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Distribution of multiple myeloma in India: Heterogeneity in incidence across age, sex and geography

Kaustubh Bora

Haematology Division, ICMR – Regional Medical Research Centre, N.E. Region, 786010, Dibrugarh, Assam, India

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ABSTRACT

Background: This study aimed to investigate the distribution of multiple myeloma (MM) in India and provide a comprehensive narrative about its incidence, including differential patterns across age, sex and geography.
Methods: MM cases diagnosed during 2012-14 were obtained from 27 populations based cancer registries in India by consulting the latest National Cancer Registry Programme reports. Crude (CR) and age-specific (ASR) rates of MM incidence were determined. Age-adjusted rates (AARs) were estimated by standardizing the CR values using age-specific weights recommended for LMIC countries (including India) for men and women separately, along with the corresponding 95% confidence interval (95% CI) measures.
Results: Altogether, 1916 MM cases (male/female: 1123/793) were documented (*i.e.* 1.19% of all cancers, 95% CI: 1.14–1.24%). Overall CR of MM in India was 1.27 (95% CI: 1.20–1.35)/ 100,000 in men and 0.95 (95% CI: 0.89–1.02)/ 100,000 in women, while the corresponding AARs were 1.13 (95% CI: 1.07–1.20) and 0.81 (95% CI: 0.75 – 0.88) per 100,000 respectively. The ASR values increased steadily with age. Most cases belonged to the 60–69 yrs bracket. However, regional and sex-specific differences in MM profile were observed. MM incidence was highest in the Southern and Northern zones, and least in the Northeast. The Northern and Central zones had higher proportion of MM in the 50–59 yrs age group, whereas Eastern zone had higher proportion of cases aged 70 yrs and above.
Conclusion: Incidence of MM in India is presented. Marked variations in MM incidence were noted with respect to age, sex and geography.

1. Introduction

Multiple myeloma (MM) is the second most frequent haematological malignancy (~15%), that is responsible for nearly 20% of all haematological malignancy-related deaths [1–3]. As per GLOBOCAN data from the International Agency for Research on Cancer (IARC), there were an estimated 114,000 new MM cases globally in 2012. [4]. More recent estimates suggested 159,985 newly diagnosed MM cases worldwide (*i.e.* about 0.9% of all cancers and 1.1% of all cancer deaths) in 2018 [5]. MM incidence displays striking dissimilarities across ethnicities [6–8]. For instance, African Americans are nearly two to three times more likely to be diagnosed with MM than European Americans [6,7]. These disparities may be due to differences in genetic susceptibility and the heterogeneity of molecular alterations underlying MM pathogenesis in various racial groups [6,9].

In comparison to Western nations, incidence data regarding MM from Asia is relatively scarce; particularly from low- and middle-income countries (LMIC) where cancer registries and vital registration systems are either non-existent or have low coverage [4,5]. Asians in general have a lesser incidence of MM than Caucasians [6,10–12]. In India as well, MM incidence is stated to be less than that in the Western countries [6]. Hospital based studies have reported certain unique features in MM patients from India, *viz.* greater proportion of symptomatic anaemia and skeletal abnormalities, higher serum creatinine, lesser proportion of hypercalcaemia, etc. [13–16]. Such sporadic studies have also indicated the possible presence of some epidemiological peculiarities in the Indian setting, namely: an earlier age of onset (median age at diagnosis nearly a decade younger than in the USA) and a greater incidence of MM in the young (age < 40 years) than in the Western populations [14–18]. In fact, MM patients in India tended to be younger than MM patients of Indian descent living in the USA [19]. These peculiarities have crucial implications because they may influence disease pathogenesis and presentation [20–23], presence of secondary complications [24,25], choice of treatment and special medical requirements [25–27], and determine prognosis and survival [23,28,29]. India is a vast country with marked diversity in terms of ethnicity, demography and environmental conditions across its various regions. However, a systematic analysis about the country-wide incidence patterns of

E-mail address: kaustubhbora1@gmail.com.

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MM from India is lacking. Therefore, it is of interest to derive population level estimates for MM incidence in India and further analyze them as a function of age, sex and geographical region. This study investigates the incidence of MM across India and examines the differential patterns in terms of age, sex and geography.

2. Materials and methods

2.1. Data sources

The population based cancer data in India is collected through Population Based Cancer Registries (PBCRs) under the National Cancer Registry Programme (NCRP) network of Indian Council of Medical Research (ICMR). As cancer is not a notifiable disease in India, hence the cases are registered primarily through active methods. All cancer cases in a registry area are sought from hospitals, diagnostic labs and death certificate records and coded as per International Classification of Diseases (ICD) codes. Information is then abstracted from the records in a core proforma (common and standardized for all Indian PBCRs). Further, to avoid registering cases from a floating population, a cancer patient is accepted as belonging to a particular registry by verifying the area of living (for at least 1 year at the time of first cancer diagnosis) through personal interview with the patient/relative/attendant [30,31]. In accordance with IARC norms, the registry data undergo many quality checks (*viz.* range, unlikely, consistency, family checks) during data entry and subsequent phases (*viz.* duplicate removal for current and previous years, re-abstracting audit, evaluating diagnostic information by indicators like proportion of microscopically verified cases, etc.) [31]. Cases with possible errors are sent back for re-verification and the corrections received thereafter are updated [31].

The latest NCRP reports (released in March 2016) cover the 2012 to 2014 period. They provide data from 27 PBCRs and represent authoritative reports, collated following uniform data collection and quality control measures. They are available online in the public domain (http://www.ncdirindia.org/NCRP/ALL_NCRP_REPORTS/PBCR_REPORT_2012_2014/index.htm). The number of incident MM cases (code C90 under ICD-10) during 2012-14 was extracted from each PBCR annexure report in an age-wise (grouped under age categories: 0–4 yrs, 5–9 yrs, 10–14 yrs, 15–19 yrs, 20–24 yrs, 25–29 yrs, 30–34 yrs, 35–39 yrs, 40–44 yrs, 45–49 yrs, 50–54 yrs, 55–59 yrs, 60–64 yrs, 65–69 yrs, 70–74 yrs, 75+ yrs) and sex-wise manner for the current study. The area catered by each PBCR and their estimated population during that period were recorded [30] (shown in Supplementary material 1). Geo-politically, India is organized into six zones (*i.e.* Northern, Southern, Eastern, Western, Central, and Northeastern) vide Part-III of the States Reorganization Act (1956) and North Eastern Council Act (1971). Based upon the geographical location, the 27 PBCRs were grouped into one of these six zones for comparison.

2.2. Data analysis

The frequency distribution of MM in different zones and the relative contribution of MM to the overall cancer burden during 2012-14 were determined along with 95% confidence intervals (CIs).

The PBCR-wise crude rates (CRs) of MM incidence provided by the NCRP for 2012-14 were noted. The CR estimations were further extended to the national and zonal levels (with 95% CI). Besides, the age-specific rates (ASRs) of MM were determined in 10 year age-categories (*viz.* 0–9 yrs, 10–19 yrs, 20–29 yrs, 30–39 yrs, 40–49 yrs, 50–59 yrs, 60–69 yrs, and ≥70 yrs) so as to identify the decadal age group with the highest MM incidence. The ASR estimates were complemented by calculating the proportion of MM across these 10 yr age-categories. The proportion of MM in the young (age < 40 yrs) was also ascertained separately.

The CRs were adjusted for age to rule out variability owing to differences in age structure. These age-adjusted rates (AARs) were determined through direct age standardization [32] by employing the latest age- and sex-specific weights for Asian men and women, as proposed by the International Network for Demographic Evaluation of Populations and Their Health (INDEPTH) network for use in LMIC nations (including India) [33]. The corresponding 95% CI limits were estimated by Poisson approximation.

Moreover, age adjustments were carried out separately over the age ranges of 35–64 years (most vulnerable age for cancer in general), 50 years or above (since MM incidence is stated to rise particularly beyond the fifth decade), and less than 40 years (*i.e.* younger population) in order to calculate the truncated rates (TRs) of MM incidence, *i.e.* $TR_{35–65\ yrs}$, $TR_{\geq 50\ yrs}$, and $TR_{<40\ yrs}$, respectively. As mentioned above, INDEPTH suggested weights for the concerned age categories were used [33].

3. Results

3.1. Relative contribution of MM to cancer burden and MM distribution in India

During 2012-14, overall 161,363 incident cancer cases (males = 82026, females = 79,337) were documented in India under the 27 PBCRs of NCRP. Of these, 1916 were MM cases, consisting of 1123 males (58.6%) and 793 females (41.4%). Thus, MM accounted for 1.19% (95% CI: 1.14–1.24%) of all cancers in India [0.99% (95% CI: 0.93%–1.07%) in females and 1.36% (95% CI: 1.29–1.45%) in males]. The relative contribution of MM to the cancer burden in the various PBCRs and zones are presented in Supplementary materials 2A-2D.

The number of MM cases (sex-wise) in the individual PBCRs is listed in Supplementary materials 3 & 4. The Southern zone contributed to the highest proportion (44.9%) of MM cases, which together with the Northern (20.5%) and Western (19.4%) zones accounted for approximately 85% of the total MM cases (Supplementary material 5). The remaining 15% of the MM cases were from the Northeastern (9.6%), Eastern (3.5%) and Central (2.1%) zones. This pattern was reflected in both the sexes (Table 1).

3.2. Crude MM incidence in India

The CRs for MM incidence in India were 1.27 (95% CI: 1.20–1.35) per 100,000 in men and 0.95 (95% CI: 0.89–1.02) per 100,000 in women. It ranged from 0 to 4.2 per 100,000 in men, and from 0 to 3.1 per 100,000 in women amongst the different PBCRs (Supplementary materials 6 A & 6B); and from 0.41 to 2.72 per 100,000 in men, and 0.32 to 2.05 per 100,000 in women amongst the different zones (Supplementary materials 6C & 6D).

3.3. Age and MM incidence in India

The ASRs of MM incidence in men and women for the different

Table 1
Distribution of male (N = 1123) and female (N = 793) multiple myeloma cases in PBCRs spread across different zones of India.

Zones	Male multiple myeloma cases (N = 1123)			Female multiple myeloma cases (N = 793)		
	n	%	95% CI	n	%	95% CI
North	239	21.3	18.9 - 23.8	154	19.4	16.8 - 22.3
South	485	43.2	40.3 - 46.1	376	47.4	43.9 - 50.9
East	46	4.1	3.1 - 5.4	21	2.7	1.7 - 4
West	224	19.9	17.7 - 22.4	148	18.7	16.1 - 21.5
Northeast	105	9.4	7.8 - 11.2	78	9.8	7.9 - 12.1
Central	24	2.1	1.4 - 3.2	16	2.0	1.3 - 3.3

Abbreviations: PBCR, population based cancer registry; CI, confidence interval.

Table 2
Age-specific incidence of multiple myeloma (per 100,000 population) in males among different age-groups in individual PBCRs of India.

PBCRs *(time period)*	Age-specific incidence rate (per 100,000 population) in different age-groups among males							
	0 - 9 yrs	10 - 19 yrs	20 - 29 yrs	30 - 39 yrs	40 - 49 yrs	50 - 59 yrs	60 - 69 yrs	≥ 70 yrs
Delhi *(2012)*	0	0	0.06	0.68	2.08	9.43	12.97	24.34
Patiala *(2012 - 2014)*	0	0	0	0.65	0.53	4.04	7.43	10.21
Bangalore *(2012)*	0	0	0	0.33	0.53	3.17	6.36	17.93
Chennai *(2012 - 2013)*	0	0	0	0.36	0.88	4.39	7.46	18.77
Thiruvananthapuram *(2012 - 2014)*	0	0	0.14	0.44	3.21	7.79	16.02	26.83
Kollam *(2012 - 2014)*	0	0	0	0.37	1.48	7.97	17.34	24.63
Kolkata *(2012)*	0	0	0	0	1.67	3.68	7.77	14.54
Ahmedabad (Urban) *(2012 - 2013)*	0	0	0	0.2	0.38	2.42	5.47	4.48
Mumbai *(2012)*	0	0	0	0	0.8	3.62	8.65	17.57
Pune *(2012 - 2013)*	0	0	0	0.3	0.63	1.64	4.46	7.8
Aurangabad *(2012 - 2014)*	0	0	0	0	0	4.93	1.18	3.99
Barshi (Rural) *(2012 - 2014)*	0	0	0	0	1.15	0	3.66	0
Barshi (Expanded) *(2012)*	0	0	0	0	0.85	0	0	0.87
Nagpur *(2012 - 2013)*	0	0	0	0.23	0	1.66	3.51	4.53
Wardha *(2012 - 2014)*	0	0	0.27	0.32	0.73	1.05	5.25	2.89
Kamrup (Urban) *(2012 - 2014)*	0	0	0	0	0	4.07	14.93	22.69
Dibrugarh *(2012 - 2014)*	0	0.24	0	0	0.38	2.4	6.44	7.51
Cachar *(2012 - 2014)*	0	0	0	0	0.31	0.49	0.81	4.07
Manipur *(2012 - 2014)*	0	0.1	0.11	0.3	0.96	2.29	2.57	3.13
Meghalaya *(2012 - 2014)*	0	0	0	0	0	0	1.3	0
Mizoram *(2012 - 2014)*	0	0	0	0	0	0.8	1.52	4.46
Nagaland *(2012 - 2014)*	0	0	0	0	0	0	0	0
Naharlagun *(2012 - 2014)*	0	0	0	0	0	0	0	0
Pasighat *(2012 - 2014)*	0	0	0	0	0	0	0	0
Tripura *(2012 - 2014)*	0	0.09	0	0.22	0.41	0.62	2.21	3.95
Sikkim *(2012 - 2014)*	0	0	0	0	0	0	0	0
Bhopal *(2012 - 2013)*	0	0	0.23	0.62	0.78	5.31	7.42	6.55

Abbreviations: PBCR, population based cancer registry.

Table 3
Age-specific incidence of multiple myeloma (per 100,000 population) in females among different age-groups in individual PBCRs of India.

PBCRs *(time period)*	Age-specific incidence rate (per 100,000 population) in different age-groups among females							
	0 - 9 yrs	10 - 19 yrs	20 - 29 yrs	30 - 39 yrs	40 - 49 yrs	50 - 59 yrs	60 - 69 yrs	≥ 70 yrs
Delhi *(2012)*	0.15	0.07	0	0.3	2.1	6.43	9.69	12.74
Patiala *(2012 - 2014)*	0	0	0	0.23	1.64	2.99	3.14	5.31
Bangalore *(2012)*	0	0	0.1	0	1.23	5.2	13.31	4.68
Chennai *(2012 - 2013)*	0	0.15	0	0.12	1.21	4.68	4.16	5.88
Thiruvananthapuram *(2012 - 2014)*	0	0.13	0	0.87	1.72	6.01	10.42	8.96
Kollam *(2012 - 2014)*	0	0.34	0	0.74	1.96	5.78	14.54	11.7
Kolkata *(2012)*	0.41	0	0	0.53	0	2.63	4.71	4.43
Ahmedabad (Urban) *(2012 - 2013)*	0	0	0	0.11	0.67	2.89	2.07	4.54
Mumbai *(2012)*	0	0	0.09	0.1	0.65	1.14	8.4	9.61
Pune *(2012 - 2013)*	0	0	0.09	0	0.51	2.74	1.94	2.44
Aurangabad *(2012 - 2014)*	0	0	0	0	0.48	1.63	0	0
Barshi (Rural) *(2012 - 2014)*	0	0	0	0	0	0	1.62	4.71
Barshi (Expanded) *(2012)*	0	0	0	0	0	0.66	1.11	0
Nagpur *(2012 - 2013)*	0	0	0	0	0.57	1.38	0.68	0
Wardha *(2012 - 2014)*	0	0	0	0	0.78	2.4	1.32	1.94
Kamrup (Urban) *(2012 - 2014)*	0	0	0	0.25	1.28	3.27	6.8	2.64
Dibrugarh *(2012 - 2014)*	0.29	0	0	0	0.4	2.74	4.42	6.04
Cachar *(2012 - 2014)*	0	0	0	0	0	1.11	1.72	0
Manipur *(2012 - 2014)*	0	0	0	0.15	0.39	1.74	3.14	2.24
Meghalaya *(2012 - 2014)*	0	0	0	0	0.39	0.7	0	1.52
Mizoram *(2012 - 2014)*	0	0	0	0	0	0	0	2.19
Nagaland *(2012 - 2014)*	0	0	0.45	0.62	0	0	0	0
Naharlagun *(2012 - 2014)*	0	0	0	0	0	0	0	6.46
Pasighat *(2012 - 2014)*	0	0	0	0	0	0	0	0
Tripura *(2012 - 2014)*	0	0.19	0.18	0.12	0.14	1.4	1.9	0
Sikkim *(2012 - 2014)*	0	0	0	0	2.09	0	5.63	4.16
Bhopal *(2012 - 2013)*	0	0	0	0	1.75	3.79	3.23	6.63

Abbreviations: PBCR, population based cancer registry.

PBCRs are presented in Tables 2 and 3 respectively. At the national level and considering both sexes together, it was observed that the ASR values for MM incidence tended to increase steadily with advancing age (Supplementary material 7A). It was comparable in the age-groups 0–9 yrs, 10–19 yrs, and 20–29 yrs. Thereafter, a significant upward trend in ASR values was seen through each decadal age-category ($\chi^2 = 2456.5$, $df = 4$, $P < 0.0001$ and $\chi^2_{\text{trend}} = 2328.7$, $df = 1$, $P < 0.0001$), starting from 30 to 39 yrs to 70 ys and beyond. However, a sub-group analysis

Table 4
Young multiple myeloma (i.e. age < 40 years) cases across different zones of India.

Zones	Male				Female				Both sexes			
	Total MM cases	Young MM cases (< 40 yrs)			Total MM cases	Young MM cases (< 40 yrs)			Total MM cases	Young MM cases (< 40 yrs)		
		n	%	95% CI		n	%	95% CI		n	%	95% CI
North	239	14	5.9	3.5 - 9.6	154	8	5.2	2.7 - 9.9	393	22	5.6	3.7 - 8.3
South	485	12	2.5	1.4 - 4.3	376	18	4.8	3.1 - 7.4	861	30	3.5	2.5 - 4.9
East	46	0	–	–	21	3	14.3	5 - 34.6	67	3	4.5	1.5 - 12.4
West	224	8	3.6	1.8 - 6.9	148	4	2.7	1.1 - 6.7	372	12	3.2	1.9 - 5.6
Northeast	105	8	7.6	3.9 - 14.3	78	10	12.8	7.1 - 22	183	18	9.8	6.3 - 15
Central	24	3	12.5	4.3 - 31	16	0	–	–	40	3	7.5	2.6 - 19.9
National (all zones together)	1123	45	4	3 - 5.3	793	43	5.4	4.1 - 7.2	1916	88	4.6	3.7 - 5.6

Abbreviations: MM, multiple myeloma; n number of cases; CI, confidence interval.

revealed that, in women (except in those from Western and Northern zones), the ASRs decreased after 70 yrs (Supplementary material 7B).

Supplementary materials 3 & 4 show the count and frequency of MM cases across 10 yr age-categories in different PBCRs. Altogether, majority of the newly diagnosed MM cases (31.1%, 95% CI: 29.1–33.2%) in India belonged to the 60–69 yrs age group (Supplementary material 8 A). However, zonal and sex-wise variations were present (Supplementary materials 8B & 8C). Further, 4.6% (95% CI: 3.7–5.6%) of the total MM cases throughout India were diagnosed in the young people (age < 40 yrs) (Table 4). This included 88 individuals (45 males and 43 females). The proportion of young MM cases was highest in the Northeastern zone and least in the Western zone.

3.4. Age-adjusted MM incidence in India

Collectively, AAR values for India were 1.13 (95% CI: 1.07–1.20) per 100,000 in men, and 0.81 (95% CI: 0.75-0.88) per 100,000 in women. Regional variations in AAR estimates were noticed across the six zones (Table 5). The Southern and the Northern zones had remarkably higher, while the Northeastern and the Western zones had remarkably lower AAR values as compared to the national value. The AARs of individual PBCRs are displayed in Supplementary materials 9A & 9B.

3.5. Truncated MM incidence in India

The TRs for the individual PBCRs are listed in Supplementary material 10. Amongst the various zones, the Southern zone had the highest $TR_{35–64\ yrs}$ in women, the highest $TR_{<40\ yrs}$ in women, and the highest $TR_{\geq 50\ yrs}$ in both men and women (Table 6). In contrast, the highest $TR_{35–64\ yrs}$ and $TR_{<40\ yrs}$ estimates in men were noticed in the Northern and the Central zones, respectively. On the other hand, the $TR_{35–64\ yrs}$, the $TR_{<40\ yrs}$, and the $TR_{\geq 50\ yrs}$ estimates at a national level in men and women were found to be 2.18 (95% CI: 1.99–2.35) and 1.87 (95% CI: 1.71–2.04) per 100,000, 0.05 (95% CI: 0.04-0.07) and 0.06 (95% CI: 0.04-0.08) per 100,000, and 6.84 (95% CI: 6.41–7.27) and 4.49 (95% CI: 4.14–4.83) per 100,000, respectively.

Table 5
Age adjusted incidence rate (per 100,000 population) of multiple myeloma in males and females across India during 2012-14.

Zones	Male		Female	
	AAR	95% CI	AAR	95% CI
National (all zones together)	1.13	1.07 – 1.20	0.81	0.75 – 0.88
Zonal				
North	1.94	1.87 – 2.01	1.35	1.28 – 1.41
South	1.93	1.86 – 1.99	1.40	1.33 – 1.47
East	1.24	1.17 – 1.30	0.71	0.64 – 0.78
West	0.69	0.62 – 0.76	0.47	0.40 – 0.53
Northeast	0.46	0.39 – 0.52	0.34	0.27 – 0.40
Central	1.10	1.03 – 1.17	0.82	0.75 – 0.88

Abbreviations: AAR, age-adjusted rate; CI, confidence interval.

Table 6
Truncated incidence rate (per 100,000 population) of multiple myeloma in different zones of India.

Zones	Truncated rate (TR)					
	$TR_{(35 - 64\ yrs)}$		$TR_{(< 40\ yrs)}$		$TR_{(\geq 50\ yrs)}$	
	Male	Female	Male	Female	Male	Female
North	4.22	2.94	0.11	0.1	11.52	7.2
South	3.49	3.2	0.07	0.12	11.77	7.76
East	2.08	1.33	–	0.2	7.35	3.72
West	1.41	1.11	0.03	0.02	4.19	2.67
Northeast	0.77	0.86	0.04	0.05	2.68	1.77
Central	2.58	2.14	0.14	–	6.25	4.28
National (all zones together)	2.18	1.87	0.05	0.06	6.84	4.49

4. Discussion

According to GLOBOCAN estimates, the worldwide age-adjusted incidence for MM in 2012 were 1.7 per 100,000 in men and 1.2 per 100,000 in women [4]. These rates varied between 0.4 and nearly 5 per 100,000 among different world regions. As opposed to the overall global rates, the PBCR-based age-adjusted MM rates in India in the 2012-14 period as derived in the current study [*i.e.* 1.13 (95% CI: 1.07–1.20) per 100,000 in men, and 0.81 (95% CI: 0.75-0.88) per 100,000 in women] were relatively low. But, these estimates suggest that MM incidence in India was higher than the Asian average (1 per 100,000 in men, and 0.7 per 100,000 in women), although significant differences were observed across different regions of the continent. For instance, these AARs for India were substantially higher than the GLOBOCAN AAR estimates for Eastern Asia (1 per 100,000 in men, and 0.6 per 100,000 in women) and Southeastern Asia (0.9 per 100,000 in men, and 0.8 per 100,000 in women), but lower than those for Western Asia (2.3 per 100,000 in men, and 1.7 per 100,000 in women). Although the MM incidence in Asia is relatively low than that in Europe (3.2 per 100,000 in men, and 2.1 per 100,000 in women), the Americas (3.1 per 100,000 in men, and 2.2 per 100,000 in women) and Oceania (4.2 per 100,000 in men, and 2.7 per 100,000 in women) [4], yet some Asian nations like South Korea and Taiwan have experienced a rapid surge in MM incidence recently – with industrialization, improved MM case detection and aging suspected to be the contributory factors [10,12,34]. India is the second most populous country in the world. And in view of the enhanced life expectancy, improved health care services and standards of living, and rapid urbanization that India is

currently undergoing, increased rates of MM may be expected in the future.

From the current work, it is evident that MM incidence in India exhibits considerable variation across sex, age and geographical regions of the country. A male preponderance was noticed. The MM rates (both crude and age-adjusted) in men exceeded those in women (at zonal as well as national levels), which concurs with reports from other world regions [12,35,36]. With respect to age, some hospital-based studies have previously reported a lower age of MM onset in Indian patients (median: ~55 years) [13,15,16,18,19,37]. This is nearly a decade earlier than that in the USA (median: ~67 yrs in Blacks, ~66 yrs in Hispanics, and ~71 yrs in Whites) [16,36,37]. The reported median MM onset age of around 55 years in Indians is also quite early than that in other Asian patients, *viz.* Thai (59 yrs), Chinese (59 yrs), Koreans (61 yrs), Singaporean (62 yrs), Taiwanese (63 yrs), Hong Kongese (65 years) and Japanese (66 yrs) [34], and patients from Latin America (61 yrs) [38] and Africa (62 yrs) [39]. However, the current study found that most MM patients from India overall were aged between 60 and 69 yrs at the time of diagnosis. Exceptions to this trend were seen in the Northern and Central zones where 50–59 yrs was the most common age category for MM detection, and also in the Eastern zone where the majority of the new MM patients were aged 70 yrs or older. In addition to these variations, stark differences in age-adjusted incidence existed across the different zones of India. For example, the AARs for the Northern and Southern zones were at par or higher than the global average, whereas the AAR for the Northeastern zone matched those for world regions with the lowest AAR values.

This remarkable heterogeneity in MM incidence across different zones of India may be due to the differences in environmental and lifestyle factors. This may partly explain the lesser incidence of MM in the remote Northeastern zone as compared to the MM incidence in the PBCRs located in the relatively more industrial and developed Northern and Southern zones. Urban areas are usually associated with greater environmental and occupational exposure to air pollutants, chemical carcinogens and ionizing radiation and also with lifestyle factors (*viz.* Westernized diet and greater presence of overweight/ obesity) that are known to predispose to MM [10,12,34,40–44]. Further, quality of health care resources may affect myeloma diagnosis. In general, MM incidence in urban/metropolitan areas is higher than that in rural areas [45,46]. Since MM is a rare disease and its diagnosis is lab-intensive requiring sensitive investigations, hence it may be under-reported if the available healthcare facilities for myeloma detection are inadequate. Urban and industrialized areas with better health facilities are more likely to have improved myeloma detection than their rural and less developed counterparts; and this may partly account for the higher incidence of myeloma in urban localities. In general, the healthcare resources in northeast India are modest as compared to other parts of the country [47]. However, it deserves mention that the states in the Northeastern zone otherwise have a very high burden of overall cancer in general. In fact, unlike for MM, the highest AAR values for cancer in general for both males and females in India are reported from PBCRs of the Northeastern zone (Aizawl district under Mizoram PBCR for males, Papumpare district under Naharlagun PBCR for females) [30]. In addition to environmental factors, genetic susceptibility to MM is suggested to vary by the racial background [6–9,11]. The Indian population is heterogeneous and multiracial with diverse ethnic affiliations. Thus, it is plausible that both genetic and environmental factors are collectively responsible for the heterogeneity in MM incidence noticed among the different zones in India. The urban versus rural disparities in MM incidence in India could not be explored in details in the current analyses. That was because most PBCRs in the country (listed in Supplementary material 1) cater to populations from entire state or district (s), *i.e.* both rural and urban areas fall under the geographical area of the PBCR. Cancer data from the rural and the urban areas under such PBCRs are not provided separately in the NCRP reports [30]. Only the Barshi (rural) registry covered an exclusively rural population in the 2012-14 period, where the crude and age-adjusted MM rates in men as well as women were considerably lower than those in the exclusively urban registries [namely: Chennai, Delhi, Bangalore, Ahmedabad (urban), Kolkata, Kamrup (urban), Mumbai, Pune, Nagpur, Aurangabad, and Bhopal].

The major strength of the study is the use of reliable population based data from a well validated registry program representing different parts of India which enabled a nation-wide snapshot of MM incidence profile. A possible limitation is the < 10% coverage of the total population of India by these 27 PBCRs. Nonetheless, these PBCRs constitute the only source of authentic population based cancer incidence data in India. As these registries represent various parts of the country, they portray India's cancer profile fairly well. The cancer registry data from India were classified as high quality by GLOBOCAN standards [4].

5. Conclusion

The current study catalogues the distribution of MM in India. Population based incidence of MM in India across age, sex and geography is presented. The heterogeneities in MM incidence recorded within the country may provide insights into myeloma etiologies and epidemiological trends for India in the future. The information generated would be useful in concerting and prioritizing the myeloma control efforts in the country in a more focused and streamlined manner depending upon the specific regional/ national scenario.

Author contributions

KB carried out conception of the study, data management, data analysis and interpretation, and manuscript writing.

Conflict of interest

The author declares no conflict of interests, financial or otherwise.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2019.02.010.

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