CHAPTER 4 : RESULTS

4.1 EPIDEMIOLOGY OF GYNAECOLOGICAL NEOPLASMS

4.1.1 Incidence of gynaecological neoplasms in Sarawak

Figure 4.1 shows the annual incidence of gynaecological neoplasms in Sarawak for the years 1985 to 1993. The breakdown of number of patients for cancer is given in Table 4.1. The number of gynaecological neoplasms patients seen per year during this period increased from 41 in 1985 to 113 in 1992 and dropped to 82 in 1993. The average number per year was 88. The crude incidence per 100,000 increased from 5.6 in 1985 to 12.4 in 1988 and became fairly steady till 1992 and dropped to 9.4 in 1993. The highest incidence was 13.2 which was recorded in 1992 and the lowest incidence 5.6 was recorded in 1985. There was no significant difference found between the lowest and the highest incidence (t test, p value > 0.05).

4.1.2 Most frequent gynaecological neoplasms in Sarawak

The frequency of gynaecological neoplasms in Sarawak is shown in Figure 4.2. Cervical neoplasm made up about 85.4 per cent of all gynaecological neoplasms. This was followed by endometrial neoplasm at 7.4 per cent and ovarian neoplasm at 5.7 per cent. There was only a small percentage of vulva and vaginal neoplasm i.e. 1.5 per cent of all gynaecological neoplasms reported.

Table 4. 1 : The incidence of four sites of gynaecological neoplasms among different ethnic groups in Sarawak from 1985 to 1993.

YEAR	DIAGNOSIS	RACE					TOTAL
		Chinese	Iban	Malay	Other Indigenous	Others	
1985							
	CERVIX	23	4	6	3		36
	ENDOMETRIUM	2	1				3
	OVARY			2			2
	VULVA/VAGINA						
1986							
	CERVIX	34	14	8	7		63
	ENDOMETRIUM	3		3	1		7
	OVARY	4		2	1		7
	VULVA/VAGINA		1				1
1987							
	CERVIX	27	21	10	13		71
	ENDOMETRIUM	5		2			7
	OVARY	1			1		2
	VULVA/VAGINA			1	1		2
1988							
	CERVIX	37	21	11	9	1	79
	ENDOMETRIUM	5	2	1		1	9
	OVARY		1				1
	VULVA/VAGINA	5	2	2			9
1989							
	CERVIX	23	17	19	15		74
	ENDOMETRIUM	3	1	1			5
	OVARY	5	3	2	2		12
	VULVA/VAGINA		2	1			3
1990							
	CERVIX	33	19	22	16	2	92
	ENDOMETRIUM	2		3	1		6
	OVARY	1	1	1			3
	VULVA/VAGINA						
1991							
	CERVIX	37	19	20	15	1	92
	ENDOMETRIUM	6			1		7
	OVARY		1				1
	VULVA/VAGINA						
1992							
	CERVIX	43	13	19	26		101
	ENDOMETRIUM	2	1	4		1	8
	OVARY	1	1	1			3
	VULVA/VAGINA				1		1
1993							
	CERVIX	27	21	8	7	1	64
	ENDOMETRIUM	3	2	1			6
	OVARY	4	4	2			10
	VULVA/VAGINA	1		1			2
TOTAL		337	172	153	120	7	789

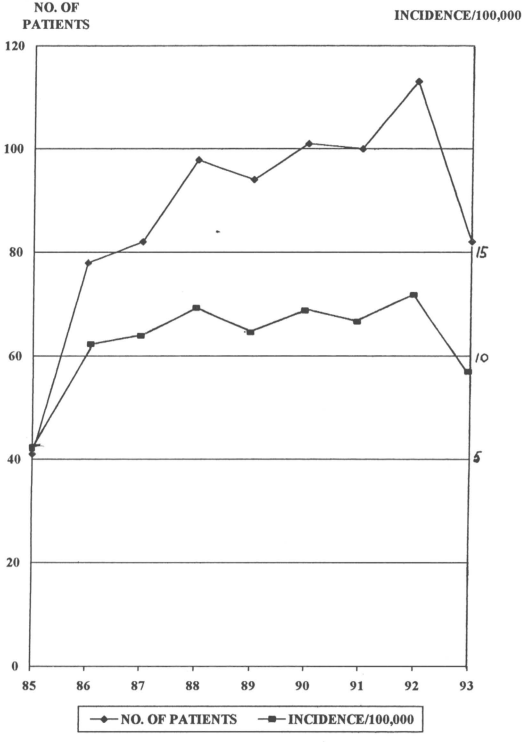


Figure 4.1 : Annual incidence of gynaecological neoplasms in Sarawak Malaysia (1985 - 1993)

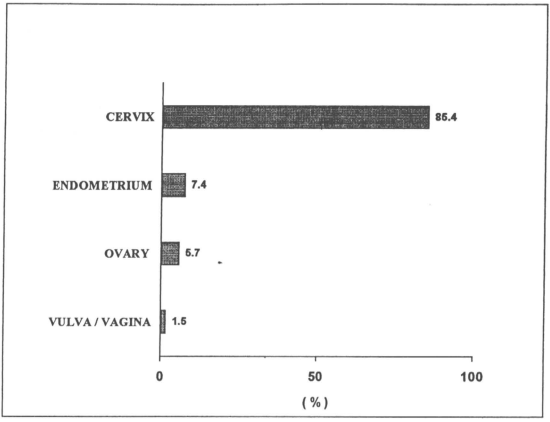


Figure 4.2 : Most frequent gynaecological neoplasms in Sarawak

4.1.3 Incidence of gynaecological neoplasms in Sarawak with respect to age

The incidence of gynaecological neoplasms in Sarawak with repect to age is shown in Figure 4.3 and the peak incidence is shown in Table 4.2.

Cervical neoplasm had been shown to be the most frequent gynaecological neoplasm among females in Sarawak. It appeared in the age group 11 - 20 years and increased rapidly after the age group 21 - 30 years and gave a peak in the age group 41 - 50 years.

The cancer of the endometrium was intially noted in age group 21 - 30 years and reached a peak in the age group 51 - 60 years. Ovarian cancer appeared in age group 11 - 20 years and reached a peak in age group 41 - 50 years. Cancer of the vulva and vagina was noted initially in age group 31 - 40 years and like endometrial cancer, reached a peak in the age group 51 - 60 years.

Incidence of gynaecological neoplasms below and above age 40 years

Table 4.3 shows the percentage of gynaecological patients below and above the age 40 years. All cancer sites were found to have a majority of patients at the age above 40 years. Surprisingly the percentage of endometrial cancer cases which were below 40 years appeared to be very high (40.0%) compared to other cancer sites i.e. cervical cancer (27.2%), vulva and vagina cancer (15.4%) and ovarian cancer (7.0%).

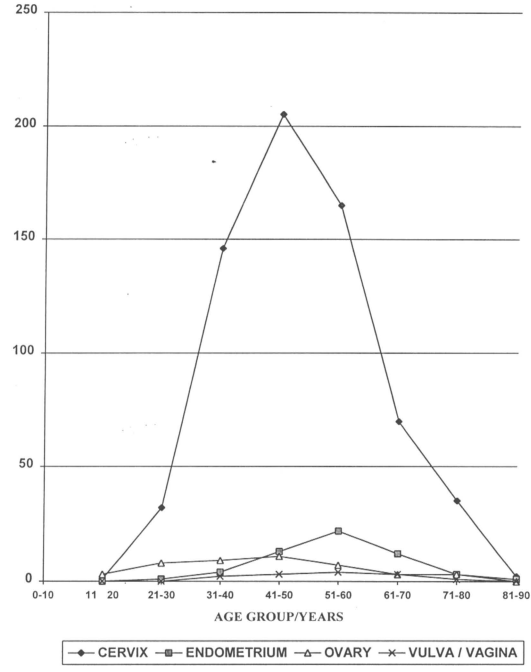


Figure 4.3 : Incidence of gynaecological neoplasms with respect to age (years) in Sarawak (1985 - 1993)

SITE	Age first appeared (age group in years)	Peak incidence (age group in years)
CERVIX	11 - 20	41 - 50
ENDOMETRIUM	21 - 30	51 - 60
OVARY	11 - 20	41 - 50
VULVA/VAGINA	31 - 40	51 - 60

Table 4.2 : Age first appeared and peak incidence of four cancer sites of gynaecological neoplasms in Sarawak

SITE	Below age 40 years		Above age 40 years	
	No.	%	No.	%
CERVIX	179	27.2	479	72.8
ENDOMETRIUM	22	40.0	33	60.0
OVARY	3	7.0	39	93.0
VULVA/VAGINA	2	15.4	11	84.6
TOTAL	206		562	

* No. of patients with no age record : 21

Table 4.3 : Incidence of gynaecological neoplasms in Sarawak below and above the age 40 years.

4.1.4 Incidence of gynaecological neoplasms in Sarawak with respect to ethnic group

The incidence of gynaecological neoplasms in Sarawak with respect to ethnic group is shown in Figure 4.4. The Chinese formed the largest proportion of all gynaecological neoplasms patient i.e. 42.6 per cent, followed by the Ibans (21.9 %), the Malays (19.4 %) and other Indigenous groups (15.2 %). The other patients include Indians, Eurasian and Indonesians which made up only a small proportion of all gynaecological neoplasms patients i.e. 0.9 per cent.

The crude incidence according to ethnic group for 1985 to 1993 is shown in Figure 4.5. The incidence of gynaecological neoplasms among the Chinese is higher than the other ethnic groups.

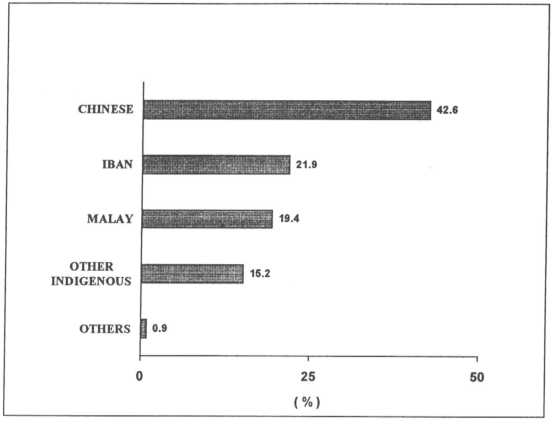


Figure 4.4 : Frequency of gynaecological neoplasms in Sarawak with respect to ethnic group

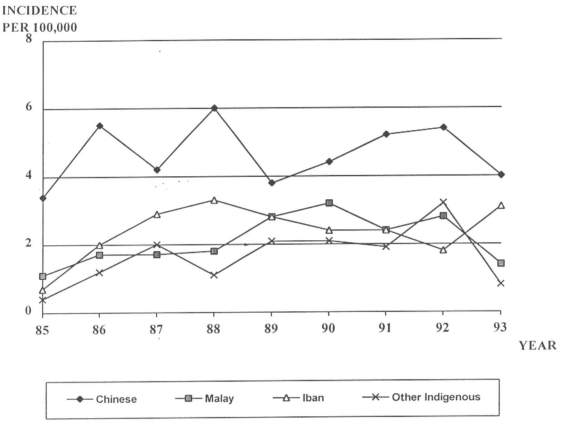


Figure 4.5 : Crude incidence of gynaecological neoplasms in Sarawak with respect to ethnic groups for years 1985 to 1993.

4.1.5 Incidence of gynaecological neoplasms in Sarawak with respect to ethnic group and cancer sites

Figure 4.6 shows the incidence of four different sites of gynaecological neoplasms in four major ethnic groups in Sarawak, namely the Chinese, Malays, Ibans and Other Indigenous groups. All ethnic groups showed very high frequency of cervical cancer very low frequency of vulva/vaginal cancer. Among the Chinese and the Malays endometrial cancer ranked second followed by ovarian cancer whereas among the Ibans and other Indigenous groups, ovarian cancer precedes endometrial cancer. The other races were not assessed due to the small number of patients.

Chinese

Among Chinese females, cancer of the cervix (84.5 %) formed the highest proportion of all gynaecological neoplasms. This is followed by endometrium (9.2 %), ovary (5.1 %) and vulva or vagina (1.2 %).

Malay

Cancer of the cervix was also found the be a common neoplasia among Malay females in Sarawak. It accounts for 81.7 per cent of all gynaecological neoplasms, followed by endometrial cancer (9.2 %), ovarian cancer (7.2 %) and vulva or vaginal cancer (1.9 %).

Iban

As noted for the Chinese and Malay females, cancer of the cervix was the most frequent neoplasia among the females of the ethnic group Iban. It made up about 86.1 per cent of all gynaecological neoplasms. Endometrial cancer seems to be less frequent (5.2 %) compared to ovarian cancer (7.0 %) and followed by vulva or vaginal cancer (1.7 %).

Other Indigenous Groups

In the Other Indigenous Groups females, a majority of patients (92.5 %) were cases of cervical cancer, and only a small proportion of ovarian cancer (2.5 %), endometrium (3.3 %) and vulva or vagina (1.7 %).

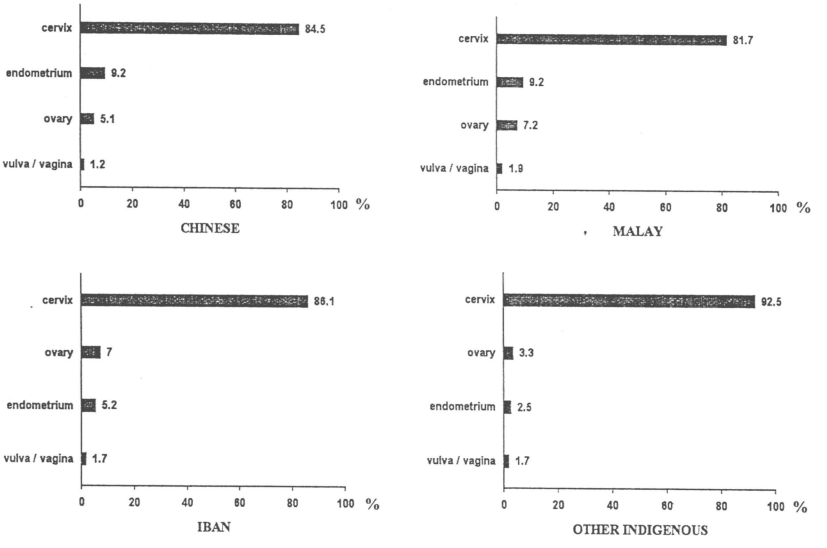


Figure 4.6 : Most frequent gynaecological neoplasms in four major ethnic races in Sarawak.

4.1.6 Ethnic composition with respect to cancer sites

Figure 4.7 shows the ethnic composition with respect to four major cancer sites of gynaecological neoplasms in the population studied.

Cervix neoplasm

For cervix neoplasm, the highest percentage was found among the Chinese i.e. 42.4 per cent. This was followed by the Ibans (22.3 %), Malays (18.7 %) and the Other Indigenous Groups (16.6 %).

Endometrial neoplasm

As noted for cervix neoplasm, the Chinese formed the highest group of endomerial neoplasm cases i.e. 54.4 per cent. However, the Malays (24.6 %) showed a higher frequency of endometrial neoplasm compared to the Ibans (15.8 %). The Other Indigenous Groups (5.2 %) formed only a small proportion of cancer cases.

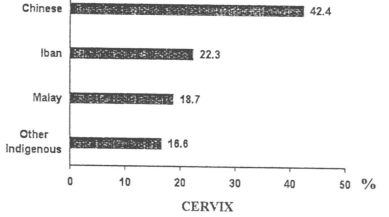
Ovarian neoplasm

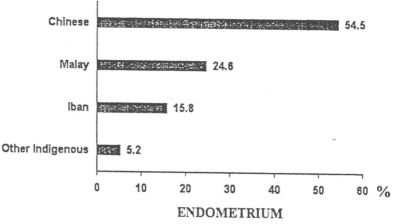
For ovarian neoplasm, the Chinese remain the leading ethnic race for this disease, with a percentage of 38.6 cases. The Ibans (27.3 %) formed the second highest ethnic

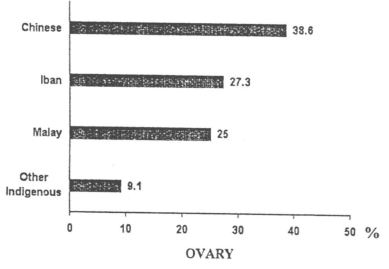
group with ovarian neoplasm, followed by the Malays (25.0 %) and Other Indigenous Groups (9.1 %).

Vulva or vaginal neoplasm

The Chinese (33.3 %) formed the highest group of vulva or vaginal neoplasm cases while Other Indigenous Groups (16.7 %) formed the lowest percentage. The Malays and the Ibans shared the same proportion of cases i.e. 25.0 per cent







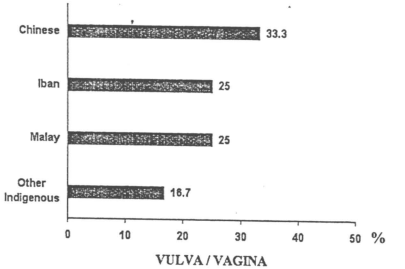


Figure 4.7 : Ethnic composition in four sites of gynaecological neoplasms in Sarawak

4.1.7 Incidence of cervix neoplasm in Sarawak

Figure 4.8 shows the crude incidence of cervix neoplasm cases with respect to ethnic groups in Sarawak, namely the Chinese, Malays, Ibans and other Indigenous groups. The Chinese showed higher incidence of cervical neoplasm compared to the other ethnic groups.

4.1.8 Incidence of cervix neoplasm cases in Sarawak with respect to age

The frequency of cervix neoplasm cases with respect to age in three major ethnic races in Sarawak is shown in Figure 4.9. All three ethnic groups demonstrated a similar pattern of age variations among cervix neoplasm cases. They showed high percentage of cases between the age of 31 to 60 years and gave peak incidences in the age group 41 - 50 years i.e. 30.7, 29.9 and 35.8 per cent among the Chinese, Indigenous Groups and the Malays respectively. Among the Malays, one case was found to be under the age of 20 years. The Chinese showed a higher frequency of cases (10.8 %) in the age group 71 - 80 years compared to the Indigenous Groups (1.9 %) and the Malays (0.0 %).

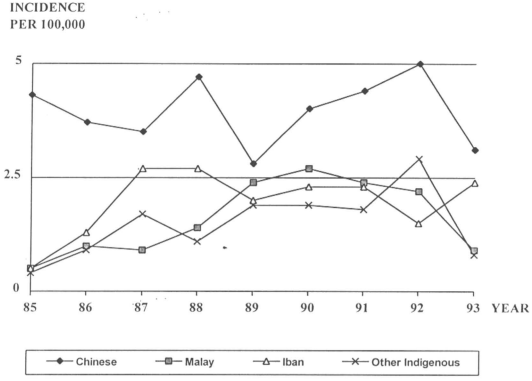


Figure 4.8 : Crude incidence of cervical neoplasm in Sarawak with respect to ethnic groups for years 1985 to 1993.

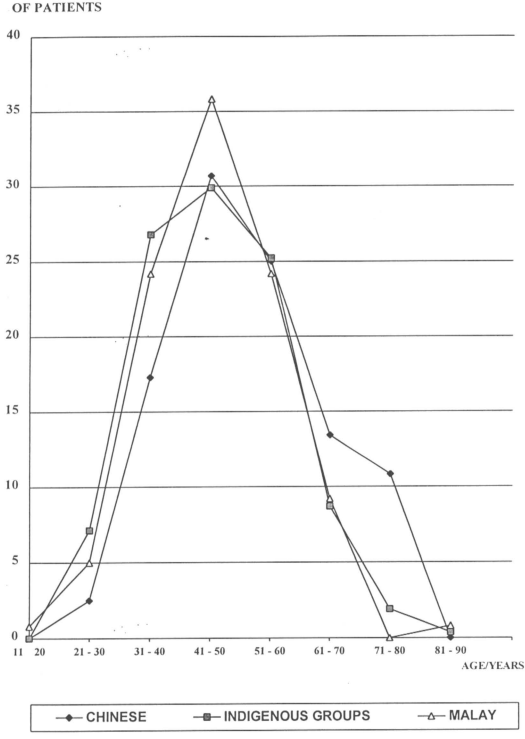


Figure 4.9 : Frequency of cervical neoplasm in Sarawak with respect to age and ethnic group

Table 4.4 shows the age standardized rate (ASR) for cervical neoplasm in Sarawak. The ASR for cervical cancer in Sarawak (9.9) is lower than the ASR reported in the 1996 Penang Cancer Registry (15.03). The ASR for the Chinese (15.5) and the Ibans (10.7) appeared to be much higher than the Malays (6.3) and the other Indigenous groups (5.4).

Table 4.4 : The incidence and age standardised rate for cervical cancer in Sarawak (1993)

AGE	NO.	INCIDENCE RATE
10 - 14	0	0.0
15 - 19	0	0.0
20 - 24	1	1.2
25 - 29	2	1.3
30 - 34	3	4.3
35 - 39	8	14.5
40 - 44	9	19.9
45 - 49	12	34.6
50 - 54	9	30.7
55 - 59	8	36.0
60 - 64	6	29.0
65 - 69	3	22.4
70 - 74	2	17.3
75 - 79	0	0.0
TOTAL	63	
CRUDE RATE PER 100,000		7.3
AGE STANDARDIZED RATE		9.9
ASR FOR CHINESE		15.5
MALAY		6.3
IBAN		10.7
OTHER INDIGENOUS		5.4

4.2 SEROLOGY OF CERVICAL CARCINOMA

4.2.1 Seroreactivity against HPV 16 E7 in cervical carcinoma patients and normal pregnant women

The prevalence of HPV 16 E7 protein in the sera of cervical carcinoma patients and normal pregnant women is shown in Table 4.5. Among the cervical carcinoma patients, 27.5% were IgA positive, 23.2% were IgG positive, 56.5% were IgM positive and 13.0% were positive to both IgG and IgA. Among the normal pregnant women, 15.6% were IgG positive, 15.6% were IgA positive, 62.5% were positive to IgM and 3.0% were positive to both IgG and IgA. Out of 69 sera samples of cervical carcinoma tested, 34.8% were seronegative to all immunoglobulin classes. 28.1% of the 32 sera samples from normal pregnant women were seronegative to all immunoglobulin classes. These differences appear not to be significant (t test, p value < 0.05)

Table 4. 5 : Seroprevalence of HPV 16 E7 in cervical carcinoma patients and normal pregnant women

Immunoglobulin	**Cervical carcinoma patients** (N = 69) No. of positives (%)	**Normal pregnant women** (N = 32) No. of positives (%)
IgG	16 (23.2)	5 (15.6)
IgA	19 (27.5)	5 (15.6)
Both IgG and IgA	9 (13.0)	1 (3.0)
IgM	39 (56.5)	20 (62.5)

4.2.2 Seroprevalence of HSV-II and CMV in cervical carcinoma patients and normal pregnant women

The seroreactivity of sera from cervical carcinoma patients and normal pregnant women against HSV-II and CMV is shown in Table 4.6. The seropositivity to HSV-II and CMV was very high in the sera from cervical carcinoma patients i.e. 95.6% and 98.6% respectively. For the normal pregnant women, the percentage of seropositivity was slightly lower compared to cervical carcinoma patients i.e. 84.0% were positive to HSV-II and 86.4% were positive to CMV. The difference between the antibody levels among cervical carcinoma patients and normal pregnant women for both infections were not significant (t test, p value < 0.05).

Table 4. 6 : Seroprevalence of HSV-II and CMV in cervical carcinoma patients and normal pregnant women

Viral Antibody	**Cervical carcinoma patients** (N = 69) No. of positives (%)	**Normal pregnant women** (N = 44) No. of positives (%)
HSV 2 / IgG	66 (95.6)	37 (84.0)
CMV / IgG	68 (98.6)	38 (20.4)

4.2.3 Seroprevalence of EBV-associated antibody titres in cervical carcinoma patients and normal pregnant women

Table 4.7 shows the percentage of seropositivity to EBV-associated antibody titres among cervical carcinoma patients and normal pregnant women. The incidence among normal pregnant women appeared to be slightly higher for the various EBV-associated antibody titres compared to cervical carcinoma patients. Both groups showed a majority of seropositivity to VCA/IgG antibody titres i.e. 88.4% in cervical carcinoma patients and 95.4% in normal pregnant women. The percentage positive for VCA/IgA were low for both groups i.e. about 4.2% in cervical carcinoma patients and 6.8% in normal pregnant women. For EA/IgG, seropositivity among cervical carcinoma patients and normal pregnant women were 14.1% and 29.5% respectively.

The geometric mean titre (GMT) values of the three antibodies did not differ significantly between cervical carcinoma patients and normal pregnant women (t test, p value < 0.05). For VCA/IgG, the GMT values for cervical carcinoma patients and normal pregnant women were 34.9 and 44.9 respectively. The GMT values for VCA/IgA and EA/IgG were very low in both groups i.e.10.0.

Table 4. 7 : Seroprevalence of EBV-associated antibodies in cervical carcinoma patients and normal pregnant women

EBV Antibody	Cervical carcinoma patients (N = 69)		Normal pregnant women (N = 44)	
	No. of positives (%)	GMT	No. of positives (%)	GMT
VCA / IgG	61 (88.4)	34.9	42 (95.4)	44.9
VCA / IgA	3 (4.2)	10.0	3 (6.8)	10.0
EA / IgG	10 (14.1)	10.7	13 (29.5)	10.0

4.2.4 Seroprevalence of HSV-II, CMV and EBV in HPV-seropositive and HPV-seronegative cervical carcinoma patients

The prevalence of HSV-II, CMV and EBV in HPV-seropositive (positive for IgA and/or IgG) and HPV-seronegative cervical carcinoma patients is shown in Table 4.8. The prevalence of HSV-II and CMV infection among HPV-seropositive and HPV-seronegative cervical carcinoma patients appeared to be similar, ranging from 88.0% to 100.0%. For EBV IgG anti-VCA, HPV-seropositive cases showed higher percentage of infection (80.0%) compared to HPV-seronegative cases (34.0%). Both HPV-seropositive and HPV-seronegative cases were observed to have low infection of EBV IgA anti-VCA and EBV IgA anti-EA (0.0% to 24.0%).

Table 4.8 : Seroprevalence of HSV-II, CMV and EBV in HPV-seropositive and HPV-seronegative cervical carcinoma patients

Viral Antibody	HPV-seropositive (N = 25) No. of positives (%)	HPV-seronegative (N = 44) No. of positives (%)
HSV-II/IgG	22 (88.0)	44 (100.0)
CMV/IgG	25 (100.0)	43 (98.0)
EBV VCA/IgG	20 (80.0)	15 (34.0)
EBV VCA/IgA	3 (12.0)	0 (0.0)
EBV EA/IgG	6 (24.0)	4 (9.0)

4.2.5 Seroprevalence of HSV-II, CMV and EBV in HPV-seropositive and HPV-seronegative normal pregnant women

Table 4.9 shows the prevalence of HSV-II, CMV and EBV in HPV-seropositive and HPV-seronegative normal pregnant women. The prevalence of HSV-II, CMV and EBV infection in HPV-seropositive nomal pregnant women showed a similar pattern with the HPV-seronegative normal pregnant women. Both HPV-seropositive and HPV-seronegative normal pregnant women were found to have high percentage of HSV-II and CMV (73.9 % to 100.0%). The percentage of EBV VCA/IgG infection were slightly lower for both HPV-seropositive and HPV-seronegative normal pregnant women, i.e. 66.7 % and 65.2 % respectively. For EBV VCA/IgA and EA/IgG both

HPV-seropositive and HPV-seronegative normal pregnant women showed low infection ranging from 11.1 % to 34.8 %.

Table 4.9 : Seroprevalence of HSV-II, CMV and EBV in HPV-seropositive and HPV-seronegative normal pregnant women

Viral Antibody	HPV-seropositive (N = 9) No. of positives (%)	HPV-seronegative (N = 23) No. of positives (%)
HSV-II/IgG	9 (100.0)	17 (73.9)
CMV/IgG	9 (100.0)	17 (73.9)
EBV VCA/IgG	6 (66.7)	15 (65.2)
EBV VCA/IgA	1 (11.1)	4 (17.4)
EBV EA/IgG	2 (22.2)	8 (34.8)