SUMMARY OF FINAL REPORT

TITLE:

Study to assess prognostically important features of breast carcinoma in a Sri Lankan population.

RESEARCH INSTITUTE:

Department of Pathology Faculty of Medicine, Colombo.

CHIEF SCIENTIFIC INVESTIGATOR:

Dr M. D. S. Lokuhetty

PERIOD OF CONTRACT:

23.3.98 - December 2000 (However work started only in April 1998 after obtaining the necessary consumables.)

SCIENTIFIC BACH GROUND AND SCOPE / OBJECTIVES OF STUDY

Breast carcinoma is the commonest cause of cancer death among women world wide including Sri Lanka. Post surgical therapeutic decisions for breast cancer are made, based only on clinical and morphological features in Sri Lanka. Immune prognostic markers are not widely used. There fore post surgical therapeutic decisions made and the therapeutic regimes used may not be accurate unless clinical and morphological features alone could reliably determine the risk for metastatic and recurrent disease.

Objectives of the study were to identify important clinical and morphological features and the status of immune prognostic markers of breast carcinomas in Sri Lanka. Immune prognostic marker status of breast carcinoma was also compared with the clinical and morphological features and fine needle aspiration biopsy results to look for any associations. The risk for recurrent and metastatic disease assessed by clinical and

morphological features were compared with the risk assessed by immune prognostic markers.

EXPERIMENTAL METHOD:

Relevant clinical and morphological features of a consecutive sample of 126 breast carcinoma patients presenting to the 2nd investigator during the study period was collected. Representive samples of tumour tissue were assessed immunohistochemically for oestrogen receptors and over amplification of Her2neu. Patients were categorized in to high and low risk groups for recurrent and metastatic disease considering both clinical and morphological features and immune markers. Associations between clinical and morphological features and the immune markers and the agreement between the levels of risk as assessed by clinical and morphological features and immune markers were determined by using standard statistical tests.

RESULTS OBTAINED:

Mean age of breast carcinoma patients in the study was 54.8. The highest frequency of breast carcinoma was seen in the 41-50 year age group. A majority (61.3%) of patients were postmenopausal. Breast carcinoma occurring in a familial setting was rare. At clinical examination mean size of the tumour was 4.16cm, however by gross examination mean size was smaller (2.95cm). Most tumours measured between 2.1-5cm.
Ipsilateral axillary lymph nodes were clinically palpable in 43% of patients. 44.4% had axillary lymph node metastasis. Fine needle aspiration test was a useful test to diagnose malignancy in our setting (in 83.3% patients) before definite surgical intervention.
Invasive duct carcinoma was the commonest histological type (82.5%). Majority of breast carcinomas were moderately differentiated (43.3%).

46% of breast carcinomas expressed oestrogen receptor positivity with 31.7% showing moderate / strong positivity. 48.4% tumours over expressed the oncogene Her2neu out of which 38.1% showed moderate and strong over expression.

Out of all clinical and morphological features and the fine needle aspiration results studied significant relationships were demonstrated only between the following.

Positive ER status was associated with the clinically palpable lymph nodes. Positive Her2neu status was associated with fine needle aspiration results and the mitotic count.

The level of agreement between the risks for recurrent and metastatic diseases assessed by clinical and morphological features and the risk assessed by the immnuhistochemical markers also indicate very poor levels of agreement.

CONCLUSIONS AND RECOMMENDATIONS:

It is apparent that ER and Her2neu status cannot be assessed by considering most common clinical and morphological features of breast carcinoma.

The level of risks for recurrent and metastatic disease assessed by clinical and morphological features do not agree well with the risk assessed by immune markers.

There fore it is recommended that oestrogen receptor status and Her2neu status be assessed in every breast carcinoma specimen before planning out post surgical therapy to invidualize treatment depending on the risk for recurrent and metastatic disease.

Since 2+ positivity for Her2neu is currently considered equivocal, facilities to perform fluorescent in situ hybridization to detect Her2neu gene amplification is recommended especially when specific therapy with Trastuzumab is planned.

PAPERS PUBLISHED ON WORK DONE UNDER CONTRACT RG / 98 / M /04

Presentations -

1. **Her2neu status of breast carcinoma in Sri Lanka – Oral presentation**
    - College of Surgeons annual sessions 2000
    - Sri Lanka Medical Association 114th Sessions, March 2001.

    Won H. K. T. Fernando award for best oral presentation on cancer.

    Won Channa Goonerathne memorial award for best cancer research done in year 2000.
2. **Impact of Her2neu status of breast carcinoma in Sri Lanka. – Oral presentation**

    Presented at the World Congress in Surgery in August / 2001 at Brussels Belgium.
3. **Is it possible to assess immune prognostic marker status of breast carcinoma by clinical and morphological features? – Oral presentation**

    College of Pathologists annual academic sessions - August 2001 in Kandy
4. The final report of the study **Prognostically important features of breast carcinoma among Sri Lankan women** has been nominated from Department of Pathology for the University of Colombo Research award for year 2000.

Publications -

1. Work done on prognostically important features of breast carcinoma in Sri Lanka will be submitted for publication in the Ceylon Medical Journal in due course.
2. Impact of Her2neu status of breast carcinoma in Sri Lanka will be submitted for publication in the World Journal of Surgery as requested by the editor of that journal subsequent to the oral presentation in Brussels Belgium in August 2001.