CHAPTER-VII

SUMMARY
Summary:

Since limited information is available on the underlying molecular etiology of cervical cancer disease development and progression in Assam and other parts of northeast India, which incidentally has a high load of cervical cancer disease patients of different grades of severity; the present case-control prospective study to explore the demographic profile, clinical risk factor, viral, and genetic risk factors for cervical cancer diseases in Assam using molecular diagnostic tools.

The following are the highlights of the data generated from the present study:

From the present study we can conclude that:

- Cervical cancer is mostly prevalent amongst the middle aged women of the age group 31-50 year.
- Early sexual activity and/or marriage, teenage pregnancy, illiteracy or low literacy, high parity was the major clinical risk factors for cervical cancer development in our cohort. Lower socioeconomic status and religion wise Hindus were found to be more predisposed to development of cervical cancer in our region.
- HPV infection (85/102, 83.33%) is the predominant factor for cervical cancer development in our cohort (p<0.001).
- HPV infection is significantly associated with the development of cervical cancer in the early reproductive phase ≤ 50 years of life (p <0.001).
- Our study observation showed, HPV16 (89.41%) being the most predominant genotype (p=0.003) followed by HPV 18 (3.52%).
- Down-regulation or improper activation of Th1 immune modulator profile both at serum as well as cervical tissue level plays a key role in cervical cancer development.
- TNF-α expression, which is a key anti-neoplastic cytokine, was found to be down-regulated gradient in cervical anomalies, the lowest expression being in cervical cancer cases.
- HPV induced down-regulation of pro-inflammatory cytokine NF-kβ, which in turn was found to be statistically associated with TNF-α down-regulation at both mRNA and protein levels is a key factor in the development of HPV16 related cervical neoplasia.
Limitations of the study:

Some of the limitations of the study are mentioned below:
The study had to be conducted with a limited number of cervical tissue samples, but since the Gauhati Medical College and hospital, Guwahati is a referral centre for the entire Assam and many parts of NE India, non-biased representation of cases belonging to both tribal and non-tribal background could be enrolled and studied.

Although several genotypes have been found to be involved in invasive cervical cancer development, our study is confined to screening of only HPV16 and HPV 18 genotypes which have been shown to be associated with majority of the cases worldwide, national wise and from the limited data available from northeast India.

Genetic alteration based analysis of the key cytokines like TNF-α etc. couldn’t be included within the study period.

Although there were limitations in the study, a conscious effort was made to elucidate the clinical and immunological parameters which critically influencing HPV related cervical cancer development in northeast India. This is the first study from northeast India which has highlighted the role of deregulation in immunological profile in the pathogenesis of cervical anomalies and carcinoma with underlying HPV infection; and we are hopeful that our study may be the platform for further scientific studies.
Conclusion:

To conclude, present study shows that apart from some demographical, clinical and sociological factors; infection with HPV16 is the most important factor associated with cervical cancer disease burden in our study cohort. Deregulation in the immunological profile of the host, resulting in suppression/inadequate activation of Th1 cytokine profile is a deciding factor in the progression of HPV16 mediated cervical anomalies to cancer. Evaluation of key cytokines like TNF-α has high prognostic significance for stratifying patients with high risk of progression to HPV infected cervical anomalies severities, and may be used for therapeutic targeting for controlling the disease at an earlier stage, therefore decreasing the mortality and morbidity rate associated with the disease.