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RESEARCH ARTICLE

Molecular Profile and Clinical Outcomes in Cancer Subjects: Experience from a Tertiary Referral Centre in Bihar

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Abstract

Background: Personalised therapy methods have been made possible by molecular profiling, which has transformed cancer diagnosis and treatment. Nevertheless, little information about molecular profiles and their relationship to clinical outcomes is available from tertiary care facilities in eastern India.

Objective: At a tertiary referral centre in Bihar, India, the goal is to assess clinical outcomes and examine the genetic profiles of cancer subjects.

Methods: From January 2022 to December 2023, retrospective observational research was conducted at Katihar Medical College & Hospital in Katihar, Bihar, India. Included were 65 cancer subjects who had molecular profiling. Analysis was done on information on molecular markers, tumour histology, treatment responses, demographics, and survival results.

Results: Among 65 subjects (mean age 58.3 ± 12.7 years, 60% male), lung cancer was the most common (32.3%), followed by breast (24.6%) and colorectal cancer (18.5%). Molecular profiling revealed EGFR mutations in 45.7% of lung cancer subjects, HER2 overexpression in 43.8% of breast cancer subjects, and KRAS mutations in 33.3% of colorectal cancer subjects. Subjects with targetable mutations showed significantly better progression-free survival compared to those without (median 14.2 vs 8.6 months, $p<0.05$). Overall response rate was 68.4% in the molecularly profiled cohort.

Conclusion: Molecular profiling significantly impacts treatment outcomes in cancer subjects. Our findings

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from Bihar demonstrate the feasibility and clinical utility of implementing molecular diagnostics in resource-limited settings, emphasizing the need for expanded molecular testing capabilities in eastern India.

Keywords: Molecular profiling, Cancer outcomes, Targeted therapy, Precision medicine, Bihar

INTRODUCTION

With an expected 19.3 million new cases and 10 million deaths worldwide in 2020, cancer is still the biggest cause of death worldwide[1]. In India, cancer incidence has been steadily rising, with approximately 1.39 million new cases diagnosed annually[2]. The advent of molecular profiling has transformed cancer care by enabling precision medicine approaches that target specific genetic alterations driving tumorigenesis[3].

Molecular profiling involves the comprehensive analysis of genetic, epigenetic, and proteomic alterations in tumor tissues, allowing for the identification of actionable mutations that can guide targeted therapeutic interventions[4]. This approach has demonstrated significant improvements in patient outcomes across various cancer types, including lung, breast, colorectal, and other solid tutors[5–7].

Despite the proven benefits of molecular profiling, its implementation in resource-limited settings, particularly in eastern India, remains challenging due to infrastructure limitations, cost constraints, and lack of trained personnel[8]. Limited data exists regarding the molecular landscape of cancers and associated clinical outcomes from tertiary care centres in Bihar, one of India's most populous states.

The present study meant to gauge the molecular profile of cancer subjects and analyse clinical outcomes at Katihar Medical College & Hospital, a tertiary referral canter serving the population of north Bihar and adjoining areas. This study represents one of the first comprehensive analyses of molecular profiling and its clinical impact in this geographical region.

MATERIALS AND METHODS

Study Design and Setting

The Department of Medical Oncology at Katihar Medical College & Hospital in Katihar, Bihar, India, was the site of this retrospective observational study. The trial ran from January 2022 to December 2023, and all subjects had to be followed up with for at least six months.

Study Population

65 consecutive cancer subjects who had molecular profiling done during the study period were included

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in the research. Histologically proven malignancy, sufficient tissue samples for molecular analysis, molecular profiling conducted at our centre or related laboratories, full clinical and follow-up data accessible, and age ≥18 years were the requirements for inclusion. Subjects who were lost to follow-up within three months or had inadequate molecular profile data were not included.

Molecular Profiling Methods

Formalin-fixed paraffin-embedded (FFPE) tumour tissue trials were used for molecular profiling. The following techniques were used:

1. NGS, or next-generation sequencing: For thorough genomic profiling, targeted gene panels of 50–400 genes were employed.

2. Real-time PCR for certain mutations (EGFR, KRAS, and BRAF) using polymerase chain reaction (PCR)

3. Protein expression analysis using immunohistochemistry (IHC) (HER2, PD-L1, MSI indicators)

For gene amplifications and translocations, use Fluorescence In Situ Hybridisation (FISH).

Data collection

The following information was gathered from electronic medical records:

• Features of the tumour (primary location, histology, grade, stage).

• Demographics (age, gender, smoking history, family history).

The results of the molecular profile

• Specifics of the treatment (immunotherapy, targeted therapy, chemotherapy)

• Response evaluation based on RECIST v1.1 standards

• Survival results (total survival, survival without advancement)

• Adverse events and profiles of toxicity

Interpretation of Statistics

The patient information and molecular findings were gathered using descriptive statistics. Frequencies and percentages were used to represent categorical variables, whereas means ± standard deviation or medians with interquartile ranges were used to represent continuous data. The Kaplan-Meier method was used for survival analysis, and the log-rank test was used for comparisons. Multivariate analysis was performed using Cox proportional hazards regression. The threshold for statistical significance was set at $p<0.05$. The SPSS version 26.0 was used for all analyses.

Ethical Considerations

The Katihar Medical College & Hospital Institutional Ethics Committee gave consent to the project. All subjects gave penned informed consent for the use of clinical data for research and molecular profiling.

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RESULTS

Attributes of the Patient

In all, 65 subjects participated in the research. Table 1 provides a summary of the clinical and demographic characteristics. With a male preponderance (60 percent, n=39), the average age was 58.3 ± 12.7 years (range: 28-79 years). Most of the subjects (72.3%) were from rural Bihar and the surrounding regions of Jharkhand and West Bengal.

Table no.1: Patient Demographics and Clinical Characteristics

Characteristic	N (%)
Age (years)	
Mean ± SD	58.3 ± 12.7
<50	18 (27.7)
50-65	32 (49.2)
>65	15 (23.1)
Gender	
Male	39 (60.0)
Female	26 (40.0)
Primary Timor Site	
Lung	21 (32.3)
Breast	16 (24.6)
Colorectal	12 (18.5)
Gastric	6 (9.2)
Ovarian	5 (7.7)
Others	5 (7.7)
Stage at Diagnosis	
Stage I-II	18 (27.7)
Stage III	23 (35.4)
Stage IV	24 (36.9)

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Molecular Profile Analysis

Molecular profiling revealed actionable mutations in 78.5% (n=51) of subjects. The allocation of molecular adjustments by tumor type is presented in Table 2.

Table no.2: Molecular Alterations by Tumor Type

Tumor Type	Total (n)	Actionable Mutations	Specific Alterations
Lung Cancer	21	15 (71.4%)	EGFR: 10 (47.6%), ALK: 3 (14.3%), ROS1: 2 (9.5%)
Breast Cancer	16	12 (75.0%)	HER2+: 7 (43.8%), HR+: 9 (56.3%), BRCA1/2: 4 (25.0%)
Colorectal	12	8 (66.7%)	KRAS: 4 (33.3%), PIK3CA: 3 (25.0%), MSI-H: 2 (16.7%)
Gastric	6	4 (66.7%)	HER2+: 2 (33.3%), MSI-H: 1 (16.7%), PD-L1+: 3 (50.0%)
Ovarian	5	5 (100%)	BRCA1/2: 3 (60.0%), HRD: 4 (80.0%)

Treatment Outcomes

Based on molecular profiling results, 51 subjects (78.5%) received targeted therapy or personalized treatment approaches. The overall response rate (ORR) in the molecularly profiled cohort was 68.4% compared to 42.9% in subjects without actionable mutations (p=0.045).

Treatment Response by Molecular Status:

- Complete Response (CR): 8 subjects (12.3%)
- Partial Response (PR): 36 subjects (55.4%)
- Stable Disease (SD): 15 subjects (23.1%)
- Progressive Disease (PD): 6 subjects (9.2%)

Survival Analysis

The median follow-up period was 18.2 months, with a range of 6 to 36 months. Subjects with actionable mutations had a substantially greater duration of progression-free survival (PFS) than those without susceptible to assault alterations (median PFS: 14.2 vs. 8.6 months, HR=0.62, 95% CI: 0.39-0.98, p=0.041).

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The 12-month overall survival rate for subjects with actionable mutations was 78.4%, while the 12-month overall survival rate for those without was 64.3% (p=0.158). Subgroup analysis showed that subjects who got matched targeted treatment did better than those who received conventional chemotherapy alone.

Adverse Events

With grade 3–4 adverse events ensuing in 23.5% of subjects undergoing targeted drugs compared to 42.9% of subjects getting conventional chemotherapy, targeted treatments were generally well-tolerated (p=0.087). In the targeted treatment group, tiredness (41.2%), rash (29.4%), and diarrhoea (35.3%) were the most frequent side effects.

Challenges and Limitations

Several challenges were encountered during the implementation of molecular profiling:

1. Tissue adequacy for molecular testing (18.2% initial failure rate)
2. Turnaround time for results (median 14 days)
3. Cost considerations and insurance coverage limitations
4. Access to targeted medications in rural settings

DISCUSSION

This study embodies one of the first comprehensive analyses of molecular profiling and clinical outcomes from a tertiary care center in Bihar, providing valuable insights into the implementation of precision medicine in resource-limited settings in eastern India.

Our findings demonstrate that molecular profiling is feasible and clinically beneficial in this setting, with 78.5% of subjects harbouring actionable mutations. This rate is comparable to larger studies from developed countries, suggesting that the molecular landscape of cancers in Bihar is like global patterns[9'10].

The high prevalence of EGFR mutations (47.6%) in lung cancer subjects in our cohort is consistent with data from other Asian populations[11]. Similarly, the HER2 positivity rate of 43.8% in breast cancer subjects aligns with global statistics[12]. These findings support the implementation of routine molecular testing in our population.

The sizable recovery in progression-free survival (14.2 vs 8.6 months) among subjects with actionable mutations underscores the clinical utility of molecular profiling. This 5.6-month improvement in PFS translates to meaningful clinical benefit and quality of life improvements for subjects and their families.

Our study also highlights several implementation challenges specific to resource-limited settings. The initial tissue adequacy failure rate of 18.2% emphasizes the need for improved biopsy techniques and sample handling protocols. The 14-day median turnaround time for molecular results, while

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acceptable, could be further optimized through local laboratory capacity building.

Cost remains a significant barrier to widespread implementation of molecular profiling in Bihar. Despite government insurance schemes, many subjects face out-of-pocket expenses for molecular testing and targeted therapies. This economic challenge necessitates policy interventions and pharmaceutical access programs to ensure equitable access to precision medicine.

The geographic distribution of our subjects, with 72.3% from rural areas, reflects the tertiary referral pattern in Bihar. This finding emphasizes the need for strengthening molecular diagnostics capabilities in district-level hospitals to reduce patient travel burden and improve access to care.

Compared to international studies, our overall response rate of 68.4% in molecularly profiled subjects is encouraging[13,14]. However, the relatively meek improvement in overall survival suggests that longer follow-up periods are needed to fully evaluate the survival advances of molecular profiling in our population.

The lower rate of grade 3-4 adverse events in subjects receiving targeted therapy (23.5% vs 42.9%) supports the amended tolerability profile of precision medicine approaches. This finding is particularly relevant in the Indian context, where subjects often present with advanced disease and compromised performance status.

CONCLUSION

This study reveals the viability and clinical efficiency of employing molecular profiling in a tertiary care center in Bihar, India. Despite resource constraints, molecular testing significantly improved treatment outcomes, with subjects harboring actionable mutations showing superior pfs and response rates.

The high prevalence of actionable mutations (78.5%) in our cohort supports the routine implementation of molecular profiling in cancer care in Bihar. However, several challenges including tissue adequacy, cost considerations, and access to targeted therapies need to be addressed through systematic interventions.

Our findings provide a foundation for expanding precision medicine initiatives in eastern India and similar resource-limited settings. The experience from Katihar Medical College demonstrates that with appropriate planning and resource allocation, molecular profiling can be successfully integrated into routine cancer care, ultimately improving patient outcomes.

The success of this initiative at our center serves as a model for other tertiary care institutions in Bihar and neighbouring states. Continued efforts to build local capacity, reduce costs, and improve access to molecular diagnostics will be necessary for achieving the full potential of precision medicine in this region.

Future research ought to hub on larger, multicentre studies with prolonged follow-up periods to validate these outcomes and explore the cost-effectiveness of molecular profiling in the Indian healthcare context. Additionally, studies investigating the integration of

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liquid biopsies and emerging biomarkers could further enhance the molecular profiling capabilities in resource-limited settings.

LIMITATION

Several constraints ought to be addressed. First, the findings are not as universally applicable as they may be due to the retrospective approach and limited sample size. Second, there's a chance that the analysis's diverse tumour kinds included complicating variables. Third, the comparatively brief follow-up period may have underestimated long-term survival benefits. Finally, selection bias cannot be excluded, as molecular profiling was not performed uniformly in all eligible subjects due to resource constraints.

FUTURE DIRECTIONS

Based on our experience, several recommendations emerge for expanding molecular profiling in Bihar and similar settings:

1. **Capacity Building:** Training programs for pathologists and laboratory technicians in molecular diagnostics
2. **Infrastructure Development:** Establishment of regional molecular laboratories with appropriate quality control measures
3. **Policy Interventions:** Inclusion of molecular testing and targeted therapies in government insurance schemes
4. **Telemedicine Integration:** Use of digital platforms for molecular tumor boards and treatment planning
5. **Research Collaboration:** Multi-center studies to generate larger datasets and validate findings.

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CONFLICT OF INTEREST

Regarding this work, the authors disclose no conflicts of interest.

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