CONCLUSION

The expression of miR-21 was significantly higher while let-7a showed a low level of expression in primary cervical cancer tissues. However, such a reciprocal kinetics was not observed in tissues of LSIL and HSIL which over-expressed let-7a. While miR-21 showed direct association, let-7a expression was inversely related to STAT3 expression and activation in HPV16-positive cervical cancer lesions. Both, miR-21 and let-7a were found differentially expressed with respect to levels of oncoprotein E6 in HPV-positive lesions. Over-expression of miR-21 was found associated with elevated levels of other STAT3 regulated gene products MMP-2 and MMP-9 and decreased levels of its known target gene products, PTEN and TIMP-3.

Overall, miR-21 and Let-7a appear as integral components of STAT3 signaling and may be responsible for maintaining activated state of STAT3 and increased expression of its downstream genes during cervical carcinogenesis. Targeting STAT3 by siRNA, curcumin and stattic molecule, and targeting miR-21 by antisense or small-molecule compounds may represent new targeted therapeutic strategies for human cancers, including cervical cancer. Let-7a mimics could contribute in developing novel treatment strategy for cervical cancer. By regulating miR-21, STAT3 might also be involved in the regulation of other critical cellular events. Therefore, it is important to further explore the link between STAT3 and miRs and their interacting circuit that contribute to carcinogenesis. These studies might provide leads to future development of alternative strategies that target STAT3 and miRs in treatment of diseases, such as cancer. Nevertheless, miR-21 and Let-7a alongwith STAT3 could become clinically useful biomarkers to identify pre-invasive, progressive, lesions and may prove useful targets for pharmacological intervention for control of cervical cancer.