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CASE STUDY

A RETROSPECTIVE AUDIT OF DIAGNOSTIC DELAY IN LYMPHOMA PATIENTS IN WEST BENGAL, INDIA

Bidyut Mandal, Anish Bandyopadhyay, Pratyusha Mukherjee, *Abhishek Basu, Avik Maji and Prof S.K.Sikdar

Department of Radiation Oncology, Medical College Hospital, Kolkata

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ABSTRACT

Introduction: Prior to diagnosis lymphoma patients often have multiple primary care consultations, resulting in diagnostic delay. They are less likely to be referred urgently to hospital and often present in advanced stage or land up in emergency. This is a dismal picture for an otherwise curable disease. There is a paucity of studies in Indian context examining this diagnostic delay. We retrospectively examined this diagnostic delay and clarify its impact on clinical stage and outcome in our institution.
Objectives: To estimate mean diagnostic delay of presentation and to find impact of diagnostic delay on stage of disease presentation, treatment outcome & Progression free survival.
Material and Methods: We have analysed histopathlogically confirmed 250 lymphoma patients, excluding extra nodal presentations, in a retrospective single institutional epidemiological study. Follow up time is Date of treatment completion to date of last contact, local recurrence, distant metastasis or death. Statistical analysis was done by bivariate analysis using IBM SPSS software v.23
Results: Mean diagnostic delay is 302 days, including delay in tertiary care of 60days.56%patients had CR,6%PR ,28% SD. Simple correlation between PFS & Range of diagnostic delay(R=.488). The lesser the primary care delay, better is the treatment response (p 0.00). Beyond a delay of 300 days, patients presented with advanced stage.
Conclusions: In developing country like India delayed presentation due to diagnostic delay is taking a toll on treatment outcome. More evidence is needed as well as interventions to reduce time to diagnosis such as public education campaign and GP decision making aids.

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INTRODUCTION

Prior to diagnosis lymphoma patients often have multiple primary care consultations, resulting in diagnostic delay. They are less likely to be referred urgently to hospital and often present in advanced stage or land up in emergency. This is a dismal picture for an otherwise curable disease. There is a paucity of studies in Indian context examining this diagnostic delay. We retrospectively examined this diagnostic delay and clarify its impact on clinical stage and outcome in our institution. The literature regarding the length of diagnostic delays has several common themes. With the exception of cancer registry studies, most of the studies report conflicting findings from relatively small numbers of patients; generalisation from these data is difficult. This is compounded by different healthcare settings, different methods of measuring delays, the potential confounding effect of lead-time bias, and variations between cancers; and is reflected in the conflicting findings from this literature. In cancer patients, morbidity and psychological outcomes may be more important than mortality. Psychological distress correlates positively with total diagnostic delay (Risberg *et al*, 1996), itself a reason to minimise delays.

***Corresponding author:* Abhishek Basu,**
Department of Radiation Oncology, Medical College Hospital, Kolkata.

Aims & Objectives

- To estimate median diagnostic delay of presentation and to find impact of diagnostic delay on stage of disease presentation
- Relationship of diagnostic delay on treatment outcome
- Evaluating impact of diagnostic delay on Progression free survival

MATERIALS AND METHODS

- **Study design**: Retrospective, Epidemiological, Single institutional Study

- **Study period**: December 2010- February 2015
- **Study population**: 250 patients
- **Inclusion criteria**: Histologically confirmed lymphoma patients.
- **Exclusion criteria**: Extra-nodal sites of presentation.
- Retrospective data collection was undertaken by assessment of medical case records of lymphoma patients during study duration to Radiotherapy dept. of our hospital.

Statistical Analysis

Follow up time was calculated from Date of treatment completion to the date of last contact, local recurrence, distant metastasis or death.

Diagnostic delay was calculated From the first day of GP contact to histopathological confirmation (Primary care delay) + referral delay + delay due to metastatic work up & treatment initiation in our hospital. (Secondary care delay)

All analysis were performed by Bivariate analysis, using SPSS v23 IBM software. (Table – 1)

Table 1. Statistical analysis

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.699[a]	.488	.474	9.488

a. Predictors: (Constant), RANGE OF DIAGNOSTIC DELAY

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	3088.318	1	3088.318	34.303	.000[b]
	Residual	3241.076	36	90.030		
	Total	6329.395	37			

a. Dependent Variable: PFS
b. Predictors: (Constant), RANGE OF DIAGNOSTIC DELAY

RESULTS

In our study we found that, Median age of presentation was 38 years with male Preponderance (Male : Female = 3:1). Most common presentation was stage II. (Mean follow up period was 44 month, mean diagnostic delay was 302 days, (primary care delay 242 days) Including mean delay for initiation of treatment in tertiary care hospital was 60 days.(referral & secondary care delay) In subset analysis we found that Hodgkin's Lymphoma caters 62% of study Population, while 38% cases were from NHL(DLBCL). Pie diagram showing stage wise presentation of lymphoma patients in our study. Stage II was most common, though about 30% study population presented with advanced stage, i.e, stage 3 & stage 4 (18% & 12% respectively). Follow up till date of 30 patients was done radio-logically by PET-CT and in 230 patients response was evaluated clinically by detailed physical examination, blood parameters & imaging (USG, CT scan) When we assessed response of patients under study, we found that 48% patients achieved complete response, 6% patients partial response, while percentage of stable disease & progressive disease were 28 % & 6% respectively. 4% patients defaulted treatment and 8% patients died during follow up periods. Beyond a range of delay of 301-400 days there is a transition of disease spectrum from Stage II to more advanced stages i.e. Stage III and Stage IV (p 0.00) (Fig - 4). The lesser the diagnostic delay i.e. less than 300 days the better is the treatment response (p 0.00). Beyond this cut off limit, patients presented with advanced stage.

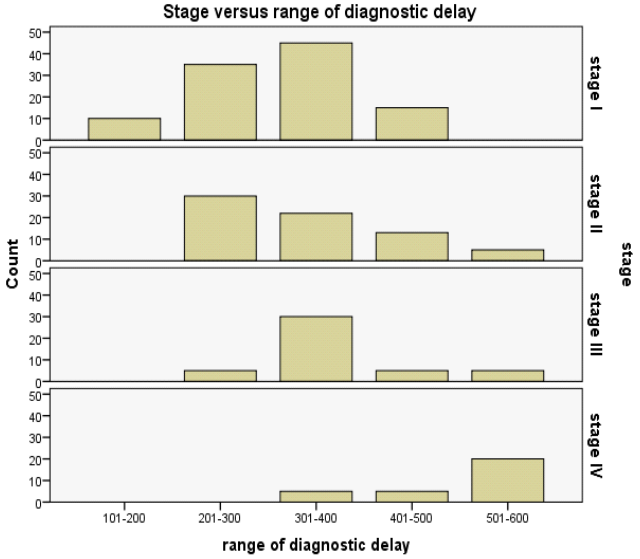

Fig. Bar dig showing stage of lymphoma patients versus range of diagnostic delay

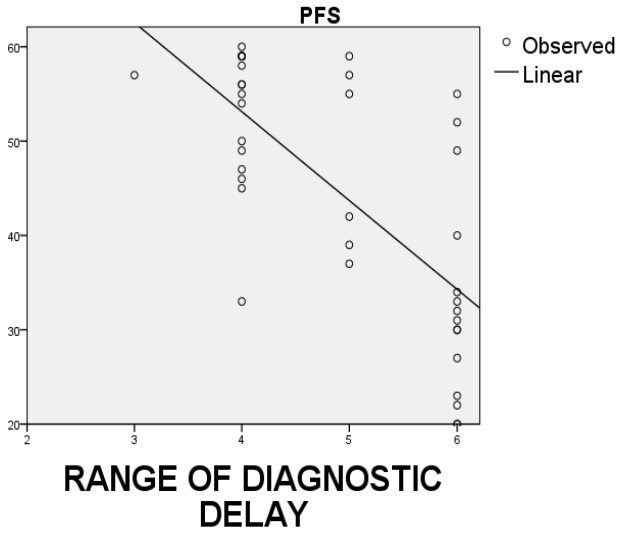

Fig. Diagram showing linear relationship between PFS & Range of diagnostic delay

Median PFS has not been reached in Stage I and II patients whereas it is 42 months in Stage III and Stage IV patients. Simple correlation between PFS & Range of diagnostic delay (R=.488) & significant (p<0.001). (Fig – 5)

DISCUSSION

Statement of principal findings – It is one of the few studies to report delays in lymphoma in Indian Scenario. Mean diagnostic delay of 302 days still suggests that diagnostic process could be quicker. Primary care delay contributed more than referral & secondary care delays. More the delay, more advanced stage presentation and consequently poorer outcome.

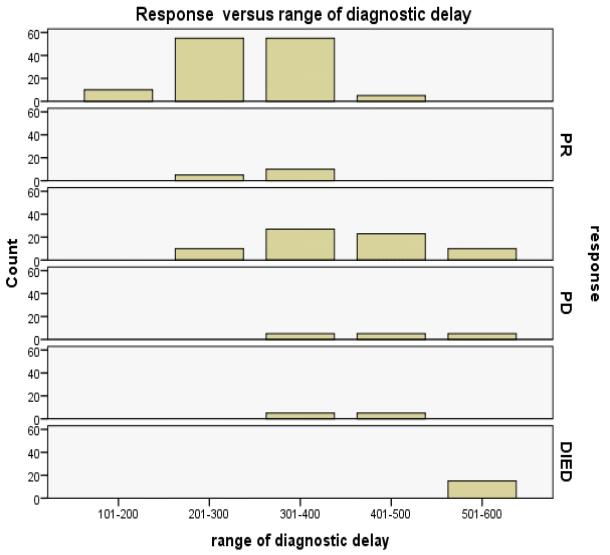

Fig. Bar diagram showing relationship between response of patients with range of diagnostic delay

Our study has few limitations like…

The sample size was small, only 250 patients. Single Institutional & Retrospective study. Aggressiveness of presentation not taken into consideration. The patient interval (date of first symptom onset to first help seeking) not taken into consideration as this is a retrospective study. Potential for recall bias.

Implication of the study

Reductions in delays may improve survival. Longer delays in lymphoma may occur because of the insidious onset of nonspecific symptoms, which may occur on top of appearance of node or lump. Delays may improve in the future with more opportunistic screening, although the effect of this on survival is unknown. The effects of the introduction of a national screening programme are unknown. While there is insufficient evidence at present to prove that shorter delays are associated with better prognosis, there is considerable logic that this should be the case, given the potential for curative treatments. There is clear potential to reduce delays with the anticipated outcome of improved survival. The finding that primary care delay was the longest suggests that while further reductions in referral delays and secondary care delays may result in better psychological outcomes, attempts to improve clinical outcomes (earlier stage diagnosis and improved survival), must be directed at patient and/or primary care delays.

Controversy raised by this study

From our study we came to know that a large proportion of our study population first visited Quacks & Homeopaths & other practitioners of alternative medicines and this could contribute to the diagnostic delay. But as this was a retrospective study we could not find any further details apart from few telephonic conversations with the patient and their relatives, which are not conclusive to make a strong comment. Regarding this issue we intend to do a prospective study with more type of cancer patients in future.

Future research direction

Prior to the development and evaluation of interventions to reduce delay (Jensen *et al*, 2002), further work needs to be performed in order to elucidate the separate contributions of patient and primary care delays to the overall delays. There may be variation between delays and socio-demographic factors, and local or regional variations; these need quantifying prior to intervention. Findings from the ever-increasing evidence based on the reasons for patient delays in most cancers, and the smaller evidence base regarding primary care delays (Spellman *et al*, 1999) will inform the development of the interventions. Lastly, in developing country like India delayed presentation due to diagnostic delay is taking a toll on treatment outcome. More evidence is needed as well as interventions to reduce time to diagnosis such as public education campaign and GP decision making aids.

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