Review of Literature
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Previously gynaecological carcinoma was diagnosed on the basis of symptoms and mostly at an advanced stage histologically, Rubin in 1910 first reported 3 cases of incipient carcinoma of the cervix and in two of his cases extension into the glands of the cervix was observed (Reddy and Sarada, 1976). Broders in 1932, introduced the term “Carcinoma in situ” and classified early malignant lesions as:

(1) Carcinoma in situ with involvement of surface epithelium.

(2) Carcinoma in situ with glandular involvement.

(3) Questionable stromal involvement.

The first two are grouped under carcinoma in situ. The role of vaginal smear in detection of cancer was first described by Papanicolaou in 1928. Carcinoma fundus and cervix were classified as exfoliative lesions by Papanicolaou and Traut WHO in 1943 published a method of vaginal smear for diagnosing uterine cancer.

Papanicolaou and Traut (1943), particularly in the early days of cyto diagnosis took samples chiefly from the posterior fornix of the vagina. Berg and Durfee (1958) demonstrated that
vaginal sample was seemed particularly suitable for investigating endometrial carcinoma.

Davis (1962) suggested the idea of conducting mass examinations of self collected irrigation specimens, such systems have been tested satisfactorily by other investigators, since then Kawashima et al tried his technique, in Japan in 1966. Richart and Vaillant (1965) and Reagan and Lin (1967) reported that vaginal irrigation resulted in inadequate diagnostic accuracy in the screening for early cervical cancer.

Nelson and Hall (1968) consider a typical smear benign. Hammond et al (1968) consider atypical smears changes as negative.

Wahi et al (1969) studied factors influencing cancer of uterine cervix by vaginal cytology and concluded that carcinoma cervix accounted for 30.6% of all cancers. The youngest patient was 18 years and oldest 80 years, carcinoma was higher in the group 45-54 years of age. Wahi et al (1969), Rao et al (1973), Chakravarty at al (1976) reported dysplasia from 2.3 - 7.5%.

Figg et al (1970) reported that one sixth of their cases of cancer were found in patients with atypical smear.
Aikat et al. (1974) studied cervical smears of 19,574 women of different ages. Malignancy was detected in 341 women (17/1000) of whom 77 (4/1000) were clinically non suspected. Dysplasia was present in 301 women (15/1000), mostly they were mild in type. Dysplasia was seen starting usually at 25 years, carcinoma in situ at 35 years and invasive carcinoma at 45 years. Dysplasia was found in 6.58% in the age group of 21—30 years. Dyaplasia and malignancy were more common in women with multiple pregnancies. 18.8% of malignancy were present in nulliparous women. Women had no complaints whatsoever, though 53.1% were suffering from dysplasia 22% from carcinoma in situ end 5.9% from invasive carcinoma. Biopsy could be taken from 154 women, which confirmed diagnosis, 22 women suffering from carcinoma in situ were clinically free from malignancy. There were 301 smears with dysplasia, mild 231, moderate 53, severe 17.

Herbert et al (1976) on analysis of atypical smears continued to find cases of carcinoma in situ. In 10% cases repeat smears progressed to higher abnormality. Persistent atypical smear required tissue for adequate histologic evaluation. Nyirjesy (1972) arid Hulka (1968) have reached to similar conclusions.

Hameed et al (1976) studied 300 vaginal smears. The incidence of cancer cervix was 2%. Out of 143 cases belonging
to the age group of 20-30 years none had cancer smears. The incidence was 2.22% in the age groups of 31-40 years and 41—50 years. There was 13.64% incidence amongst 22 cases of age group of above 50 years.

Bhaskaran et al (1978) studied 2741 patients, 620 were inflammatory. In 221 cells were scanty. cytological assessment was possible in 1900 cases. Mild dysplasia was seen in 16.6%. moderate in 6%. severe in 5.9% carcinoma in situ in 3.8% and malignancy in 11.6%. Average age of mild dysplasia was 31.4 years, carcinoma in situ 34.3 years and invasive carcinoma 42.2 years. Dysplasia was seen most often in the younger age group (18.7%). 204 biopsies were available in the invasive group, two were reclassified as carcinoma in situ and 2 as severe dysplasia after biopsy. In carcinoma in situ 65 biopsies were available, 2 turned out to be micro-invasive carcinoma and 4 moderate dysplasia by biopsy. There were 3 cases of over diagnosis in severe dysplasia and under diagnosis in 4 cases. The same occurred with moderate and mild dysplasia.

Mishra and Das (1979) studied 100 cases by vaginal cytology in precancerous lesions. Maximum number of abnormal smears observed in cases of erosion cervix, with cervicitis (6.6%) and erosion with hypertrophy of cervix (80%). Incidence of dysplasia increased with age, parity and low socio-
economic group. Biopsy confirmed carcinoma in situ in one which showed severe dysplasia.

Jamila at al (1980) did cervical smear study in 1000 kashmiri women, selection for cases were patients erosion or chronic vaginal discharge. Dysplasia was seen in 2.5% case., carcinoma in situ in 3 patients and invasive carcinoma in 11 patients, normal smear in 6.5%. remaining smears showed inflammatory changes and abnormal smear were 3.90%. Mild dysplasia in 10 cases, moderate in 10 cases, and severe in 5 cases out of the 25 cases of dysplasia. Mean age group of mild and moderate dysplasia wan 26 years, severe 28 years, carcinoma in situ 30 years and invasive carcinoma 55 years. Cervical biopsy was done in all the cases of severe dysplasia and had later on total abdominal hysterectomy performed Irradiation therapy or Wertheim’s hysterectomy was done for the invasive carcinoma of the cervix.

Szczepanik and Helpap (1983) histologically analysed 135 cases of suspicious or positive colposcopic or cytologic findings. In cases of colposcopically detectable atypical changes or suspicious findings as well as of cytologic dysplasia or carcinomas the histologic diagnosis were almost the same. In 3 years they performed colpoascopic, cytologic and histologic examination in 6,872 patients. Histologically analysed 135 cases of suspicious or positive colposcopic or cytologic findings.

In 1943 Papanicolaou and Traut diagnosed uterine cancers by vaginal smear examination, but results were poor showing variable accuracy rate (18.94% of accuracy). Cary (1943) was the first to develop a practicable technique of aspiration to draw an intra uterine sample.

Later on various other workers had diagnosed endometrial carcinoma by studying ecto-cervical sample, (Ayre 1947) and endocervical samples (Reagan and Sanmerville 1954), (Boschanfl 1956). By these studies accuracy rate for endometrial carcinoma was 70% and 61% respectively.

Williams and Stewart (1947) diagnosed cases of endometrial carcinoma by endometrial aspiration. Two hundred cases of more than 36 years of age were studied. All cases showed proliferative phase except six of slight hyperplasia in post menopausal group.
In 1949 Papanicolaou performed cytological diagnosis of uterine cancer by examination of uterine secretions. 3.22% cases of adenocarcinoma were diagnosed.

Hecht (1952) studied 125 cases by endometrial aspiration. Age group varied from 34-71 years, 86 cases with menorrhagia, metrorrhagia and bleeding P/V off and on 52 cases were postmenopausal. 16 patients had adenocarcinoma of endometrium, 12 were in postmenopausal and 4 among premenopausal group. 6 of these cases were diagnosed by endometrial smear.

Ayre (1955) developed his new method. Natural bristles were fixed to tip of cannula used to scrape the walls of uterine cavity. The material was smeared on slide and studied.

Hecht (1956) did a study of endometrial aspiration smear in endometrial lesions. An accuracy of 92.3% in the use of aspiration smear in corporal carcinoma was found. Jordan and Bader (1956) found an accuracy of 76% in vagino cervical smear whereas 84% in endometrial smear by endometrial aspiration technique.

Hecht (1956) studied 901 cases by endometrial aspiration smear between 26-71 years average being 51 years. 18.97% cases were bleeding postmenopausally, 5.77% had adenocarcinoma of the endometrium. In the postmenopausal
group 73.07% had positive smears. 57.69% cases of adenocarcinoma were detected by vaginal and cervical smears. Endometrial aspiration smear accurately detected 92.31%. There were 4 false positive In 69.17% curettings were performed. In 30.83% both the uterus and curettings were available. There were 6 cases in which adenocarcinoma of the endometrium was repeatedly diagnosed by endometrial smears and missed by curettage, removal of uterus showed adenocarcinoma in all these cases.

Timonen and Purola (1962), Johnsen et el (1973) and Burk et al (1974) diagnosed, endometrial carcinoma by vaginal and cervical smears. Results were showing 42.2% accuracy. Fox (1962) did endometrial brushing in 500 patients to correlate cytologic and histologic findings obtained by curettage or hysterectomy.

Slaughter end Schewe (1962) performed 433 biopsies on 406 patients. 92% had abnormal vaginal bleeding. There were 68 patient in whom a diagnosis of malignancy of the endometrium was established, 57 patients (84%) had endometrium with biopsies which were reported as showing either malignancy or premalignancy of the endometrium. In 52 of these 68 patients of malignancy final diagnosis was confirm by hysterectomy. There were 11 instances in which no tissue was obtained with suction curettage in cases of endometrial
carcinoma. 9 of these were diagnosed by D & C and remaining by hysterectomy. Carcinoma cervix was the final diagnosis in 39 of the 406 cases with endometrial biopsy. There were 25% cases in which no tissue was obtained initially by use of a suction curette but in which diagnosis was established by a repeat biopsy, D & C or hysterectomy. An accuracy of 76% was achieved in diagnosing carcinoma of endometrium.

Slaughter (1962) performed biopsy of endometrium by Novak suction curettage and reported 76% accuracy for endometrial cancer.

Rascoe (1963) conduct & his study on 6416 patients and obtained vaginal and aspiration smear and performed diagnostic curettage, 103 malignancies were diagnosed.

Wildhack and Graham (1964) reviewed patients with postmenopausal bleeding. A total of 638 cases were reviewed and biopsy was done, 149 were rejected. 489 cases were considered suitable. endometrial biopsy was performed in 302 (61%) of the cases. Procedure was carried in cancer of corpus (71%) and benign postmenopausal bleeders (53%). In 187 cases (39%) endometrial biopsy could not be performed. Majority of the patients were in the age group 50-70 years. Cancer was diagnosed in 131 cases, 116 adenocarcinoma, 11 adenocanthomas carcinoma and 2 metastatic lesions. In 121
cases the diagnosis was benign. In 50 cases tissue was insufficient for histologic diagnosis.

Denis and Barnett (1973) stated that vacuum curettage was applied for diagnosing uterine carcinoma in patients with abdominal uterine haemorrhage. 640 patients underwent suction curettage by Vabra aspirator. 18 were diagnosed as adenocarcinomas. There was high accuracy in diagnosing endometrial hyperplasias.

American Cancer Society (1973) stated that to approach 90-95% accuracy of current screening methods for endometrial malignancy, it is necessary to obtain cells directly from cavity.

Mathews et al (1973) did a comparison of vacuum aspiration and conventional curettage in abnormal, uterine haemorrhage. Vacuum aspiration proved to be more effective than curettage in obtaining at least some material from inside the uterus. 10% cases of vacuum aspiration were abandoned because of the inability of cannula to be introduced. Aspiration technique for cytological diagnosis is available for more than 35 years and reports accuracy up to 84 to 93%.

Cohen et al (1974) performed screening for endometrial cancer by vabra aspirator and reported an accuracy of 95% over all with 100% correlation is cystic and adenomatous hyperplasia and frank carcinoma. Aspiration device with 84.4%
accuracy for detecting endometrial adenocarcinoma was accepted.

Issac's and Withoite (1974) strongly proposed the validity of aspiration cytology. According to this study, the diagnosis of endometrial carcinoma by cervicovaginal smear does not approach the accuracy enjoyed by squamous cell carcinoma of the cervix. This study employed a new disposable endometrial aspirator. There were 160 postmenopausal women in whom an endometrial smear was obtained as an office procedure. There were 186 aspirates obtained in hospital patients. The smear was taken just prior to diagnostic curettage. The accuracy of the endometrial smear was same as obtained by curettage (85.7%).

Muenzer et al (1974) obtained endometrial aspirates in 983 out patients and in 500 patients hospitalized for diagnostic D & C or hysterectomy. All hospitalized patients were aged 40 or above. The outpatient group varied from 29-81 years. Endometrial carcinoma was diagnosed histologically on surgical specimen in 32 of the 500 hospitalized In 27 (84.4%) of the 32 cases endometrial carcinoma was detected by cytologic examination of the aspirate. In 5 patients (15.6%) the aspirate did not show malignant cells, although adenocarcinoma was found in the surgical specimen. In 6 cases adenocarcinoma was suspected from examination of the aspirate and was not found
histologically, 4 of these cases revealed endometrial curettings that were abnormal but benign including 3 with endometrial polyps. This study showed 84.4% accuracy in detecting endometrial adenocarcinoma by aspiration.

Vassilakos et al (1975) reported diagnostic accuracy of 99% cases by jet wash technique. By endometrial aspiration one unsatisfactory case was observed. Diagnosis, by Jet technique has been found to be extremely accurate, the accuracy rate approaching 90 to 100% for both cancerous and precancerous lesions.

Bernard et al (1977) studied the correlation between series of cases between intrauterine lavage and pathological examination of endometrium and surgical samples.

Dilatation and curettage was found by Vuopala (1977) to be most reliable technique for diagnosis of intrauterine abnormalities. It was the standard technique by which most other techniques were compared.

Unfortunately false negative rate could be documented by only removal of uterus. In the course of research, malignant cells were detected in 75% of initial stage, while only 40% cases at stage two showed malignant cells.
Chausson et al (1978) had presented a review of patients in whom suction and curettage of endometrium was performed as an office procedure. A total of 978 curettage were performed. In 14 cases the procedure was not completed primarily due to stenosis. 15 cases of adenocarcinoma, adenomatous hyperplasia of the endometrium were diagnosed.

The work on intracavity washing method indicated by various workers for early diagnosis of adenocarcinornna in various pathologies of endometrial mucosa was examined by Gambotto et al (1978). 29 patients with various endometrial pathologies were considered and the findings of cytological and histological examinations as the material obtained from the washing fluid were compared with those histological examination of the endometrium obtained by curetting. The value of the method was confirmed when the washing matter was examined histologically.

Haack et al (1979) did diagnostic vabra curettage without anaesthesia. The diagnostic certainly was just as good as with conventional curettage under anaesthesia.

Nikitina et al (1979) examined cytologically 172 uterine aspirations. Cancer in 89, non cancer process in 71 and in 12 cases aspiration specimens were obtained in reproductive period in proliferative and secretory phases of menstrual cycle.
It was shown that in a group of histologically verified observation in 45.8% a gynaecologist failed to recognize the true endometrial effect; some cytological criteria elaborated were suggested, their combination helped to precisely diagnose cancer cytologically in 93.2% while various forces of hyperplasia in 89.8%.

Bibbo et al (1979) performed a study with endometrial aspiration and vaginal ectocervical and endocervical smears and correlated with D & C or hysterectomy. Diagnosis for 33 adenocarcinomas and one carcinosarcoma by vaccum was 100%. In 5 cases of atypical hyperplasia the detection rate was 100% by vaccum aspiration, while the vaginal ectocervical and endocervical aspirates were diagnostic in 67% of cases each. In the 5 cases of a typical hyperplasia the detection rate was 100% by vaccum aspiration and 20% by the vaginal ectocervical smears and endocervical aspiration. 30 cases of adenomatous hyperplasia were detected by vaccum aspiration but only 6% vaccum aspiration technique was more reliable in the detection of endometrial adenocarcinoma and its precursors.

Wolinska et al (1979) demonstrated a clear cell adenocarcinoma of endometrium using the cytological technique. Kawada (1979) in an important research finding stated that endometrial carcinoma is easily curable if detected early.
Ambiya et al (1981) made a study of 50 cases of endometrial aspirates. There were 43 cases with hypermenorrhoea, 22 of them showed stromal elements and 10 showed broken glandular elements. No material could be obtained in 5 cases. In 1 case of suspected adenocarcinoma adenocarcinomatous cells could be obtained on aspiration which was confirmed on biopsy. In this study 90% cases had either hypermenorrhoea or post menopausal bleeding.

Favre et al (1982) studied intrauterine washing cytology of the 1,378 washings in 37.7% no anomalies, in 44.7% only benign disorders, in 2.4 cells suspected of being malignant, and in 5.2% malignant cell and 9.9% unfit for study. A total of 620 patients had biopsy curettage or hysterectomy for histologic studies. On histologic finding in 213 cytologically normal smears only 40.8% of them were confirmed histologically normal, 52.5% histology showed benign lesions of the endometrium mostly diffuse hyperplasias or polyps. Histologic findings in 317 cases where cytology showed benign lesions were normal endometrium 23.6%, benign changes 68.4%, adenocarcinoma of endometrium 1.5% unsatisfactory 6.6%. Among the 24 cases of cytology suspected of being malignant histologic examination confirmed 8 adenocarcinomas, 2 suspicious lesions and 14 benign disorders. Among the 66 cases with cytologically malignant specimens, histology
confirmed malignancy in 59 instances, 7 (10.6%) did not correlate. The results show that a positive correlation with histology existed in 89.4% of the cases with a cytologic diagnosis of malignant disease.

Agarwal et al (1985) studied aspiration cytology smear of 200 cases. Proliferative phase was found in 35.5% cases, secretory phase in 45% cases, simple and cystic hyperplasia was seen in 2.5% cases and 3% cases were of malignancy and in 2% cases material was inadequate for diagnosis. In all the above cases endometrial biopsy was done and histopathological finding were studied. 41% cases were of proliferative phase, 43% of secretory phase. 7% cases of simple and cystic hyperplasia, 1% of adenomatous hyperplasia, 2.5% cases of malignancy and 3% cases inadequate. Positive correlation between cytological and histological findings in malignant cases was 83.3% while in hyperplasia was 63.3%. In suspicious or atypical cases correlation was 100%. The patients studied were between the age of 40-70 years. Most of the patients in the study were multiparous. 95 patients were postmenopausal and 15 cases were premenopausal.

Glenthaj A. et al (1986) studied brush cytology from the uterine cervix, incidence rate per 100,000 is still around 18 Demark.
Cherkis RC et al (1988), studied significance by normal endometrial cells detected by cervical cytology of 440 women with normal endometrial cells endometrial evaluation. Endometrial disease was identified in 64 (35.7%) of these patients having endometrial sampling or hysterectomy within 12 month of the cytological evaluation. These lesion included 21 cases (11.7%) of endometrial carcinoma 23 cases (12.9%) of endometrial hyperplasia and 20 cases (11.2%) of adenocarcinoma.

Lopolla et al 1990 studied endopap device for the cytologic detection of uterine cervix and its precursors: a comparison of the endopap with fractional curettage or Hysterectomy was done in 249 patients with symptoms. The sensitivities for the detection of primary corpus cancer and hyperplasia were 0.90 (59/66) and 0.58 (18/31) respectively. All six cases of typical endometrial hyperplasia were detected by the endopap device. Malignant endopap cytologic finding were present in 4 of 10 patients with a primary adnexal malignancy and normal endometrial histologic finding were present in 4 of 10 patients with a primary adnexal malignancy and normal endometrial histologic findings. 92% of primary uterine cervical cancers were detected by endopap cytologic sampling. The specificity
for the cytologic diagnosis of benign conditions was 0.93. Endopap cytologic sampling has a reasonably high sensitivity for the detection of uterine cancers and preinvasive endometrial lesions with a high risk of progression to carcinoma.

Paowati et al (1991) studied false negative pap smears from women with cancerous and precancerous lesions of the uterine cervix from 1980 to 1989. The 4,781 cases of cancerous (2814 invasive carcinoma & 593 carcinoma-in-situ) and precancerous lesions (418 severe dysplasia, 748 moderate dysplasias and 208 mild dysplasia included 70 cases (1.5%) with false negative smears. These 70 cases included 43 invasive carcinoma (61.4%), 17 carcinoma in situ and adenocarcinoma in situ (24.2%) and 10 dysplasia (14.4%) all were diagnosed histologically. The mean age of women with false negative smears was 44.1 +/- 13.7 years. Review of the original cytologic samples showed a screening error in 41 cases (58.5%), interpretation error in 2 cases (2.9%) and a sampling error in 27 cases (38.6%).

Zuna Re Erroll et al (1996) studied retrospectively the utility of the cervical cytologic smear in assessing endocervical involvement by endometrial carcinoma preoperative smear and endocervical curettage were compared with the status of the endocervix in the hysterectomy specimens. Two patients of
malignant endocervical cells are identified in the 25 positive smears (1) a sloughing pattern which was the classic round cell pattern associated with the exfoliation of endometrial cancer cells (2) an abraded pattern in which the cancer cells were present as loosely cohesive sheetlike groups that retained the original cells shape.

Kin Tj kimts et al 1999 studied to evaluate the efficiency of the follow-up methods and routes of AGUS detected on cervicovaginal pap smears in 407, 451, Of which 326 patients were identified as AGUS of 326 patients 268 was followed by repeat pap smears cone biopsy or endometrial curetting.

The incidence of AGUS on pap smears is approximately 0.08% mean age of the patients was 43 years (22-79 cases) most common complains was vaginal bleeding. Gross findings of cervix were normal to mild erosion. Benign lesions detected during follow-up were 6 micro glandular hyperplasia, 5 atypical squamous metaplasia of cervix, 2 cervical endometrosis & uterine adenomyosis. The premalignant or malignant lesions of the cervix were 4 ISIL, 24 HGIL and 4 invasive adenocarcinoma. The neoplastic lesions of the uterine were 6 endometrial hyperplasia 11 endometrial adenocarcinoma. 77 (25%) of 268 patients followed up were identified as having clinically significant lesions of cervix or uterus, The detection
rates of abnormal lesions were 3.1% in repeated papsmears (3/98). 6.3.6% with cone biopsy (35/55) and 29.7% with endometrial curettage (19/64).

Chun AB et al 2000 studied significance ACUS on routine cervical cytologic testing in 48890, women over period of 12 month. Of 48890 smear 141 (0.29%) were diagnosed with AGUS of these 64 (51.2%) were monitored further 26 (66.7%) were of squamous origin 4 (10.3%) had glandular cervical lesions, 2 benign polyps and 2 carcinoma-in-situ. 7(19.9%) had endometrial lesions, one had ovarian cystoadenocarcinoma of this study it was concluded that incidence of AGUS was 0.29%.

Obenson K. Abreo f et al 2000 studied cytohistologic correlation between AGUS & biopsy detected lesions in post menopausal women. They studied retrospectively 30 patients overage 50 had cervical smears interpreted as AGUS and had follow-up biopsies within 12 months following the abnormal smear. Of these 5 smears had AGUS favour reactive revealed abnormal histology in four cases, 3 endometrial polyps & one squamous carcinoma. Two smears interpreted as AGUS favour dysplasia revealed squamous intra-epithelial lesions. on biopsy in both cases, 17 smears interpreted as AGUS favour endometrial cells, revealed abnormal histology in 13 cases, endocervical polyps, 6 endometrial polyps 3 endometrial
hyperplasia & 3 adenomyosis six patients with smears interpreted as AGUS, unclassifiable, revealed abnormal histology in 5 cases: two endocervical polyps, one endometrial polyp, one endometrial carcinoma & one ovarian carcinoma so, it was concluded that cervical smears was highly predictive of abnormal lesions detected by histologic examination.