Summary and Conclusion

Ninety-two cases of breast cancer were studied histopathologically (for typing, grading of the tumors and other histopathological changes in different types) and immunohistochemically for evaluation of microvessel density and tumor-associated macrophage density in relation to different histopathological types, tumor grade, tumor size, lymph node status, stage, 2-years recurrence, distant metastases, 5-year overall survival and other data.

The cases were selected to represent a spectrum of breast carcinomas including DCIS (n=7) one of low grade, 2 intermediate and 4 high grade, IDC (n=39) 3 GI, 18 GII, and 18 GIII, ILC (n=20) 8 of GII and 12 GIII, medullary carcinoma (n=6) 3 of GII and 3 GIII, mucinous carcinoma (n=6) 5 of GII and 1 GIII, papillary carcinoma (n=6) all of GII and paget's disease (n=8) one of GI, 4 GII, and 3 GIII.

This study revealed that higher grades were associated with more 2-years recurrence rates, distant metastases development and low 5-years overall survival rates. Also, a highly significant positive correlation was found between grade, vascular invasion and tumor necrosis. But there was no significant correlation between grade and lymphocytic infiltration.

Concerning lymph node status in this work, findings are consistent with better prognosis in case of involved lymph nodes up to 3 regarding 2-years recurrence, development of distant metastases and overall survival compared with cases with lymph node involvement more than 3.

The current study demonstrated that a highly significant direct correlation between the stage, tumor size and recurrence; and a highly significant inverse correlation between the stage, tumor size and 5-year overall survival were reported.

This study revealed that positive vascular invasion and tumor necrosis are associated with worse prognosis and outcome of breast cancer. But, there was statistically insignificant inverse correlation between lymphocytic infiltrate and recurrence, distant metastases and overall survival.

The current investigation demonstrated that advanced stages were associated with lower lymphocytic infiltration and more vascular invasion, however, there is insignificant correlation between stage and tumor necrosis.

This study reported high significant correlation between MVD, tumor grade, vascular invasion and tumor necrosis, however, border-line significant correlation with lymphocytic infiltration (P= 0.054). High MVD is associated with more 2-years recurrence and shorter overall survival.

There was no significant correlation between MVD, lymph node status, tumor size and stage in the current study.

As regards TAM density, there was high positive correlation with tumor grade. High TAM density was associated with heavy lymphocytic infiltration, vascular invasion, tumor necrosis, more 2-years recurrence and shorter overall survival.

But, no significant correlation between TAM density and lymph node status, tumor size and stage could be found.

A highly significant positive correlation between the TAM density and MVD was detected in the current investigation.

In conclusion:

- MVD and TAMs density were found individually to be important prognostic factor (more recurrence rate and shorter overall survival). So, MVD and TAM level can provide additional prognostic significance and help in the identification of patients who need postoperative adjuvant therapy.

- This research clearly indicated that TAMs infiltration correlates with increased microvessel density in breast cancer. These findings suggest that the prognostic implications of the TAM density are due to the involvement of TAMs in tumor angiogenesis. So, Immunodetection of TAM infiltration on surgical specimens can be useful for clinical prediction of breast cancer patients.

- TAMs have multiple effects on tumor progression. They exhibit tumoricidal activity toward one fraction of cancer cells. Evidence suggests that TAMs can interact with cancer cells and microenvironment; release growth factors, cytokines, proteolytic enzymes, and other inflammatory modulators. This induces tissue matrix remodeling and angiogenesis, and simultaneously enhances tumor cell migration and invasion, and metastasis.

- Understanding the interplay between inflammatory and tumor cells in breast cancer will permit the development of new cancer therapeutic strategies aimed to modulate the interaction between tumor and stromal cells. The elucidation of the mechanisms by which tumor-associated macrophages cooperate with tumor growth will also aid in the design of approaches to boost anti-tumor immunity.

- Additional studies are recommended to study TAM density and MVD in a larger number of cases to define its importance in breast carcinoma and other types of breast cancer.

- From this study, it was suggested that combining immunotherapy with angiostatic therapy will result in improved and possibly synergistic antitumor responses and better prognosis for breast cancer patients.