# INTERLEUKINE-6 (IL-6) AND TRANSFORMING GROWTH FACTOR-α (TGF-α) AS PREDICTORS OF MOLECULAR RESPONSE FAILURE IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA (CML)

Thesis

Submitted for Partial Fulfillment of Master Degree inClinical and Chemical Pathology

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**2016**

# Abstract

CMLis a clonal myeloproliferative neoplasm characterized by a specific translocation t(9; 22) (q34; q11).The novel chimeric protein BCR-ABL with un controlled elevated tyrosine kinase activity dictates the pathophysiology of the disease. Current established first line therapy for CML is tyrosine kinase inhibitors (TKI). The firstgeneration includes imatinib (IM) and masylate. Newer TKIs, nilotinib and dasatinib have been commercially available and are indicated for patients who developed resistance or intolerance to IM.

Monitoring of IM response is done according tohematological,cytogenic and molecular finding .Recently complete molecular response (CMR ) has been established as a gold standard for the outcome prediction. Also Many studies prove that the lack of early molecular response (EMR) (BCR-ABL$^{IS}$ ≤ 10% cut off) at 3 months was associated with a low rate of achieving subsequent CMR **(Dave Levitanet al., 2016).**

The mechanisms of resistance to IM are generally complex and likely to be a result of intrinsic and extrinsic causes. The extrinsic causes defined as the dynamic microenvironment around cancer primitive cells in the BM .This microenvironment with high concentration of growth factors and cytokines necessary for hematopoiesis.

In this study, our aim was identifying early predictors of suboptimal response or failure to IM. So we conducted this study to identify if high Interleukin -6 (IL-6) and transforming growth factor – α (TGF-α) levels at time of diagnosis can be used as a predictive of IM response and to clarify the association between there levels at time of diagnosis and the incidence of achieving of early molecular response (EMR).

This study included newly diagnosed 30 adult patients with Philadelphia positive (Ph$^{+}$) CML which were evaluated by molecular analysis at diagnosis and after 3months of IM therapy. The patients are divided into 2 groups(improved and non- improved). The levels of (IL-6) and (TGF-α ) before treatment were

assayedandreal time quantitative PCRfor BCR − ABL / ABL was done for each patient at beginning of IM supplementation and at end of 3 months.

The study concluded that levels of (IL-6) and (TGF − α) were elevated in CML patient regards to health peopleand there was association between high levels of relevant biomarker and failure of achieving EMR.

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**2016**