Online Journal of Gynecology, Obstetrics and Maternity Care
ISSN: 2642-0163

Research Article *Volume 2; Issue 1*

Challenges in Management of Endometrial Cancer in Low Resource Settings

Chhabra S* and Gangane N

Obstetrics Gynaecology, Mahatma Gandhi Institute of Medical Sciences, India

***Corresponding author:** Shakunthala Chhabra, Obstetrics Gynecology, Mahatma Gandhi Institute of Medical Sciences Sevagram-442102, Wardha, Maharashtra, India, Tel: +917152284342; Email: chhabra_s@rediffmail.com; schhabra@mgims.ac.in

Received Date: May 31, 2019; **Published Date:** July 03, 2019

Abstract

Background: It is believed that because of abnormal uterine bleeding (pre-, peri-or postmenopausal), most constant first symptom of endometrial cancer, care is usually sought early. But in developing countries this may not happen. Also while most of often EC occurs in postmenopausal women, mostly 61-70yrs, some might get it at younger age with challenges in management.

Objectives: Present study was conducted to look at challenges in management of EC in women from low resources.

Material Methods: Present study was conducted in the department of Obstetrics & Gynecology of a rural tertiary care centre after approval of ethics committee of the institute with help from pathology. Histopathologically proved EC cases managed over a period of 9 years were included and details of their management were analyzed.

Results: Of the 62 patients of EC, 11 (17.74%) were premenopausal and 51 post-menopausal, 57 (91.94%) were of Type I 5 (8.06%) Type II. Fifty-four (93%) out of total 62 women could be evaluated completely surgically also, with available facilities and had myometrium involvement diagnosed on histopathology, 4 only by imaging. Nineteen women had one third thickness, 12 half thickness, 2 two third thickness, 21 had full thickness of uterine myometrium involvement. Peritoneal washings were submitted for cytology only in 8 patients, 4 (50%) were positive for EC, Two of those 4 had tubectomy years back. All four had myometrium involvement of more than half thickness. Of 4 cases with negative washings, 3 had tubectomy and no myometrium involvement. Out of 34 cases in whom lymph nodes were submitted, three (8.8%) had positive lymph nodes and had half to full thickness myometrium involvement on histopathology. All 4 patients of less than 40 years were of Type I EC, 3 stages I and one stage III. All had surgery, followed by chemo radiotherapy. Overall of the 62 patients of EC, 18 (29.03%) were of stage I A, 20 (32.26%) stage I B, 4 (6.45%) Stage II, 6 (9.68%) stage III A, 3 (4.84%) stage III B, 3 (4.84%) stage III C, (12.9%) were stage IV B. So over all 50% were beyond stage I, almost 18% stage III.

Conclusion: In resource poor women in whom EC is increasing, are not being diagnosed in early stages with limitations in availability and use of technology available. Peritoneal cytology and linkage of myometrium histopathology and also myometrium involvement and lymph node involvement need more research.

Citation: Chhabra S and Gangane N. Challenges in Management of Endometrial Cancer in Low Resource Settings. Online J Gyne Obste Maternity Care 2019, 2(1): 180009.

Keywords: Endometrial cancer; Endometrial thickness

Abbreviations: HIS: Hospital Information System; ET: Endometrial Thickness; FIGO: Federation of Gynecology and Obstetrics; ER: Estrogen Receptors; PR: Progesterone Receptors; MPA: Medroxyprogesterone Acetate; TNM: Tumour Node Metastasis;

Introduction

Background

Endometrial cancer, with maximum incidence believed to be in postmenopausal women of 61-70 years, tends to be the most common genital tract cancer in the developed countries [1,2], is increasing in developing countries too. Also women of younger age, (less than 40 years), are being diagnosed with EC. It is believed that because of abnormal uterine bleeding (pre-, peri-or postmenopausal), the first and most constant symptom of EC, women usually seek care early. Clinical examination, imaging tests and pathological examination help in early diagnosis. But in developing countries this may not happen. Also elderly women with atrophic endometrium might not take care needed for diagnosis of cause of spotting. Disease might progress before diagnosis and such EC Type II are more dangerous too. So final outcome differs.

Objectives

Present study was conducted to look at challenges in management of endometrial cancer in women from low resources in a low resource region [3,4].

Material Methods

The present study was conducted with his to pathologically proved EC cases admitted over a period of 9 years in the department of Obstetrics & Gynecology of a rural tertiary care centre. Earlier analysis was also looked into. History details, clinical examination, investigations and management were analysed through records in Hospital Information System (HIS) and patient's records.

Results

Of the 62 patients of EC, 11 (17.74%) were premenopausal and 51 post-menopausal. All the 11 (100%) premenopausal women had endometrial thickness (ET) of >5mm on sonography. Of the 51 postmenopausal women, also 43 (84.31%) had ET >5mm and 3 had ET <5mm. In 5 patients ET was not known as USG report had not mentioned [5, 6]. These women had undergone vaginal hysterectomy with postoperative diagnosis of EC of the 62 patients managed over study period, 57 (91.94%) were of Type I and only 5 (8.06%) Type II. Over all 18 were of stage IA, 20 IB, 4 stage II, 6 stage IIIA, 3 stage IIIB, 3 stage IIIC1, and 8 were IVB. Four (6.45%) women were of less than 40 years, 3 with stage IA and one III B too. Of 19 (30.65%) patients between 40-49 years 6 (31.5%) were of IA, 7 (11.29%) I B, 2 III A, one III B and 3 (4.83%) IVB. Overall 68.5% cares were beyond stage II. Of the 25 (40.32%) cases of 50 to 59 years, 7 (28%) were of stage I A, 10 (40%) stage I B, 2 (8%) stage II, 2 (8%) IIIC1 and one (4%) was IVB. Of the 11(17.74%) women of 60 – 69 years, one (9%) had IA EC, 3 (27%) IB, 2 (18 %) stage II, one (9%) IIIB and 3(27%) IVB. Of 3 women of 70 years, one (33.3%) was IA, one (33.3%) IIIA and one (33.3%) had IVB EC. Forty-seven (75.81%) women had endometroid EC, 9 (14.52%) endometroid ca with squamous metaplasia, one (1.61%) endometroid with squamous cell carcinoma and 5 (8.06%) had serous carcinoma. Fifty-four (93%) out of total 58women evaluated completely with available facilities, had myometrial involvement diagnosed on histopathology after surgery (four by imaging), 19 had one third thickness, 12 half thickness, 2 had third thickness, and 21 had full thickness myometrial involvement. Peritoneal washings were submitted for cytology only in 8 women and 4 (50%) were positive for EC. Of these 4 cases 2 had tubectomy years back. All four had myometrial involvement of more than half thickness. Of the 4 cases with negative washing, 3 had tubectomy years back. There was no myometrium involvement in these four women. Out of 34 cases in whom lymph nodes were submitted, three (8.8%) were positive. These women with positive nodes had half to full thickness myometrial involvement on histopathology (Table 1,2,3).

Age group (years)	Parity	Type of end= etrid cancer and size of uterus										Total	Total (%)
		TAH+ BSO	Extende Dtotal Hystere Ctomy	Wertheim s's hyste rectomy	Vaginal Hysterecto my	Racio therapy	Chemo therapy	Chemo therapy+ Radio therapy	Surgery+ Radioth erapy	Surgery + Radiotharapy + Chemotherapy	NONE		
<40 years	P_{0-2}	2	0	2	0	0	0	0	0	4*	0	4	100.00
	P_{3-5}	0	0	0	0	0	0	0	0	0	0	0	0.00
	P_{5+}	0	0	0	0	0	0	0	0	0	0	0	0.00
	Total	2	0	2	0	0	0	0	0	4*	0	4	100.00
40- 49 years	P_{0-2}	1	0	4	1	0	0	1	0	5*	0	7	36.87
	P_{3-5}	3	0	5	0	1	0	1	0	7*	2	12	63.16
	P_{5+}	0	0	0	0	0	0	0	0	0	0	0	0.00
	Total	4	0	9	1	1	0	2	0	12T	2	19	100.00
50-59 years	P_{0-2}	5	0	4	0	0	0	0	2*	6*	0	9	36.00
	P_{3-5}	6	0	7	0	1	0	1	3*	9*	1	16	64.00
	P_{5+}	0	0	0	0	0	0	0	0	0	0	0	0.00
	Total	11	0	11	0	1	0	1	Si	15*	1	25	100.00
60- 69 years	P_{0-2}	0	0	1	0	0	0	0	1*	0	0	1	9.
	P_{3-5}	0	0	3	0	0	0	2	1*	2*	1	6	54.55
	P_{5+}	0	0	3	0	0	1	0	1*	2*	0	4	36.36
	Total	0	0	7	0	0	1	2	3i	4*	1	11	100.00
>70years	P_{0-2}	0	0	1	0	0	0	0	1*	0	0	1	33.33
	P_{3-5}	1	0	1	0	0	0	0	1*	1*	0	2	66.67
	P_{5+}	0	0	0	0	0	0	0	0	0	0	0	0.00
	Total	1	0	2	0	0	0	0	2*	1*	0	3	100.00
Total		18	0	31	1	2	1	5	10*	36*	4		
%		29.	0.00	50.00	1.61	3.23	1.61	8.06	16.10	58.00	6.45	62	

Table 1: Age, parity and management.

Age group (years)	Myometrial involvement	Peritoneal Washing						Lymph Node involvement					
		Positive		Negative		Not submitted		Involved		Not involved		Not sampled	
<40 years	Not involved	0	0.00	0	0.00	1	25.00	0	0.00	1	25.00	0	0.00
	≤ ½ involved	0	0.00	0	0.00	2	50.00	0	0.00	2	50.00	0	0.00
	> ½ involved	0	0.00	0	0.00	1	25.00	0	0.00	1	25.00	0	0.00
	Total	0	0.00	0	0.00	4	100.00	0	0.00	4	100.00	0	0.00
40 - 49 years	Not involved	0	0.00	0	0.00	2	11.76	0	0.00	0	0.00	2	16.67
	≤ ½ involved	0	0.00	0	0.00	8	47.06	1	100.00	5	83.	2	16.67
	> ½ involved	1	100.00	1	100.00	7	41.18	0	0.00	1	17.	8	66.67
	Total	1	100.00	1	100.00	17	100.00	1	100.00	6	100.00	12	100.00
0 - 59 years	Not involved	0	0.00	0	0.00	3	12.50	0	0.00	1	7.	2	20.00
	≤ ½ involved	0	0.00	0	0.00	14	58.33	0	0.00	10	71.	4	40.00
	> ½ involved	1	100.00	0	0.00	7	29.17	1	100.00	3	21.	4	40.00
	Total	1	100.00	0	0.00	24	100.00	1	100.00	14	100.00	10	100.00
60 - 69 years	Not involved	0	0.00	0	0.00	2	28.57	0	0.00	0	0.00	2	40.00
	≤ ½ involved	0	0.00	1	50.00	4	57.14	1	100.00	4	80.00	0	0.00
	> ½ involved	2	100.00	1	50.00	1	14.29	0	0.00	1	20.00	3	60.00
	Total	2	100.00	2	100.00	7	100.00	1	100.00	5	100.00	5	100.00
>70 years	Not involved	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	≤ ½ involved	0	0.00	0	0.00	1	33.33	0	0.00	0	0.00	1	100.00
	> ½ involved	0	0.00	0	0.00	2	66.67	0	0.00	2	100.00	0	0.00
	Total	0	0.00	0	0.00	3	100.00	0	0.00,	2	100.00	1	100.00
Total	n	4	6.45	3	4.84	55	88.71	3	4.84	31	50.00	28	45.16

Table 2: Age, Myometrial Involvement, Peritoneal Fluid Cytology and Lymph Node involvement.

Age	Management	Type and stage of a endometrial cancer																n	%
		Type 1								Type 2									
		I		II		III		IV		I		II		III		IV			
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%		
<40 years	surgery	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	Surgery ± radiotherapy ±chemotherapy	3	75.00	0	0.00	1	25.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	4	6.45
	chemotherapy±rediotherapy	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	None	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	Total	3	75	0	0	1	25	0	0	0	0	0	0	0	0	0	0	4	6.45
49 years	surgery	1	5.26	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	1	1.61
	Surgery ± radiotherapy ±chemotherapy	10	52.63	0	0.00	2	10.53	1	5.26	0	0.00	0	0.00	0	0.00	0	0.00	13	20.97
	chemotherapy±rediotherapy	0	0.00	0	0.00	1	5.26	2	10.53	0	0.00	0	0.00	0	0.00	0	0.00	3	4.84
	None	2	10.53	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	2	3.23
	Total	13	68	0	0	3	16	3	16	0	0	0	0	0	0	0	0	19	30.65
50-59 years	surgery	1	4.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	1	1.61
	Surgery ± radiotherapy ±chemotherapy	12	85.71	2	8.00	4	16.00	0	0.00	2	8.00	0	0.00	1	4.00	0	0.00	21	33.87
	chemotherapy±rediotherapy	0	0.00	0	0.00	0	0.00	1	4.00	1	4.00	0	0.00	0	0.00	0	0.00	2	3.23
	None	1	4.00	0	0.00	0	0.00	0	0.00	0	0	0	0.00	0	0.00	0	0.00	1	1.61
	Total	14	56	2	8	4	16	1	4	3	12	0	0	1	4	0	0	25	40.32
60-69 years	surgery	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	Surgery ± radiotherapy ±chemotherapy	4	36.36	1	9.09	1	9.09	1	9.09	0	0.00	0	0.00	0	0.00	0	0.00	7	11.29
	chemotherapy±rediotherapy	0	0.00	1	9.09	1	9.09	2	18.18	0	0.00	0	0.00	0	0.00	0	0.00	4	6.45
	None	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	Total	4	36	2	18	2	18	3	27	0	0	0	0	0	0	0	0	11	17.74
>70 years	surgery	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	Surgery ± radiotherapy ±chemotherapy	1	33.33	0	0.00	1	33.33	0	0.00	0	0.00	0	0.00	0	0.00	1	33.33	3	4.84
	chemotherapy±rediotherapy	0	0.00	0	0.00	0	0	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	None	0	0.00	0	0.00	0	0	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	Total	1	33	0	0	1	33	0	0	0	0	0	0	0	0	1	33	0	4.84
Total		35	56.45	4	6.45	11	17.74	7	11.29	3	4.84	0	0.00	1	1.61	1	1.61	62	100.0

Table 3: Age, Type, Stage and Management of Endometrial cancer.

All 4 patients of less than 40 years were of Type I EC, 3 stage I and stage III. They had Wertheim's hysterectomy followed by chemo radiotherapy in one. Of the 18 women of 40-49 years with stage IA, 8 had total abdominal hysterectomy with bilateral salpingo-oophorectomy and chemo radiotherapy. They had myometrial involvement diagnosed post-operative after histopathology examination. Eight women had Wertheims' hysterectomy followed by chemo radiotherapy. One with other comorbidities received radiotherapy and one did not receive any treatment as she did not follow after diagnostic curettage. Of the 20 women with IB disease, 5 had TAH with BSO followed by chemo radiotherapy, 10 had Wetheims's hysterectomy and chemo radiotherapy, and 2 had Wertheims' hysterectomy and radiotherapy.

One woman who had vaginal hysterectomy with post-operative diagnosis of EC, received chemo radiotherapy and 2 did not receive any treatment as they did not follow. All 4 women of Stage II, EC had Wertheims' hysterectomy followed by chemo radiotherapy. Of the 6 cases of stage IIIA, 3 had TAH and BSO and chemo radiotherapy, 2 had Wertheim's hysterectomy and chemo radiotherapy and one could have only staging laparotomy followed by chemo radiotherapy as she was too advanced for surgery. Of the 3 cases of stage IIIB, 2 had Wertheim's

hysterectomy and chemo radiotherapy and one had chemo radiotherapy. Of the 3 women with IIIC1, one had TAH with BSO and chemo radiotherapy and 2 had Wertheim's hysterectomy and chemo radiotherapy. Of the 8 women of stage IVB, one had TAH and BSO with chemo radiotherapy and 2 had Wertheim's hysterectomy with chemo radiotherapy and 5 had chemo radiotherapy. Over all four patients did not receive any treatment as they failed to follow up after endometrial curettage which revealed EC. Of the 57 patients who were of EC Type I, 50 (87.71 %) had oestrogen receptors and 48 (84.21%) had progesterone receptors. Of the 5 patients EC Type II, one (20%) had oestrogen receptors and one (20%) had progesterone receptors. Depending on ORPR women received progesterone therapy during follow up.

Discussion

Amant et al., reported that bleeding made diagnosis early, so most women with EC had early-stage disease at presentation [7]. But in resource poor women where EC is increasing, EC cases are not being diagnosed in early stages. In the present study of the 62 patients of EC, 18 (29.03%) women were of stage I A, 20 (32.26%) stage I B, 4 (6.45%) Stage II, 6 (9.68%) stage III A, 3 (4.84%) stage III B, 3 (4.84%) stage III C and 8 (12.9%) were stage IV B. So over all 50% cases were diagnosed beyond stage I and almost 18% were stage III at diagnosis. In the present analysis even of 4 young women (less than 40 years) one had stage III disease at diagnosis and of 40-49 years also 68.5% were beyond stage I. Fifty-four (93%) out of total 58 patients evaluated (four only by imaging) by uterus histopathology also had myometrial involvement on histopathology . Of these 54 patients, 19 (35%) had one third thickness myometrial involvement, 12 (22%) had half thickness, 2 (3%) had two third thickness, and 21 (38%) had full thickness mytometrial involvement. In low resources setting with limitation in availabity and use of preoperative imaging technology myometrial diagnosis is after histopathology. Of the 8 cases where peritoneal washings were sent, 4 (50%) had positive peritoneal washings and they had tubectomy and more than half myometrial involvement. Of the 4 with negative washing, peritoneal 3 had tubectomy with no myometrial involvement. While extra uterine spread is a well recognized poor prognostic factor in EC the clinical significance of malignant cells, in peritoneal cavity is not clear. However disease spread seems obvious due to myometrial involvement in all the cases where peritoneal washings were positive. Cytology needs to be sent in all the EC cases. Research is needed about adjutant chemo radiotherapy in such cases even if surgery was appropriate. Some researchers have suggested that positive cytology has no association with survival [8-10], but others have observed worse outcomes for patients with positive cytology, even after controlling for other prognostic factors [11,12]. Whether or not peritoneal cytology is an independent prognostic factor is debated, though currently cytology has been removed from the staging system [13.] The findings also suggested tubectomy did not change the findings. In all the cases perioneal washings should be sent and more research is needed.

Three (8%) women had positive lymph nodes out of 34 patients in whom lymph nodes were submitted. Though in small numbers lymph nodes positivity had good correlation with myometrial involvement. Panici et al. in a randomized trial of over 500 patients with stage I EC reported no difference in disease-free survival (80% vs. 82%) or overall survival (90% vs. 86%) between the lymphadenectomy and no lymphadenectomy groups [14]. Bristow et al. in retrospective study of 40 patients with stage IIIC showed a significant disease-specific survival benefit of 37.5 months versus 8.8 months from debulking macroscopic adenopathy with node-positive advanced disease [15]. Surgery is the therapy of choice. Some authors argue that patients with stage 1A and grade 1 or 2 are unlikely to have lymph node involvement, and systematic lymphadenectomy is not indicated in these patients [16, 18]. In 1988, the international federation of gynecology and obstetrics (FIGO) cancer committee changed the staging of endometrial carcinoma from a clinical one to a surgicopathologic one. The emphasis in the new FIGO system was changed to the pathologic findings in the uterus, cervix, adenexa, and pelvic and or periaortic nodes, and peritoneal cytologic findings. The major changes in this staging system were the use of the depth of myometrial invasion and the identification of tumor cells in peritoneal cytologic examination and of invasion in the retroperitoneal lymph nodes [19]. More research is needed about pelvic lymphadenectomy.

Expression of estrogen receptors (ER) and progesterone receptors (PR) is reported in most EC, but in amounts lower than can be identified in normal cycling endometrium (Soper 1990). Response to hormonal therapy is quite variable, and a number of pathological factors contribute to this variation, like hormonal therapy is more likely to be effective in grade 1 or 2 endometrioid tumours. In a large clinical trial of Medroxyprogesterone Acetate (MPA), the response rate was 37% for grade 1, 23% for grade 2 and 9% for grade 3 tumours [20]. Women with receptor positive disease had also been shown to have a higher chance of responding to hormonal therapy.

In a randomised trial, the response rate observed in patients with ER and PR positive disease was around 25% and 37%, respectively, but was only 7–8 % in patients with ER/PR negative disease [21]. Based on these results, it seems that positivity of ER and/or PR could be a predictive factor of response to hormonal therapy and so should be determined before initiating hormonal therapy. In the present study of the 57 patients of EC Type I, 50 (87.71 %) had oestrogen receptors and 48 (84.21%) progesterone receptors, and of the 5 patients of Type II EC, one (20%) had oestrogen receptors and one (20%) progesterone receptors and 3 (60%) were ER PR negative. However more research is needed on this aspect also. Djordjevic, [22], reported that serous and clear cell carcinoma tended to be negative, for antibodies directed towards ER and PR. This was also evident in the present study, 87% of Type I ER and 84% PR, however only 20% of Type II were ER and PR positive. Follow up was not part of the present study.

Out of the total 62 patients of EC, over all 14(22.6%) had TAH with BSO, 4 (6.5%) had extended total hysterectomy, 31 (50%) had Wertheim's hysterectomy. One (1.6%) woman had vaginal hysterectomy, and EC was diagnosed on histopathology after hysterectomy after evaluation with imaging. Two (3.2%) received radiotherapy, 6 (9.7%) chemo radiotherapy. Four patients did not receive any treatment as a result of failure to follow up. Traditionally, surgical staging for EC has been accomplished with open laparotomy. Kornblith [23], reported that laparoscopy had higher scores on several quality-of-life measures over the 6-weeks recovery period compared to laparotomy patients. But a meta-analysis of survival data from three randomized trials did not detect a survival difference between surgical approaches [24]. Vandenput [25], reported approximately 10-15% of cases of EC disease outside the uterus accounting for more than 50% of all uterine cancer-related deaths, with survival rates as low as 5 to 15%. Therefore, treatment often consisted of radical surgery followed by combination of radiation, chemotherapy, and novel therapeutic agents.

The treatment paradigm for advanced FIGO stage III and IV EC has shifted to a multimodality approach that includes surgery, chemotherapy, and radiation therapy, with cytoreduction being the most crucial aspect. Multiple retrospective studies addressed the advantages of optimal cytoreductive surgery in stage III and IV EC. Each study demonstrated a significant progression-free and overall survival advantage when optimal cytoreduction was achieved [26, 27].

Staging (pre-therapeutic and postsurgical), using both classification systems (TNM and FIGO), may be the most important thing in the comprehensise therapeutic decision. Present analysis had advanced cases even in young women. Treatment was individuated. Adjuvant and neoadjuvant therapy have specific indications, according to NCCN Guidelines recommendations, guided by the tumor type, grading, stage and recurrence rate [28]. EC has a good therapeutic response if the diagnosis is early established and the treatment is immediately initiated and a 5-year survival rate of over 50%, even for tumours of stage III B, [29]. Surgery remains the main therapeutic method. Pre-therapeutic staging (TNM) helps in surgical procedures. Although early-stage endometrial cancer is treatable with surgery and adjuvant therapy, long-term outcomes for patients with advanced disease are poor, and the activity of chemotherapy or hormonal therapy in this setting is very low. 20-30% of endometrial cancers have microsatellite instability, and PD-1 inhibition is much less efficacious in patients with microsatellite-stable disease [30].

Over all the median age at diagnosis reported is the sixth decade, with abnormal uterine bleeding at presentation in 90% of the patients. Surgical treatment, including complete hysterectomy, removal of remaining adnexal structures, and an appropriate surgical staging, represents the milestone of curative therapy for patients with EC. Adjuvant therapy is necessary in patients at high risk of recurrence. Conservative treatment approaches should be used in selected cases for women with a desire of fertility preservation [31]. Since overweight and obesity have reached epidemic proportions in many Asian countries, especially in India, it becomes imperative to be prepared for increase in EC [32,33]. Also in women with abnormal uterine bleeding and endometrial hyperplasia concurrent EC needs to remembered and ruled out [34]. Pap's smear may not help, though substantial information of endometrium may be valuable [35-37] and malignant cells do give evidence of advanced EC [38-41]. It seems a lot of more research is needed, especially because there are chances of increase in EC in populations, more so in younger age with management challenges.

References

1. Weiss NS, Szekely DR, Austin DF (1976) Increasing incidence of endometrial cancer in the United States. New England journal of medicine 294(23):1259-62.

2. Varughese J, Richman S (2010) Cancer care inequity for women in resource-poor countries. Reviews in Obstetrics and Gynecology 3(3):122.

3. Tabor A, Watt HC, Wald NJ (2002) Endometrial thickness as a test for endometrial cancer in women

with postmenopausal vaginal bleeding. Obstetrics & Gynecology 99(4):663-70.

4. Larson DM, Johnson KK, Reyes CN Jr, Broste SK (1994) Prognostic significance of malignant cervical cytology in patients with endometrial cancer. Obstetrics & Gynecology 84(3):399-403.

5. Nguyen TN, Bourdeau JL, Ferenczy A, Franco EL (1998) Clinical significance of histiocytes in the detection of endometrial adenocarcinoma and hyperplasia. Diagnostic cytopathology 19(2):89-93.

6. Tabor A, Watt HC, Wald NJ (2002) Endometrial thickness as a test for endometrial cancer in women with postmenopausal vaginal bleeding. Obstetrics & Gynecology 99(4):663-70.

7. Amant F, Moerman P, Neven P, Timmerman D, Van Limbergen E, et al. (2005) Endometrial cancer. The Lancet 366(9484):491-505.

8. Ebina Y, Hareyama H, Sakuragh N, Yamamoto R, Furuya M, et al (1996) Peritoneal cytology and its prognostic value in endometrial carcinoma. International surgery 82(3):244-8.

9. Kasamatsu T, Onda T, Katsumata N, Sawada M, Yamada T et al. (2003) Prognostic significance of positive peritoneal cytology in endometrial carcinoma confined to the uterus. British journal of cancer 88(2):245-50.

10. Fadare O, Mariappan MR, Hileeto D, Wang S, Mcalpine JN et al. (2005) Upstaging based solely on positive peritoneal washing does not affect outcome in endometrial cancer. Modern pathology 18(5):673-80.

11. Katz LA, Andrews SJ, Fanning J (2001) Survival after multimodality treatment for stage IIIC endometrial cancer. American journal of obstetrics and gynecology 184(6):1071-1073.

12. Santala M, Talvensaari Mattila A, Kauppila A (2002) Peritoneal cytology and preoperative serum CA 125 level are important prognostic indicators of overall survival in advanced endometrial cancer. Anticancer research 23(3C):3097-1093.

13. Cooke EW, Pappas L, Gaffney DK (2011) Does the revised International Federation of Gynecology and Obstetrics staging system for endometrial cancer lead to increased discrimination in patient outcomes? Cancer 117(18):4231-4237.

14. Panici PB, Basile S, Maneschi F, Lissoni AA, Signorelli M et al. (2008) Systematic pelvic lymphadenectomy vs no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. Journal of the National Cancer Institute 100(23):1707-1716.

15. Bristow R, Zahurak M, Alexander C, Zellars R, Montz F (2003) FIGO stage IIIC endometrial carcinoma: resection of macroscopic nodal disease and other determinants of survival. International Journal of Gynecological Cancer 13(5):664-672.

16. Morrow CP, Bundy BN, Kurman RJ, Creasman WT, Heller P, et al. (1991) Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study. Gynecologic oncology 40(1):55-65.

17. Creutzberg CL (2005) Lymphadenectomy in apparent early-stage endometrial carcinoma: do numbers count? Journal of clinical oncology 23(16):3653-3655.

18. Kehoe SM, Miller DS (2011) The role of lymphadenectomy in endometrial cancer. Clinical obstetrics and gynecology 54(2):235-44.

19. Mikuta JJ (1993) International Federation of Gynecology and Obstetrics staging of endometrial cancer 1988. Cancer 71(S4):1460-1463.

20. Thigpen JT, Brady MF, Alvarez RD, Adelson MD, Homesley HD, et al. (1999) Oral medroxyprogesterone acetate in the treatment of advanced or recurrent endometrial carcinoma: a dose-response study by the Gynecologic Oncology Group. Journal of Clinical Oncology 17(6):1736.

21. Decruze S, Green J (2007) Hormone therapy in advanced and recurrent endometrial cancer: a systematic review. International Journal of Gynecological Cancer 17(5):964-78.

22. Djordjevic B, Westin S, Broaddus RR (2102) Application of immunohistochemistry and molecular diagnostics to clinically relevant problems in endometrial cancer. Surgical pathology clinics 5(4):859-78.

23. Kornblith AB, Huang HQ, Walker JL, Spirtos NM, Rotmensch J et al. (2009) Quality of life of patients with endometrial cancer undergoing laparoscopic international federation of gynecology and obstetrics staging compared with laparotomy: a Gynecologic Oncology Group study. Journal of Clinical Oncology Group Study 27(32):5337-42.

24. Palomba S, Falbo A, Russo T, Zullo F (2009) Updating of a recent meta-analysis of randomized controlled trials to assess the safety and the efficacy of the laparoscopic surgery for treating early stage endometrial cancer. Gynecologic oncology 114(1):135-136.

25. Vandenput I, Amant F, Moerman P (2011) Clinicopathologic Study in Uterine Cancer. Facts, views & vision in Obst gynecol 3(3):189.

26. Lambrou NC, Gomez Marıin O, Mirhashemi R, Beach H, Salom E, et al. (2004) Optimal surgical cytoreduction in patients with Stage III and Stage IV endometrial carcinoma: a study of morbidity and survival. Gynecologic oncology 93(3):653-8.

27. Shih K, Yun E, Gardner G, Barakat R, Chi D, et al. (2011) Surgical cytoreduction in stage IV endometrioid endometrial carcinoma. Gynecologic oncology 122(3):608-11.

28. NCCN. NCCN clinical practice guidelines in oncology: uterine neoplasms, V. 1.2014. 2014.

29. Zhang Y, Wang J (20110) Controversies in the Management of Endometrial Carcinoma. Obstetrics and Gynecology International.

30. Konecny GE (2019)Inhibition of PD-1 and VEGF in microsatellite-stable endometrial cancer. The Lancet. Oncology.

31. Zhang Y, Wang J (20110) Controversies in the Management of Endometrial Carcinoma. Obstetrics and Gynecology International.

32. Ramachandran A, Snehalatha C (2010) Rising burden of obesity in Asia. Journal of obesity.

33. Kalra S, Unnikrishnan A (2012) Obesity in India: The weight of the nation. Journal of Medical Nutrition and Nutraceuticals 1(1):37.

34. Cherkis RC, Patten Jr SF, Dickinson JC, Dekanich AS (1987) Significance of atypical endometrial cells detected by cervical cytology. Obstetrics & Gynecology 69(5):786-789.

35. Kim HS, Underwood D (1991) Adenocarcinomas in the cervicovaginal papanicolaou smear: Analysis of a 12-year experience. Diagnostic cytopathology 7(2):119-24.

36. Zucker PK, Kasdon EJ, Feldstein ML (1985) The validity of Pap smear parameters as predictors of endometrial pathology in menopausal women. Cancer 56(9):2256-63.

37. Larson DM, Johnson KK, Reyes Jr CN, Broste SK (1994) Prognostic significance of malignant cervical cytology in patients with endometrial cancer. Obstetrics & Gynecology 84(3):399-403.

38. Nguyen TN, Bourdeau JL, Ferenczy A, Franco EL (1998) Clinical significance of histiocytes in the detection of endometrial adenocarcinoma and hyperplasia. Diagnostic cytopathology 19(2):89-93. Yancey M, Magelssen D, Demaurez A, Lee RB (1990) Classification of endometrial cells on cervical cytology. Obstetrics & Gynecology 76(6):1000-1005.

39. Eddy GL, Wojtowycz MA, Piraino PS, Mazur MT (1997) Papanicolaou smears by the Bethesda system in endometrial malignancy: utility and prognostic importance. Obstetrics & Gynecology 90(6):999-1003.

40. Roelofsen T, Geels YP, Pijnenborg JM, van Ham MA, Zomer SF et al (2013) Cervical cytology in serous and endometrioid endometrial cancer. International Journal of Gynecologic Pathology 32(4):390-8.

41. Guy MS, Cheng G, Post MD, Spillman MA, Behbakht K et al. (2014) Outcomes of women with atypical glandular cells on preoperative cytology and endometrial cancer. International Journal of Gynecological Cancer 24(2):266-271.