority because of low cellularity (15) and other are due to obscured by inflammation (12) and hemorrhage (11). (Table 1)

Out of the 255 PAP smears which were found to be satisfactory, 210 were reported as "Negative for intra-epithelial lesion or malignancy" (i.e. Non-neoplastic) and 45 were reported as having Epithelial cell abnormality. (Table: 2)

Among the PAP smears which were reported as non-neoplastic, inflammatory smears were 128 and this was the most common non-neoplastic finding. Among the infectious conditions, 29 cases of Bacterial Vaginosis and 5 cases of Candidiasis were reported Trichomonas infection was seen in 4 cases and or viral infection (Herpes Simplex) seen in 1 case. No cases of actinomycosis Virus or Cytomegalo virus were noted in our study. (Table: 2)

In the smears with Epithelial cell abnormalities; ASCUS was the most common subcategory comprising 25 out of 45 cases followed by LSIL comprising 8 out of 45 cases. There were 5 cases of ASCUS-H and 3 cases of High grade Squamous Intraepithelial Lesion (HSIL). 2 cases of ASC-US were accompanied with changes of reactive atypia due to co-existing infection of bacterial vaginosis and candiasis. Glandular cells Abnormality was found in 4 out of 44 cases. There are 2 cases of Atypical endocervical cells-NOS, 1 case of atypical endometrial cells-NOS and 1 case of atypical endocervical cells-favor neoplastic. No cases of endocervical adenocarcinoma in situ or frank adenocarcinoma were observed during the study period. (Table: 2) Koilocytic changes are seen in premenopausal age group in 4 cases of NILM and 6 cases of LSIL.

The age ranged from 22 to 77 years. Majority of the women belonged to age group between 31-40 years of age. The mean age for non-neoplastic lesions was 31.41 years while that for suspected neoplastic lesions was 46.9years. (Table 3)

Discharge per vagina was found as most common presenting complaint accounting for 51.37% of all cases in study Followed by Abdominal pain (17.25%). Out of 45 cases with epithelial cell abnormalities on smear, 23 (51.11%) cases were having complaint of discharge per vagina among which 13 cases detected to having ASC-US and 5 cases as LSIL and 4 cases as ASC-H on smear. 10 cases with squamous cell abnormalities on smear presented with no complaints. Other cases presented clinically with post coital bleeding, irregular menstrual bleeding uterine prolapse etc. Among the 4 cases with glandular cell abnormalities on smear, 2 cases presented with post menopausal bleeding, one case with cervical mass and the other was asymptomatic. (Table 4)

In per speculum examination, Normal cervix was the most common finding (37.64%) overall followed by cervical erosion seen in 33.72% cases. Among Smears with squamous cell abnormalities, Out of 20 cases of eroded cervix, 11 cases reported to having ASC-US, 5 cases to having LSIL, and 2 cases to having ASC-H and 2 cases of HSIL.12 (29.26%) cases among the smears with squamous cell abnormalities were having normal cervix. Other cervical findings noted in cases with squamous cell abnormalities were Cervical polyp, inflammation and haemorrhage. Among the smears with glandular cell abnormalities, a case with atypical endometrial cells on smear was having normal cervix, 2 cases with Atypical endocervical cells-NOS on smear, were having hypertrophied and eroded cervix and a case with Atypical endocervical cell favouring neoplastic cells was having hard cervix on examination. (Table 5)

Table 1: Pap smear sample Adequacy

	Cases	Percentages
Satisfactory for evaluation	**255**	**87.32%**
Unsatisfactory	**37**	**12.67%**
• Due to Low cellularity	15	
• Due to obscured by hemorrhage	12	
• Due to obscured by inflammation	10	
Total	292	**100%**

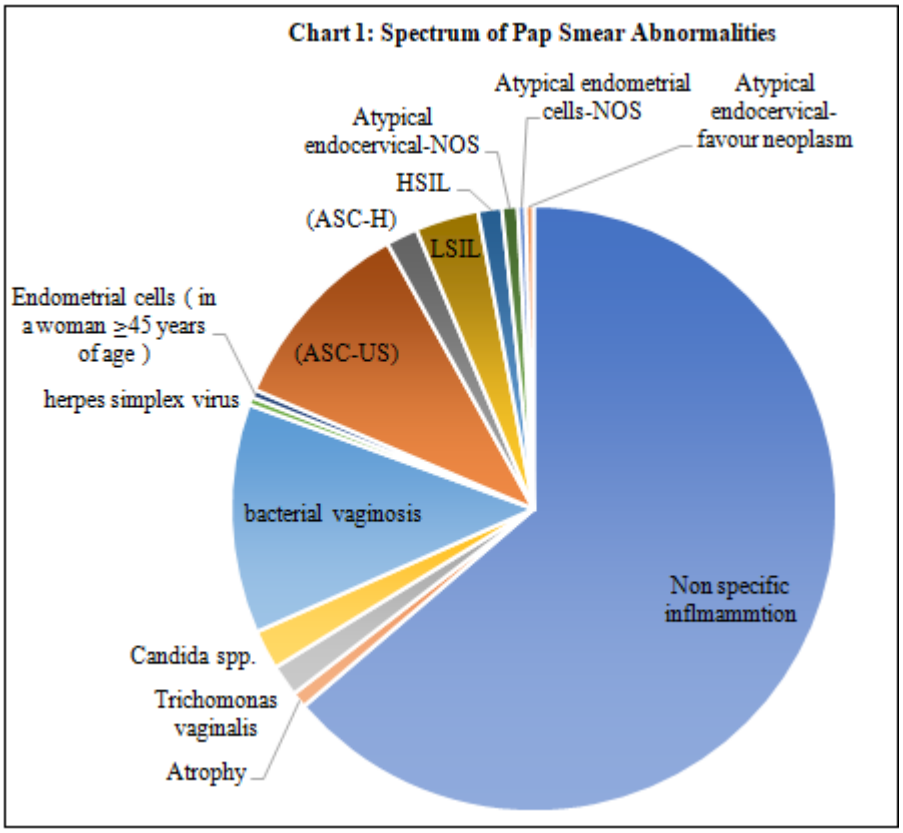

Table 2: PAP smear finding NILM vs Epithelial cell abnormality as per 2014 Bethesda System for reporting cervical cytology

NILM	NILM Without any Changes			40
	NILM WITH NON NEOPLASTIC FINDINGS	Non-neoplastic cellular variations	Squamous metaplasia	0
			Keratotic changes	0
			Tubal metaplasia	0
			Atrophy	2
			Pregnancy-associated changes	0
		Reactive cellular changes associated with	Inflammation	128
			Radiation	0
			Intrauterine contraceptive device (IUD)	0
		Glandular cells status post hysterectomy		0
	ORGANISMS	Trichomonas vaginalis		4
		Fungal organisms morphologically consistent with Candida spp.		5
		Shift in flora suggestive of bacterial vaginosis		29
		Bacteria morphologically consistent with Actinomyces spp.		0
		Cellular changes consistent with herpes simplex virus		1
		Cellular changes consistent with cytomegalovirus		0
OTHER		Endometrial cells (in a woman ≥45 years of age)		1
TOTAL				**210 (82.35%)**
Epithelial Cell Abnormalities	SQUAMOUS CELL	Atypical squamous cells of undetermined significance (ASC-US)		25
		Atypical squamous cells cannot exclude HSIL (ASC-H)		5
		Low-grade squamous intraepithelial lesion (LSIL)		8
		High-grade squamous intraepithelial lesion (HSIL)		3
		Squamous cell carcinoma		0
	GLANDULAR CELL	Atypical endocervical-NOS		2
		Atypical endometrial cells-NOS		1
		Atypical glandular cell-NOS		0
		Atypical endocervical-favour neoplastic		1
		Atypical glandular cell-favour neoplastic		0
		Adenocarcinoma in situ		0
		Adenocarcinoma		0
TOTAL				**45 (17.64%)**

Table 3: Distribution of pap smear findings among different Age groups

Age-Groups	NILM	Squamous Cell Abnormalities	Glandular Cell Abnormalities
21-30 yrs	59	5	0
31-40 yrs	85	13	0
41-50 yrs	53	10	2
51-60 yrs	9	8	1
61-70 yrs	4	3	1
71-80 yrs	0	2	0
Total	210	41	4

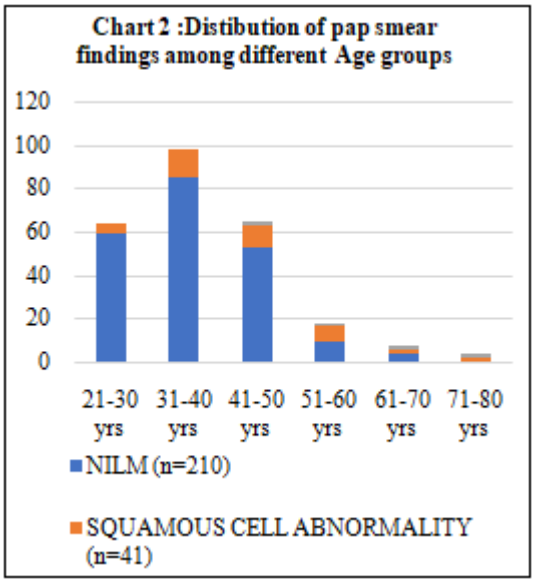

Table 4: Comparison of Pap smear findings with Clinical presentation

Clinical Symptoms	NILM	Squamous Cell Abnormality	Glandular Cell Abnormality	Total
Asymptomatic	22	10	3	35 (13.72%)
Abdominal pain	43	1	0	44 (17.25%)
Post coital bleeding	7	0	0	7 (2.74%)
Discharge	108	23	0	131 (51.37%)
Irregular menstrual bleeding	18	1	0	19 (7.45%)
Uterine prolapse	2	3	0	5 (1.96%)
Post menopausal bleeding	10	2	2	14 (5.49%)

Table 5: Comaparision of pap smear findings with Per speculum examination

	NILM	Squamous Cell Abnormality	Glandular Cell Abnormality	Total
Normal cervix	82	12	2	96 (37.64%)
Cervix Eroded	65	20	1	96 (33.72%)
Cervical polyp	2	2	0	4 (1.56%)
Haemorrhage	19	3	0	22 (8.62%)
Hypertrophied	9	0	1	10 (3.92%)
Eedematous	8	1	0	9 (3.52%)
Inflamed	25	3	0	28 (10.98%)

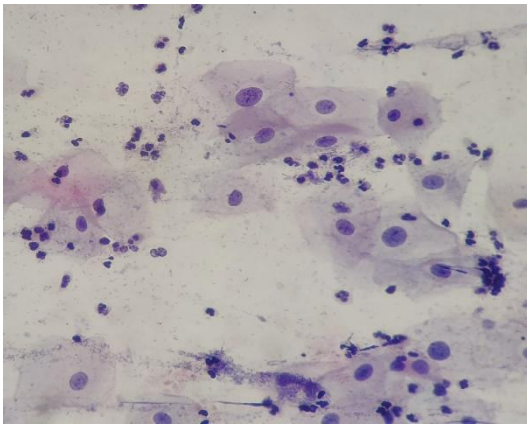

Figure 1: Atypical squamous cells-undetermined significance (ASC-US). Intermediate squamous cells with an enlarged nucleus and slight nuclear membrane irregularity.

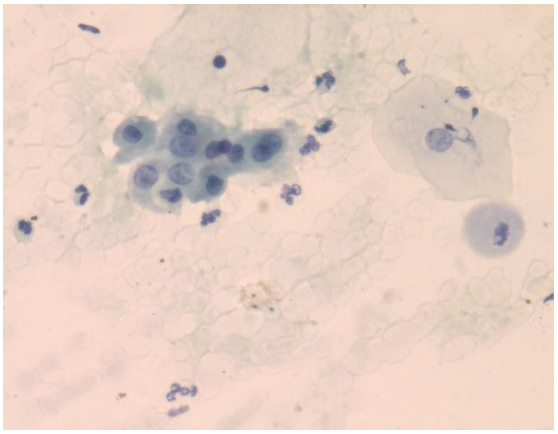

Figure 2: Atypical squamous cells-cannot exclude HSIL (ASC-H). Few small atypical metaplastic cells with high nuclear to cytoplasmic ratio, hyperchromatic nuclei and irregular nuclear membranes.

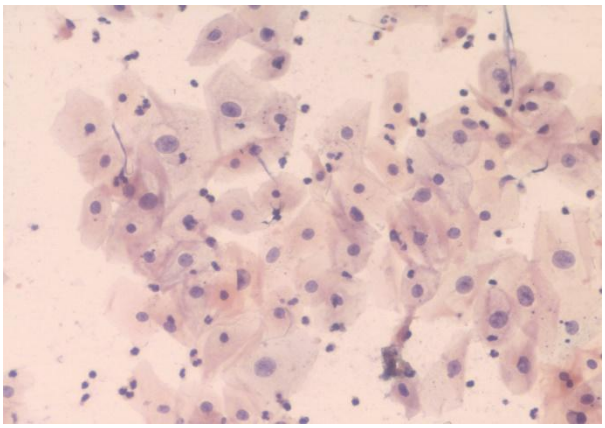

Figure 3: Low grade squamous intraepithelial lesion (LSIL). Cells are having overall large size, abnormal nuclear features including enlargement, hyperchromasiaand nuclear membrane irregularity.

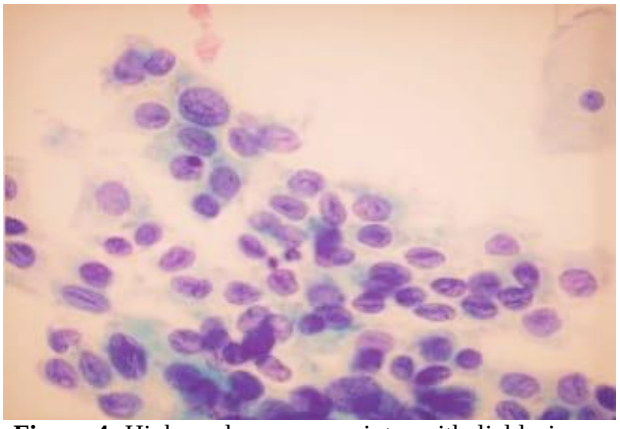

Figure 4: High grade squamous intraepithelial lesion (HSIL). Cells having variably sized, ovoid nuclei with prominent nuclear grooves

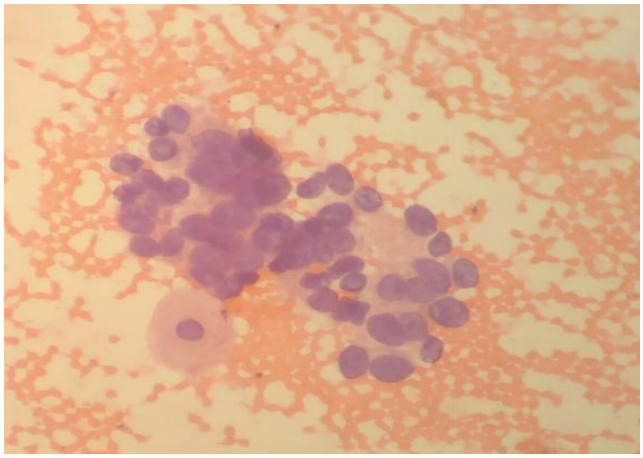

Figure 5: Atypical endocervical Cells-Favour neoplastic. Cells are having round or oval nuclei with nuclear enlargement, crowding, disordered arrangement and occasional nucleoli. Few cells are in rosette-like cellular arrangement.

4. Discussion

It is noticed that most cases included in this study visited gynecology OPD for Discharge and abdominal pain and found to having non neoplastic findings. The spectrum of Epithelial cell abnormalities has been focused on in this study.

Out of 255 cases in the study, 128 (50.19%) were found to have NILM - Inflammatory which was most common while 45 cases (16.36%) cases found to having epithelial cell abnormalities. In a study conducted by Das et al and Salvi et al similar findings were observed. [4, 5]Among Epithelial cell abnormalities, 9.09% cases having ASCUS and 2.90 % cases having LSIL. Similar findings also found in Altaf et al. [6]

In present study, most common age group was 31 to 40 years (38.43%) followed by 41 to 50 years (25.49) followed by 20 to 30 years (25.09%). In a study conducted by Pun Gurung Rashmey et al, it was found that the most common age of presentation was 30-39 years (29%), followed by 40 to 49 years (27%). The age distribution is almost the same compared to the present study. [7]The mean age for non-neoplastic lesions was 36.05 years while that for epithelial cell abnormality (ASCUS and beyond) was 46.9 years. This correlates well with study conducted by Sachen et al and Zubair et al where the mean age for epithelial cell abnormality was 49 years. [8, 9]

Mean age to develop ASC-US abnormality found to be 37.56 years and that for ASC-H to be 54. In our study, Out of 8 cases of LSIL, 3 cases found between 21-30 years age group while mean age of patients with LSIL was found to be 40.62 years. Mean age for HSIL were 45.33 yrs. an. Elhakeem et al. also noted a progressive increase in development of LSIL to invasive carcinoma with increasing age. LSIL had peak between 20-29 years, HSIL between 30-39 years. [10]. Afrakhteh et al found mean age of patients with LSIL and HSIL to be 37.7 and41.7 respectively. The results are comparable with our present study [11].

The overall most frequent presenting complaints in this study was Discharge per vagina (51.37%) followed by Abdominal pain (17.25%). Out of 45 cases with epithelial cell abnormalities on smear, 23 (51.11%) cases were having complaint of discharge per vagina among which 13 cases detected to having ASC-US and 5 cases as LSIL and 4 cases as ASC-H on smear. It is emphasized the significance of vaginal discharge and its association with neoplastic changes in the cervix. This correlates well with other studies conducted previously. [12, 13, 14, 15]

Regarding the per speculum findings, normal cervix seen in 37.64% cases followed by in cervical erosion in 33.72% cases, In a study conducted by Pushpa et al, Healthy looking cervix is seen in 26 % and Cervical erosion in 19 %. [16]. With regards to Epithelial cell abnormalities, it was seem to be more associated with Erosion of cervix which is seen in 44.44% cases with abnormal pap smears. However, for better evaluation of cervical precancerous lesioncolposcopic examination should be carried out. In study of Dipli et al, out of 150 cases of abnormal pap smear, 30.6 % cases were showing abnormal cervical findings on colposcopy.

5. Conclusion

While reviewing all the results, it is concluded that premalignant and malignant lesions of cervix are not uncommon in our set up. Cervical cytology by Pap smear is a simple, safe and effective test to detect premalignant and malignant lesions of cervix at an early stage, and thus help the clinicians in early and more efficient management of the patients. Visual inspection aided by application of acetic acid is an alternative to cytology screening, yet new techniques such as HPV DNA testing can be used to identify cervical lesions without reliance on cytology. The information obtained from this study could help the institution to know about the prevalence of various abnormal smears in this area and accordingly screening programs can be emphasized and can further be used for various other research purposes.

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