STATISTICAL SURVEILLANCE MODELING OF CHILDHOOD CANCERS

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ABSTRACT

Although, child health continues to be a priority health issue, childhood cancer is not yet a major area of focus. This article is focused on statistical analysis of trends and factors in childhood cancers in Mumbai with explorations to the Indian and global population at larger extents. With the data of 200 infant and childhood cancer patients at Tata Memorial Hospital (TMH),(1) a leading cancer hospital in Mumbai, the research explores for trend data analysis to cancer registries in Mumbai, Maharashtra, India, and in global infant and children cancer records as well, so that the trend analysis in the research suits and forecasts for global children population. Some of the findings and analyses in the research are, there is roughly around 3:1 ratio of male and female patients in infant and childhood cancer, male children are more linked to cancer. Infant cancers if diagnosed and treated early assures kind of complete cure with healthy survival. Statistical tools like the life tables, joint point analysis and smoothing constant forecasts are better ways to express data of disorders like cancers, so that forecasting the trend for the population becomes easy and individual’s traits like genetic links also could be analysed in a better way to combat the disorder completely. Data analysed by statistical tools could be better presented on advanced platforms for representation like the Alteryx an easy software tool for data representation and analysis. Gap-based and need-based predictions like the significance of gender disparity in infant and childhood cancer available and required funds for infant cancer treatments in the research open an avenue for further research in the line. The present research paper tries to give a forecast prediction study for cancer cases in Mumbai with a sample size of 200 infant patients.

KEYWORDS

Childhood Cancer, Statistical Analysis, Forecast, Prediction, Genetic Links.

INTRODUCTION

The theoretical context: Unearthing beliefs about infant cancer is 13% of the annual deaths worldwide are cancer-related and 70% of these are in the low and middle income countries. Although, child health continues to be a priority health issue. Childhood cancer is not yet a major area of focus. The research tries to emphasis on need of health facilities in the sector to ensure complete child care in a small zone like Mumbai. Mumbai, a densely populated urban metropolis on the west coast of India, occupies an area of 603.0 kms and is the smallest administrative district in the Maharashtra State. As majority of hospitals in Mumbai are maintained by Municipal Corporation and State Government, the cancer records in Mumbai are directly linked with ICMR (Indian Council of Medical Research), which is responsible for organisation of medical and public health services in the city. Main source of cancer data focused on in this research was Tata Memorial Cancer Hospital (TMH) located at Parle in Mumbai. Diagnosis and treatment of cancer is centralised only to a certain extent in Mumbai. Major cancer surgery is undertaken at all major hospitals as well apart from Tata Hospital. Therapies for cancer are also available in ten other hospitals. Out of the major collaborating hospitals for cancer treatment, one is a cancer hospital, 18 are Municipal Hospitals, 18 are Government Hospitals and 22 are Charitable Trust Hospitals(1)

Mumbai Cancer Registry maintains cancer-related information such as site of disease, histological classification, clinical extent of disease and primary treatment since 1941. Over 1,100 patients were diagnosed as cancer cases in 1941. Since then, there has been increase in patient attendance and at present over 25,000 new patients get registered and over 15,000 patients are diagnosed as suffering from cancer annually. The Population-Based Cancer Registry (PBCR) for Mumbai, then called as Greater Bombay was started in the year 1966 and TMH Cancer Registry has been the important source for getting information on resident cancer cases.(1)

TMH is a well-recognised institution. Patients from other states of India and abroad attend the hospital for expert medical care and opinion. Thus, this cancer registry has become an important source to identify resident cancer cases of PBCRs like Bhopal, Delhi, Madras and Barshi in NCRP network. As cancer is not a notifiable disease, information about patient’s health status is obtained through active follow up of patients mostly by postal inquiry.(1)

Understanding the trend of infant cancers using the cancer registry as a primary information source, statistical forecast study was performed on 200 live infant cancer patients of which 6 patients opted out of the study reducing the sample size to 194, but these 194 patients helped to give a valid forecast of infant cancer statistics in Mumbai.

Forecast of Childhood Cancer Cases

Most predominant type of cancer in infant across the globe is always leukaemia. The case records in the Mumbai Cancer Registry also show the same trend. Leukaemia is in itself a big class of multiple cancers. About 3 out of 4 leukaemias among children and teens are Acute Lymphocytic Leukaemia (ALL). Most of the remaining cases are Acute Myelogenous Leukaemia (AML). Chronic leukaemias are rare in children as ALL in children could be treated by blood transfusion therapies and bone marrow transplants.
ALL is most common in early childhood peaking between 2 and 4 years of age. Cases of AML are more spread out across the childhood years, but it is slightly more common after the first 2 years of life and during the teenage years.\(^{(2)}\) ALL is slightly more common among white children than among African-American and Asian-American children and it is more common in boys than in girls. AML occurs about equally among boys and girls of all races.\(^{(1)}\)

<table>
<thead>
<tr>
<th>Year</th>
<th>Infant Male Cancer</th>
<th>Infant Female Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 2001</td>
<td>550</td>
<td>271</td>
</tr>
<tr>
<td>2. 2004</td>
<td>543</td>
<td>253</td>
</tr>
<tr>
<td>3. 2008</td>
<td>533</td>
<td>239</td>
</tr>
<tr>
<td>4. 2011</td>
<td>145</td>
<td>55</td>
</tr>
</tbody>
</table>

**Table 2: Infant Cancer Count**

Forecast formula used for calculating the forecast number is \(F_{t+1} = F_t + (Y_t - F_t)\).

Where \(F_t\) was the average number of cancer patients and \(\alpha\) is a smoothing constant, which is taken as 0.2 in this case and \(Y_t - F_t\) is different in the average number of patients/cases and the last recorded number of patients.

\(F_{t+1}\) is the forecast of the infant cancer percentage for the next registry as per the forecast also leukemia is the most predominant type of infant cancer. Cancer registries across different places also reveal that leukemia is the most predominant type of infant cancer, not only in Mumbai or in the India, but across the globe and the forecast or the average population of infant cancer on an average for every type of infant cancer’s remains the same for every year. \(\alpha\) is the smoothing constant of the equation. Leukemia dominates as the type of infant cancer as it is a diverse type of cancer. A combination of various types of cancers of blood genetically linked and predominating the childhood population across Mumbai and also across the globe.

The forecast value for any trait using a smoothing constant used in this case as 0.2 is generally based on the last year’s value of the trait like the type of infant cancer in this state and the difference in the average and the last year’s value of the trait. As per the \(Y_t - F_t\) values, the negative values indicate that the recorded values of the last year, i.e. 2011 are less than the average values revealing some positive lines to treatment for the ailment marking towards gradual decline of the disorder in the population. The analysis here shows that some unspecified cancer, retinal cancers and renal and hepatic cancers need more research and analysis as they show a positive \(Y_t - F_t\) value. More research in these cancers along with continuation of the current trend of treatment for the other cancers could help to decrease the rate of cancer proliferation in children and combat the disorder completely.
The growth rate of the embryo is higher for males than females in different species including humans.\(^3\) Because accelerated rates of cell division and proliferation may increase the predisposed development of cancer (Preston-Martin, 1990), this inherent feature of males may explain some of the gender effect in (Childhood) cancers.\(^4\) The rate of development though remains the same for both male and infants later after birth, however, from the statistical tables and analysis, it was noted that male infant predominate female infants in the infant cancer counts linking to their embryonic growth rate characteristics without any requirement of statistical analysis. The available rate on a bar reveals that the ratio of male to female infant cancer population is roughly around 3:1.

**Statistical Analysis of Incidence of Cancer in Relatives of Childhood Cancer Patients**

The Tata Cancer statistical records reveal that there were 821 patients, around 5% of childhood cancer patients treated at Tata Memorial Hospital in the year 2013. Of all the different types of cancer leukaemia, lymphoma, bone tumours and soft tissue cancers formed about 7.5% of all other paediatric cancer patients.\(^1\)

Forecasting is one of the basic tools in management and decision making in any business process. Forecasting techniques tries to reduce the uncertainty and makes better estimates of what is likely to happen or repeat as a trend in the future.

Most of the increased cancer risk in the relatives of patients with childhood cancer could be explained by known hereditary factors; however, the genetic susceptibility may be underestimated. Although, the cancer risk in first-degree relatives is well studied, data on the cancer incidence in extended families of patients with childhood cancer are limited.

**Incidence of cancer in relatives**

<table>
<thead>
<tr>
<th>Relationship Degree</th>
<th>Incidence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 degree</td>
<td>14%</td>
</tr>
<tr>
<td>2 degree</td>
<td>7%</td>
</tr>
<tr>
<td>3 degree</td>
<td>2%</td>
</tr>
<tr>
<td>No degree</td>
<td>89%</td>
</tr>
</tbody>
</table>

In this study, the researcher assessed the occurrence of childhood and adult cancers in the extended families of 200 patients with childhood cancer included in the study. The main finding of the study was that the relatives of patients with childhood cancer were found to have an increased incidence of childhood cancer and certain adult cancers as well. Out of the 200 patients, only 194 patients did answer the question or 6 individuals who did not answer the question were ruled out in this study and the sample size for the study is now only 194 infant cancer patients. Considering the occurrence of childhood cancer, 21 of 194 patients were found to have at least one relative with a childhood tumour, cancer or adult cancer. Overall, first to third-degree relatives had a significant two-fold increased incidence of childhood tumours. The highest incidences were observed in second and third-degree relatives, although the results obtained from subgroup analyses were not statistically significant.

**SIR - Standardised Incidence Ratio** \(n=(O-E)^2/E\)

Suppose the person-time from the study group (i.e. cohort) is allocated among M cells defined by the cross-classification of various adjustment variables such as gender, race, attained age group and attained calendar year group. Let \(t_k\) represent the person-time and \(D_k\) represent the observed events that the cohort subjects contribute to the kth cell and let \(\lambda_k\) represent the standard rate for the kth cell where \(k=1, 2, ..., M\). Given this notation, the SIR is defined as:

\[
SIR = \frac{\sum_{k=1}^{M} D_k \cdot \lambda_k}{\sum_{k=1}^{M} E_k} = \frac{\sum_{k=1}^{M} (O_k - E_k)^2}{E}
\]

where the total number of events observed in the cohort is, \(D = \sum_{k=1}^{M} D_k\) and the total number of expected events is \(E^* = \sum_{k=1}^{M} E_k = \sum_{k=1}^{M} \lambda_k \cdot t_k\).

SIR 1 degree=2/21

Literature review of assessing the occurrence of childhood tumours in siblings of patients with childhood cancer or cancers in general showed similar results suggesting an approximate two-fold increased risk for childhood cancers in siblings with cancer relatives, but in most cases, the increased risk seemed to be contributed to known hereditary cancer syndromes, though the kind of cancers were different, but there was a marked ontogenic correlation in cancers in the families.\(^5\)

It was found no evidence suggesting that known hereditary syndromes could explain the observed incidence of childhood tumours in most of the cases studied with the exception of two index patients, one of whom had Down’s syndrome and one of whom had neuroblastoma type 1.\(^6\) No germline mutations were found in patients who had a relative with childhood cancer. Most of the affected relatives were of more distant relationships than first and second-degree relatives, which may suggest that it is unlikely that highly penetrant genes account for the increased incidence of childhood tumours. Genes with a recessive inheritance pattern could also contribute to the susceptibility of childhood cancer in these families. Other possible mechanisms may be the dominant inheritance of common allelic variants of susceptibility genes with low-to-moderate penetrance, possibly modifying the response to environmental factors. This needs to be further addressed in future studies.
Furthermore, it was noticed that an increased incidence of childhood cancers in the relatives of patients with adult cancer, mainly in first (SIR: 2.2, 95% CI: 1.2-3.5) and second-degree relatives (SIR: 1.4, 95% CI: 1.2-1.7). In particular, an increased incidence of Wilms tumours were observed in first to third-degree relatives. Increased leukaemia incidence was observed in first and second-degree relatives, while an increase in prostate cancer was observed in second-degree relatives.\(^{(5)}\)

In contrast to findings if the same study is done with adult patients, most previous studies have not found increased risk for adult tumours in parents or siblings except when known hereditary cancer predisposition syndromes were present. Increased breast cancer risk in mothers and sisters maybe partially, though not fully, explained by known syndromes, as previously reported.

This analysis of 200 patients thus explains that the genetic susceptibility for childhood cancer may be underestimated. Our findings lend additional support to the hypothesis that familial factors may play a role in the aetiology of childhood tumours, but may not contribute to occurrence of cancer in a child, genetic factors play a major role for occurrence of cancers in adults.

Our study of 194 infant cancer individuals could suggest that every tenth patient with childhood cancer had a relative affected by cancer in childhood or adolescence. Presently, the clinical importance of our findings is limited as it does not talk of the process of genetic link in this sample and so at this instance the researcher could not suggest any genetic counseling for families with multiple childhood tumours, cancers or adult cancers in the family also, unless indications of known hereditary syndromes occur. Although, single families with multiple childhood tumours maybe due to chance the high incidence of childhood tumours in the relatives of patients with childhood cancer. Studying families with multiple childhood tumours maybe a valuable approach to improving our understanding of the aetiology of childhood tumours and identifying candidate genes or pathways that confer increased risk for childhood cancer.

**DISCUSSION**

Most of the findings and analysis in the research are aligned around the trend setting pattern for 200 individuals from the population, so most of the data analysed though formulated for the population is always for prediction and presentation on the sample size at large, one could say that the analysis like genetic link of childhood cancers, forecast prediction from the previous values are linked to a population they are part from where the sample is drawn, basic analysis for the population is from data of the registry records, but qualitatively pulled down on this specific sample for its projection in the current scenario, the scenario for occurrence of cases may vary in different places, but stand on genetic links and male predominance in childhood cancers maybe the unified trait across the globe, this may help understanding childhood cancers in the different regions and further research for factors of childhood cancers in different regions.\(^{(3)}\) The larger percept of this research for understanding and combating childhood cancers across the globe would be:

- Do not consider infant cancers or childhood cancers or in the larger sense any type of cancer as non-curable as cancers if understood well and treated on the current time could be cured to prolong life expectancies. Death is an inevitable truth of life, so there is no escape from otherwise of cancers as well.
- Try to find ways to invest in funding infant cancer treatments to enhance healthy survival for further generations.
- Donate blood as lymphoma and blood cancers constitute the major population of infant cancers across the blood and these infants need blood transfusions and stem cell treatments.

**CONCLUSION**

Cancers could not be treated completely, but proper care and treatment could help in combating the disorder in a right way leading to increased life expectancy and survival.\(^{(6)}\) Statistical study and surveillance in the right way might help in achieving this goal for infant cancers at the pioneering stage and all cancers on a broader scale.\(^{(6)}\) Though, cancers could not be cured, but life expectancy of a patient could be increased if statistical data related to cancer is handled in the right way to forecast the trend and behaviour of the disorder.\(^{(7)}\)

The research is mainly about study of demographic factors responsible for infant cancers. The researcher tries to study the effect of these factors in occurrence and cure of the disorder in infants and by statistically testing the hypotheses framed the researcher tries to find statistical ways to analyses, handle and cure infant cancers on a broader scale. The research concludes to signify that infant cancers are not generally genetically linked, male infants are more prone to the cancers than female infants and lines of treatment to treat the most predominant type of infant cancer, which is leukaemia has improved and across the years, number of cancer cases are coming down, but treatment for some cancers like retinoblastoma and lymphoma needs more research and study.\(^{(8)}\)

**REFERENCES**