In this study the cytotoxicity and expression profiles of apoptosis gene related in human cervical cancer (HeLa) cell lines in response to Newcastle disease virus (NDV) strains AF2240 and V4-UPM were studied. NDV is a strain of avian paramyxovirus. NDV has been classified into the order Mononegavirales, family Paramyxoviridae, subfamily Paramyxovirinae and genus Rubulavirus. NDV caused severe economic losses in the poultry industry worldwide. Several local strains of Newcastle disease virus were reported to induce cytolysis to the cancerous cell lines. Strain AF2240 is a heat resistant viscerotropic velogenic NDV and strain V4-UPM is a heat resistant lentogenic which has significant higher thermostabilities of infectivity and haemagglutination were reported cytolysis leukemic cells in vitro and has shown in vivo anti leukemic agents. In this study the cytotoxicity effects of strains of NDV AF2240 and V4-UPM towards HeLa cell were determined by using standard microtetrazolium assay (MTT). Cytotoxicity dose 50% (CD$_{50}$) cells treated with different titre of NDV as haemagglutination units (HAU) as compared to the untreated cells was estimated at 72 hours post-infection. The CD$_{50}$ values obtained were 0.95 HAU and 1.0 HAU for strains AF2240 and V4-UPM, respectively. No cytolytic effect was noted towards normal cells (3T3) was observed. Both strains were also observed to inhibit HeLa cell proliferation. Morphological observations also have been done under inverted light and fluorescence microscopes. Under the inverted light microscope, the HeLa cells treated with both strains showed apoptotic features such as cell shrinkage, cell blebbing and formation of apoptotic bodies. Morphological features of apoptosis were also observed by using the AO/PI staining method under the fluorescence microscope. The AO/PI
staining demonstrated the occurrence of apoptosis which was characterised mainly by chromatin condensation, nuclear shrinkage and formation of apoptotic bodies. Evidently, both strains AF2240 and V4-UPM used in the study were found to induce cells towards apoptosis rather than necrosis. NDV strain AF2240 and strain V4-UPM was also caused genotoxic in HeLa cells after two hours treatment with CD_{10} and CD_{25} values by alkaline comet assay. Results showed that HeLa cells treated with NDV strains AF2240, V4-UPM and hydrogen peroxide gave different distribution of scores. The HeLa cells treated with hydrogen peroxide as a positive control gave more percentage at score 2, 3 and 4 for both cytotoxicity values compared to the HeLa cells treated with NDV for both strains. Observation in this study has proved the genotoxic potential of the NDV strains AF2240 and V4-UPM to induce DNA damage on HeLa cells as early as two hours following treatment at very low cytotoxicity dose (CD_{10} and CD_{25}) values. Meanwhile, the cell cycle analyses of HeLa cells treated with local strains of NDV AF2240 or V4-UPM did not induce cell cycle arrest in any specific phase. Sub-G1 phase (apoptosis peak) was found in both treated cells with a very high percentage compared to untreated cells with a small percentage. The results indicate that, the percentages of apoptosis were significantly increased (p≤0.05) in the time-dependent manner in both NDV strains treated HeLa cells. The molecular mechanisms of apoptosis may depend on the NDV strain and cell type. Six apoptosis genes were selected in this study namely Casp8, TNF-α, Bcl2 and TRAIL which focused on extrinsic pathway of apoptosis, while the gene Bax was used as an indicator for intrinsic pathway triggered by cellular stress. Lastly Myc, oncogene was used as an indicator for cell growth. From this study, NDV strain AF2240 was identified as a highly induced death receptor pathway due to the upregulation of TNF gene and the downregulation of Bax gene. Whereas NDV strain V4-UPM triggered both pathways but through the extrinsic pathway due to the very high expression of the TNF gene. The TNF gene was highly expressed due to its location and function as a stimulator of the death receptor pathway. The Casp8 gene was activated and expressed in order to enter the execution-phase of cell death. The Bcl-2 gene was continuously
observed because of its function as an apoptosis regulator. Surprisingly, no expression was detected by the TRAIL gene. NDV strain AF2240 was more effective than NDV strain V4-UPM as an apoptosis inducer. These gene expression results showed that the apoptosis occurred and led to cell death.