SUMMARY
The present work was done with the objective to study the:

- Prevalence of various risk factors associated with the development of cervical carcinoma in North Indian population.
- Genomic instability in the lymphocytes and the progress of cell cycle in response to cervical carcinoma.
- Incidence of HPV in patients with cervical carcinoma as determined by:
  i) Immunohistochemical detection of HPV-antigen.
  ii) Molecular hybridization studies using biotinylated HPV-16 DNA as probe.
- Physical status of HPV in cervical carcinoma cases and its possible bearing on carcinogenesis.

The epidemiological data on 102 patients with cervical cancer revealed that these patients were sexually active, multiparous and majority was in the age group of 40-60 years. Maximum (87.25%) number of patients had low socio-economic background and most (71.57%) were in the advanced stage of cancer at the time of diagnosis which suggested the prevalence of unhygienic health practices (followed in rural areas) and lack of Pap-smear screening (for early detection of cancer) in these patients.

The cytogenetic analysis of the lymphocytes of 30 patients with cervical cancer and 15 age matched control
women showed statistically significant (P < 0.01) increase in the frequency of SCEs in the cancer group (7.18 ± 1.23) as compared to the control group (4.68 ± 0.82). The level of TCAs was also elevated (4.77 ± 3.50) in the patients in comparison to that in the controls (2.27 ± 2.70) and the increase was statistically significant (P < 0.05). These results indicated a high degree of genomic instability associated with the cancer. The evaluation of genomic instability with respect to the stage of cervical cancer showed an increase in the frequency of SCEs with increase in the severity of the lesion. However, the frequency of TCAs was found to decrease with the progress of cancer which was due to the decrease in the chromatid type aberrations. A prolongation in the cell cycle was also observed in these patients which was evident from the high proportion of cells at M1 phase of division. The prolongation was also found to be related to the severity of the disease.

The incidence of HPV was studied in patients with cervical carcinoma by immunoperoxidase staining of the tissues to detect the presence of HPV-capsid antigen. Tissues with mild dysplasia and koilocytotic atypia (typical of HPV infection) were positive for HPV-antigen while the tissues from patients with invasive cervical carcinoma were negative. The absence of HPV-antigen was thus related to the severity of the lesion. This could be due to the decrease in the number of capsid antigen positive cells with the loss in differentiation of the tissue associated with invasive...
The incidence of HPV was also determined by dot blot hybridization analysis of the genomic DNAs extracted from biopsies of patients using biotinylated HPV-16 DNA probe. The results of DNA hybridization under low stringency conditions (42°C) showed the presence of Human papilloma virus DNA in 88 and 80% of the cases with invasive cervical carcinoma and abnormal cervical cytology, respectively. Out of these, HPV-type 16 was present in 40 and 20% of the cases as shown by the DNA hybridization under high stringency conditions. The additional signals in the dot blot under low stringency conditions, therefore, were due to HPVs other than type-16 which have homology with this type. The negative results with immunoperoxidase staining and a high incidence of HPV by DNA hybridization analysis were suggestive of the presence of viral DNA without the expression of structural capsid proteins. Thus DNA hybridization based method was more reliable than the HPV-antigen based method to study the incidence of HPV.

Southern blot hybridization analysis of four of the tissues, positive for HPV-16 DNA by dot blot hybridization, showed that HPV-16 DNA was present in episomal form in two (50%) of the tissues and was integrated into the cellular genome in the other two. The event of integration was random showing integration at different sites in these samples. These results suggest that integration, though important for carcinogenesis, is not mandatory.