Real World Multiple Myeloma Registry from Jordan, a Developing Country

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Abstract. Background and objective: Scanty reports from the middle east and north Africa (MENA) region have been published on multiple myeloma (MM). Multiple myeloma registry has been established at Jordan University Hospital (JUH) since 2009. Our work aims to review this Multiple Myeloma registry with data from 113 patients diagnosed with MM at JUH and analyze their management and course.

Methods: This is a non-interventional and retrospective analysis of the MM registry from 2009-to 2016 involving 113 patients at JUH. Statistical analysis was done using the Statistical Package for the Social Sciences (SPSS). Overall survival (OS) was analyzed with the Kaplan-Meier method. P-value was considered significant if it was (<0.05).

Results: We found no gender difference in this registry. The median age is 62 years. Most patients are in ISS stage II and III (36.28% for each). Immunoglobulin type G Kappa is the dominant subtype. Bone pain is the most common presenting symptom. The most common laboratory finding is anemia (45.6%). Most of our patients (85.2%) had received thalidomide and dexamethasone, while only 14.8% received bortezomib, thalidomide, and dexamethasone. Our patients' mean overall survival (OS) was 74 months, and the median survival was 38 months. For ISS stages I, II, and III, median OS was 96, 46, and 16 months.

Conclusion: MM in a developing country presents a challenging disease compared to industrial countries in both epidemiology and management. An improved road map in the care of MM in these countries is needed. The use of three or four drugs combination upfront is warranted. However, this is limited because of the high cost of these drugs. We expect the following decade to show better survival and quality of life for MM patients once these drugs are widely used.

Keywords: Multiple myeloma; Survival; Treatment; Thalidomide; Bortezomib.

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Introduction. Multiple myeloma accounts for 13-15% of all hematological malignancies, the second most common after non-Hodgkin lymphoma.1 It is usually a disease of older people, and its incidence is variable by geographic area, being most common in developed countries where the incidence is increasing with age.
USA data show that it is more frequent in males and black people. In industrial countries, the median patient’s age at diagnosis is approximately 66–70 years old, with 37% of patients younger than 65 years of age. Symptomatic multiple myeloma is associated with significant morbidity and mortality, especially with end-organ failure.

There have been significant improvements in treating multiple myeloma in the last few years. The introduction of autologous hematopoietic stem cell transplantation has positively impacted overall survival. In addition, novel agents such as proteasome inhibitors, immunomodulatory drugs, monoclonal antibodies, and CAR-T cells are changing the history of the disease, producing higher progression-free survival and overall survival. However, these new drugs are very expensive, and a cost/benefit balance is advisable.

Few studies have been published from developing countries describing the epidemiology of the disease, with very scanty reports from the middle east and north Africa (MENA) region. Since the population in the MENA region is expected to have a more aging population in the coming decades, the incidence is expected to increase, as shown in a recent publication from Lebanon. We are not aware of any published work on a large cohort of patients with multiple myeloma from Jordan.

The aim of this study is to review the department registry of multiple myeloma patients at Jordan University Hospital (JUH), which is representative of the whole country, over eight years with patient characteristics and disease patterns, survival, and therapy used in a real-world experience.

**Methods.** Patients. This non-interventional, single-center, retrospective study analyzes the registry of patients with newly diagnosed multiple myeloma (MM) between 01/2009 and the end of 2016.

A total of 128 patients were reviewed, representing (27.6%) of all MM patients in the country during the study period, estimated to be around 464 patients as reported by the Jordanian National cancer registry. The registry captures data prospectively. The data include patients' particulars, medical history, and diagnostic tests, including imaging tests, stage, pathology, laboratory findings, follow-up, therapy, and cytogenetics. As for the imaging tests, an x-ray of the skull and skeletal survey of the long bones and spine were done. In selected patients and in those not showing abnormal findings on x-ray images, MRI images of the spine or the suspected affected area were done. In some patients, PET scans were carried out. No patient had a low dose whole body ct scan.

Patients who entered the registry between the beginning of 2009 and the end of 2016 are the subject of this report.

This study was approved by the Institutional Review Board committee of the Cell Therapy Center and JUH, Amman, Jordan. Written informed consent that adhered to the declaration of Helsinki was obtained from all participants. The patient must be 18 years old or older.

Diagnosis of multiple myeloma, staging, and risk classification were made in accordance with ESMO guidelines.

As for the treatment, only two different reimbursable regimens were used as first-line; a combination of dexamethasone and thalidomide (DT), which was dominantly used in the first few years of the registry, and a combination of Bortezomib (Velcade), dexamethasone and thalidomide (VDT) which was used during the later years of the registry or for patients considered candidates for single autologous bone marrow transplantation (ABMT) with high dose melphalan (180mg/m²). If the patient progressed or failed first-line therapy, the reimbursed drugs were dexamethasone with melphalan or drug alone with or without palliative radiation. Subjects who had autologous bone marrow transplantation were given monthly bortezomib post-ABMT maintenance for one year. If they relapse, there was no specific reimbursable combination. Renal insufficiency was defined as per ESMO guidelines in the CRAB criteria (serum creatinine >177μmol/L (>2mg/dL).

The Statistical analysis was done using the Statistical Package for the Social Sciences (SPSS). Overall survival (OS) was analyzed with the Kaplan-Meier method. P-value was considered significant if it was <0.05.

**Results.** One hundred twenty-eight patients with MM were diagnosed and treated between 2009 and 2016 at JUH. Demographic and laboratory data are shown in table 1. The mean age was 63.3 years. Again, the distribution of ages was found to be equal in both genders, with 50% of each gender. Regarding the presenting symptomatology and findings, 61.1% complained of bone pain, with 70.5% of patients having lytic bone lesions on x-ray imaging or MRI imaging. 45.6% had symptoms of anemia, and 20% had renal insufficiency as defined by ESMO guidelines (serum creatinine >177 μmol/L (> 2 mg/dL). Concerning the immunoglobulin subtypes of multiple myeloma in the entire population, 79.1% of the patients had the IgG monoclonal band, of which 79.2% had IgG Kappa myeloma, and 20.8% had IgG lambda myeloma 13.9% of the patients had the IgA monoclonal band, of which 56.25% had IgA kappa myeloma, and 43.75% had IgA lambda myeloma. In addition, 7% of the patients had light chain myeloma. As for the ISS stage, 27.4% were stage I, 36.28% were stage II, and 36.28 were stage III. The mean and median survival for each type is shown in table 2. Survival analysis of the non-transplant population (113) patients was as follows: Median overall survival (95%
Table 1. Demographic and laboratory data of all the patients with multiple myeloma.

| Gender        | Percentage |
|---------------|------------|
| Male          | 64 (50%)   |
| Female        | 64 (50%)   |

| Age groups | Percentage |
|------------|------------|
| < 65       | 75 (58.6%) |
| ≥ 65       | 53 (41.4%) |
| Mean       | 61.3       |
| Median     | 55.3       |

| Duration of follow up | Percentage |
|-----------------------|------------|
| Mean follow up (months) | 36.8 ± 3.44 |
| Median follow up (months) | 32          |

| Presenting symptomatology* | Percentage |
|----------------------------|------------|
| Lytic lesions              | 73.5%      |
| Bone pain                  | 64.1%      |
| Anemia                     | 48.6%      |
| Renal insufficiency +      | 19%        |
| Hypercalcemia              | 12.6%      |
| Bleeding                   | 6.6%       |
| Others                     | 7.6%       |

| ISS score at diagnosis**   | Percentage |
|----------------------------|------------|
| Stage I                    | 31 (24.2%) |
| Stage II                   | 44 (34.38%)|
| Stage III                  | 53 (41.4%) |

| Disease characteristics by Immunoglobulin electrophoresis: | Percentage |
|------------------------------------------------------------|------------|
| IgG                                                        | 79.7%      |
| IgG Kappa                                                  | 79.2%      |
| IgG Lambda                                                 | 20.8%      |
| IgA                                                        | 12.5%      |
| IgA Kappa                                                  | 56.25%     |
| IgA Lambda                                                 | 43.75%     |
| Light chain                                                | 7.8%       |
| Treatment ++: DT VTD                                       | 75%        |
| VTD                                                        | 25%        |

* Some of the symptoms may overlap. DT Dexamethasone and thalidomide. VDT: Bortezomib (Velcade), Dexta and Thalidomide. ** as per ESMO guidelines. + serum creatinine > 177 μmol/L (> 2 mg/dL). ++ this treatment applies to non-transplant population. For abmt population, see text.

confidence interval [CI]) was 38.00 months (Range: 23.133-52.867). Stage I had a median survival of 96 months. Stage II had a median survival of 46 months and stage III had a median survival of 16 months (Table 2). Figure 1 demonstrates the survival difference between the ISS stage and the different immunoglobulin types of myelomas. There was a statistical significance concerning ISS stages (p < 0.05). However, the survival difference between the types of myelomas was statistically insignificant (p>0.05), as shown in table 2. Figure 1 demonstrates the survival difference between treatment regimens used. The survival analysis was not statistically significant (p > 0.05) (Table 2). Survival curves are shown in figures 1 and 2. As for the overall survival (OS) and progression-free survival (PFS) in the ABMT population, details are shown in figure 2.

Discussion. Our study involves 128 Multiple Myeloma patients who were followed at the Hematology department of JUH and was the first conducted in Jordan. The yearly number of new myeloma cases in Jordan was 58 cases per year during the registry period. During the period 2009 to 2016, it is estimated that 464 new cases were diagnosed with myeloma in the whole
Table 2. Mean and Median for Survival Time in months as per ISS stage, type of paraprotein and therapy.

| ISS        | Mean | Median | 95% Confidence Interval | Mean | Median |
|------------|------|--------|-------------------------|------|--------|
|            | Estimate | Std. Error | Lower Bound | Upper Bound | Estimate | Std. Error | Lower Bound | Upper Bound |
| Stage I    | 112.260 | 17.597 | 77.769 | 146.751 | 96.000 | 26.354 |
| Stage II   | 78.179 | 13.288 | 52.134 | 104.224 | 46.000 | 18.990 |
| stage III  | 30.291 | 7.586  | 15.422 | 45.160  | 16.000 | 4.210  |
| Overall    | 74.169 | 8.864  | 56.795 | 91.543  | 38.000 | 7.585  |

| Treatment | Mean | Median | 95% Confidence Interval | Mean | Median |
|-----------|------|--------|-------------------------|------|--------|
| DT        | 95.144 | 16.657 | 62.496 | 127.792 | 107.000 | 18.788 |
| DT        | 66.748 | 9.321  | 48.480 | 85.017  | 38.000 | 2.832  |
| Overall   | 72.557 | 8.620  | 55.662 | 89.451  | 41.000 | 8.123  |

| Types | Mean | Median | 95% Confidence Interval | Mean | Median |
|-------|------|--------|-------------------------|------|--------|
| IgG   | 63.992 | 8.606  | 47.124 | 80.859  | 36.000 | 4.234  |
| IgA   | 55.882 | 15.225 | 26.041 | 85.723  | 33.000 | 7.318  |
| Overall | 63.969 | 7.721  | 48.836 | 79.102  | 36.000 | 1.927  |

DT: Dexamethasone and Thalidomide. VTD: Bortezomib (velcade), Dexamethasone and thalidomide.

Figure 1. Survival as per stage and the abnormal IgG and IgA paraprotein detected.

Figure 2. Survival (months) as per drug combination used.

country. With 128 cases in our registry during the same period, it seems that it captured (27.6%) of all myeloma cases in Jordan, which makes it very representative of the disease in the country. There was no difference in gender distribution, as found in the Jordan cancer registry in 2012. The gender distribution is similar to that reported from Latin America but was significantly different from Iran. The median age of our patients was 55.3, and the mean age ± SD was 61.30±10.8, which is comparable to the Iranian study's mean age ± SD of 61.98±11.44 years. Other studies from the MENA region showed an even younger median age, such as the study from Algeria that showed a median age of 53 years. The age of our patients is not close to the age of 66 years reported by the Mayo clinic series. We found out that 58.6% of our patients were younger than 65 years, comparable to the Iranian study. In contrast, a Swedish study showed that 72% of their patients were older than 65 years. In a real-world study conducted in Europe, the Middle East, and Africa, 75% of patients were older than 65. The most common presenting symptom in our patients was bone pain (61.1%), similarly to the studies from Belgium, France, Germany, Italy, Spain, Switzerland, and the UK, as well as the study reported from Beijing/China. However, the registry did not capture skeletal-related events (SRE) in the disease course other than at presentation.

The prevalence of anemia during the disease is about 45.2% in our study, which is close to the prevalence reported in a recent registry study in the USA (45%). The Swedish study showed a comparable percentage of patients with anemia (49%).
The prevalence of renal dysfunction as defined by ESMO guidelines in our study was 20%, similar to that reported in European countries (20%) and in the Swedish study (18%). The Iran study reported that 33.8% of their patients had a creatinine higher than 2.

Hypercalcemia was seen in 11.6% of our patients, similar to that reported in the Mayo clinic and the Swedish studies, 13% in both. Hypercalcemia was slightly higher in the European countries study, which was reported in 19% of patients.

73.5% of our patients had osteolytic lesions by imaging (shown in table 1), comparable to the Swedish study (77%).

Figures 3 and 4 show the mean overall survival (OS) and progression-free survival in transplant patients, which was not reached during the follow-up period.

We noticed certain important findings when comparing survival results in this study with other reported studies.

For ISS stages I, II, and III, median OS were 96, 46, and 16 months, respectively. Comparing this with the RS (rescaled range) in the Swedish study, it shows a similar median survival for ISS stage I, which was 8.2 years, and lower median survival for stage II and III; 5.6 and 3.2 years, respectively.

Since most of our patients represent a typical Jordanian population in which most people are working class, lower and middle-income class, it may be possible that the poor outcome might be explained, in part, by the poor economic status of these patients. Socioeconomic status is reported to be a prognostic factor for the overall survival of multiple myeloma patients, as shown in recent publications. In the Middle East and North Africa, extreme poverty rates nearly doubled between 2015 and 2018, from 3.8% to 7.2%, according to the world bank report 2020.

Based on new data, on July 1, 2017, the World Bank classified Jordan as a lower-middle-income country. Given all these socioeconomic factors in the middle east, it is only expected to find lower survival related to multiple myeloma compared to European or industrial countries.

Since most Jordanians are ethnic Arabs, the ethnicity probably does not play a role in our study despite being reported in other countries to be of importance. Most of our patients at the time of diagnosis had ISS stage II (34.38%) and stage III (41.4%), and only 24.2% with stage I. The fact that the patients present in the advanced stage indicates a lack of proper awareness and patient education.

A study from South Korea reported that 48.8% of Multiple Myeloma patients were ISS stage II and 40.2% were ISS stage III, while only 11% were stage I. In the Swedish study, 44% of the patients were reported to be at ISS stage II at diagnosis and 33% at stage III. These findings suggest that patients in Jordan and internationally have significant MM-related organ damage at diagnosis, so initiatives facilitating earlier diagnosis are warranted.

VDT (Bortezomib, Dexamethasone, Thalidomide) was used in 14.8% of our patients, DT (Dexamethasone and Thalidomide) in 85.2%. The mean survival time for each regimen was: 95 and 66 months, respectively. Unfortunately, our institution at the time of the study did not have the approval to reimburse bortezomib until late in the registry; hence VDT was not widely used. As for the types of proteins secreted by the malignant plasma cells, the most common type was IgG (79.1%), of which 79.2% had IgG Kappa myeloma, and 20.8% had IgG lambda myeloma. 13.9% of our patients had IgA with equal IgA Kappa and Lambda distribution. Only a small number of patients (7%) had light-chain myeloma.

In our study, the mean survival time for IgG, IgA, and light chain myeloma was 64 months, 56 months, and 34 months. Mean survival for myeloma Lambda light
chains (for IgA and IgG combined) was 73 months, while for Kappa light chains (for IgA and IgG combined) was 58 months.

We believe that reporting our findings will help revisit the management pathways of multiple myeloma in a developing country with limited financial resources. We realize the lack of cytogenetic and molecular data because of non-availability at our institution. Since 2016, we have access to cytogenetics and more recent access to newer agents such as ad lenalidomide, carfilzomib, and daratumumab. However, we still have no access to CAR-T cells.

We need to bridge gaps with institutions in the industrial world to help the patients with mm. Therefore, we welcome establishing more organized collaboration and participation in clinical trials and studies with these institutions.

We believe the decade from 2017 to 2027 will show far better molecular, cytogenetic data and better survival rates.

References:

1. Palumbo A, Anderson K. Multiple myeloma. N Engl J Med. 2011 Mar 17;364(11):1046-60. doi: 10.1056/NEJMra1011442. PMID: 21410373

2. Kazandjian D. Multiple myeloma epidemiology and survival, and a unique malignancy. Semin Oncol. 2016; 43(6): 676-681. https://doi.org/10.1053/j.seminoncol.2016.11.10

3. Becker N. Epidemiology of multiple myeloma. Recent Results Cancer Res. 2011;183: 25-35. https://doi.org/10.1007/978-3-540-85772-3_2

4. Marchetti L, Galle R.P., Barosi G. Cost-effectiveness of post-autotransplant lenalidomide in persons with multiple myeloma. Mediterr J Hematol Infect Dis 2021, 13(1): e2021034.

5. Hungria VT, Masiolo A, Martinez G, Duarte GA, Bittencourt R, Peters L, Colleoni G, Oliveira LC, Crosetto E, Coelho EO, Pasquinii R, Magalhães SM, Nunes R, Neto JV, Faria RM, Souza M, Hammerschlag N, Flantl D, Navarro JR, Conte G, Gomez-Almaguer D, Ruiz-Aguilera G, Durie BG; International Myeloma Working Group Latin America. Observational study of multiple myeloma in Latin America. Ann Hematol. 2017 Jan;96(1):65-72. doi: 10.1007/s00277-016-2866-9. Epub 2016 Nov 5. PMID:27815724

6. Nnonyenun OH, Anaozeze MJ, Eunice NO, Emmanuel OO, Stella AT, Marcus Al, Taiwo BM, Oufela KO, Chinawaee AJ, Orduma JA, Dalhat GG, Otobo UI. Multiple myeloma in Nigeria: a multi-centre epidemiological and biomedical study. Pan Afr Med J. 2015 Nov 24;22:292. doi: 10.11604/pamj.2015.22.292.7774. https://doi.org/10.11604/pamj.2015.22.292.7774

PMID:29696488 PMCid:PMC4769058

7. Sadia S, Syed M, Saira P, Ali H, Basharat M, Multiple Myeloma: a Retrospective Analysis of 61 Patients from a Tertiary Care Center. Asian Pac J Cancer Prev, 2016; 17 (4), 1833-1835. https://doi.org/10.7314/APJCP.2016.17.4.1833

PMID:27221861

8. Jalaeikhoo H, Shariatfazeh M, Rajaiinejad M, Keyhani M, Zokasadi M. Retrospective Analysis of 345 Multiple Myeloma Cases: An Inves}

PMID:29385907

9. El Husseiny NM, Kasem N, El Azeem HA, Mattar MW. Multiple myeloma: a descriptive study of 217 Egyptian patients. Ann Hematol. 2014;93(1):141-5. https://doi.org/10.1007/s00277-013-1849-3

PMID:23892925

10. Mohammad L, Harir N, Braimi M, Moulessehoul S, Bekdak MA. Epidemiological, clinical and prognostic aspects of multiple myeloma eligible for therapeutic intensification followed by autologous hematopoietic stem cell in the Algerian West: report of 147 cases. Tunis Med. 2017 Jun;95(6):415-421.

PMID:2856354

11. Al-Sayaineh, Ayoub & Nimri, Omar & Arquob, Kamal & Al-Zaghhl, Marwan & Halasa, Wafa. (2016). Cancer Incidence In Jordan - 2012. https://doi.org/10.13140/RG.2.1.1251.6246

12. Moreau, J. San Miguel, P. Sonneveld, V. M. Mateos, E. Zamagni, H. Aret-Loiseau, R. Hajek, M. A. Dimopoulos, H. Ludwig, H. Einsele, S. Weeke, T. Facon, M. Cavo, E. Terpos, H. Goldschmidt, M. Attal & C. Buske. Multiple Myeloma: ESMO Clinical Practice Guidelines Ann Oncol (2017) 28 (suppl 4); iv52-iv61. https://doi.org/10.1093/annonc/mdx096

PMID:28453614

13. Kyle RA, Gertz MA, Witzig TE, Lust JA, Lacy MQ, Dispenzieri A, Fonseca R, Rajkumar SV, Offidori JR, Larson DR, Plevak ME, Therneau TM, Grepp PR. Review of 1027 patients with newly diagnosed multiple myeloma. Mayo Clin Proc. 2003 Jan;78(1):21-33. doi: 10.4065/78.1.21. https://doi.org/10.1215/10665774-12528874

PMID:12528874

14. Blimark CH, Turesson I, Genell A, Alhberg L, Björkstrand B, Carlson K, Forberg K, Julious G, Linder O, Meeuwis UL, Nahi H, Kristinsson SY; Swedish Myeloma Registry. Outcome and survival of myeloma patients diagnosed 2008-2015. Real-world data on 4904 patients from the Swedish Myeloma Registry. Haematologica. 2018 Mar;103(3):506-513. doi: 10.3324/haematol.2017.178103. Epub 2017 Dec 7. https://doi.org/10.3324/haematol.2017.178103

PMID:29217784 PMcid:PMC5830385

15. Mohy M, Terpos E, Mateos MV, Cavo M, Leijnse S, Bekmam, Bekdak MA, Legiec W, Dimopoulos M, Stankovic S, Darun MS, De Stefano V, Corso A, Kochkareva Y, Laane E, Berthou C, Salvander, H, Masliak Z, Peclétinovas V, Willenbacher W, Silva J, Lous V, Nemet D, Borbély Z, Abadi U, Pedersen RS, Cernél P, Potamianou A, Couturier C, Feys C, Thoët-Bauchet F, Boccardo M, EMMSO Investigators. Multiple Myeloma Treatment in Real-world Clinical Practice: Results of a Prospective, Multinational, Noninterventional Study. Clin Lymphoma Myeloma Leuk. - 2018 Oct;18(10):e401-e419. doi: 10.1016/j.clml.2018.06.018. Epub 2018 Jun 25. https://doi.org/10.1016/j.clml.2018.06.018

PMID:30030333

16. Yong K, Delforge M, Driessen C, Fink L, Finloos A, Gonzalez-McQuire S, Safaer R, Karlin L, Mateos MV, Raab MS, Schoen P, Cavo M. Multiple myeloma: patient outcomes in real-world practice. Br J Haematol. 2016 Oct;175(2):252-264. doi: 10.1111/bjh.14213. Epub 2016 Jul 13. https://doi.org/10.1111/bjh.14213

PMID:27411022 PMCid:PMC5096152

17. Wang L, Jin FY, Li Y, Sun JN, Zhang JJ, Zhong YP. IgA Type Multiple Myeloma, Clinical Features, and Prognosis. Chin Med J (Engl). 2018 May 20;131(10):1249-1250. doi: 10.4103/0366-6999.213513. https://doi.org/10.4013/jclin.2018.06.018

PMID:29723436 PMCid:PMC5956780

18. Ritkin RM, Abounour R, Terebelo H, Shah JJ, Gasparetto Y, Hardin J, Strinivasan S, Ranaerwa Y, Durie BG; Connect MM Registry: The Importance of Establishing Baseline Disease Characteristics. Clin Lymphoma Myeloma Leuk. 2015 Jun;15(6):368-76. doi: 10.1016/j.clml.2014.12.002. Epub 2014 Dec 11. https://doi.org/10.1016/j.clml.2014.12.002

PMID:25617035

19. Kumar SK, Dispenzieri A, Lacy MQ, Gertz MA, Buadi FK, Pandey S, Kapoor P, Dingli D, Hayman SR, Leung N, Lust J, McCurdy A, Russell SJ, Zeldenrust SR, Kyle RA, Rajkumar SV. Continued improvement in survival in multiple myeloma: changes in early mortality and outcomes in older patients. Leukemia. 2014 May;28(5):1122-8. doi: 10.1038/leu.2013.313. Epub 2013 Oct 25. https://doi.org/10.1038/leu.2013.313

PMID:30003033
22. Riva E, Bove V, Villano F, Mori M, Córdoba C, Noria A, Petruskevics P, Cardeza A, Díaz L. From guidelines to real world: results from the National Multiple Myeloma Registry in Uruguay on 222 newly diagnosed multiple myeloma patients from 2012 to 2015. Curr Med Res Opin. 2019 Jul;35(7):1197-1203. doi: 10.1080/03007995.2019.1568091. Epub 2019 Feb 8. https://doi.org/10.1080/03007995.2019.1568091

PMid:30621522

23. Remes K, Anttila P, Silvennoinen R, Putkonen M, Ollikainen H, Terävä V, Sinisalo M, Kananen K, Schain F, Castren-Kortegangas P, Järvinen TM, Pisi M, Wahl F, Dixon T, Leva A. Real-world treatment outcomes in multiple myeloma: Multicenter registry results from Finland 2009-2013. PLoS One. 2018 Dec 5;13(12):e0208507. doi: 10.1371/journal.pone.0208507. https://doi.org/10.1371/journal.pone.0208507

PMid:33489045 PMcid:PMC7813274

24. Liwing J, Uttervall K, Lund J, Aldrin A, Blimark C, Carlson K, Enestig J, Flogegård M, Forsberg K, Gruber A, Haglöf Kviele H, Johansson P, Lauri B, Mellqvist UH, Swedin A, Svensson M, Näsman P, Gahrton G, Aschan J, Nahi H. Improved survival in myeloma patients: starting to close in on the gap between elderly patients and a matched normal population. Br J Haematol. 2014 Mar;164(5):684-93. doi: 10.1111/bjh.12685. Epub 2013 Dec 9.. https://doi.org/10.1111/bjh.12685

PMid:24513224

25. Shustik, C., Bergsagel, D. E., & Pruzanski, W. (1976). Kappa and lambda light chain disease: survival rates and clinical manifestations. Blood. 1976 Jul;48(1):41-51. https://doi.org/10.1182/blood.V48.1.41.41

PMid:820387

26. Naïr B, Waheed S, Szymonifka J, Shaughnessy JD Jr, Crowley J, Barlogie B. Immunoglobulin isotypes in multiple myeloma: laboratory correlates and prognostic implications in total therapy protocols. Br J Haematol. 2009 Apr;145(1):134-7. doi: 10.1111/j.1365-2414.2008.07547.x. Epub 2008 Dec 20. https://doi.org/10.1111/j.1365-2414.2008.07547.x

PMid:19120351 PMcid:PMC3644043

27. nizes S, Symeonidou M, Zagoridis K, Bezirgianidou Z, Vrachiolias G, Spanoudaki A, Spanoudakis E. Socioeconomic Status is Globally a Prognostic Factor for Overall Survival of Multiple Myeloma Patients: Synthesis of Studies and Review of the Literature. Mediterr J Hematol Infect Dis. 2021 Jan 1;13(1):e2021006. doi: 10.4084/MJHID.2021.006 https://doi.org/10.4084/mjhid.2021.006

PMid:33489045 PMcid:PMC7813274

28. https://openknowledge.worldbank.org/bitstream/handle/10986/34496/978146816024.pdf

29. https://www.worldbank.org/en/country/jordan/brief/ja-jordan-country-reclassification

30. Marinac CR, Ghobrial IM, Birmann BM, Soiffer J, Rebbeck TR. Dissecting racial disparities in multiple myeloma. Blood Cancer J. 2020 Feb 17;10(2):19. doi: 10.1038/s41408-020-0284-7 https://doi.org/10.1038/s41408-020-0284-7

PMid:32066732 PMcid:PMC7026439

31. Drayson M, Begum G, Basu S, Makkuni S, Dunn J, Barth N, Child JA. Effects of paraprotein heavy and light chain types and free light chain load on survival in myeloma: an analysis of patients receiving conventional-dose chemotherapy in Medical Research Council UK multiple myeloma trials. Blood. 2006 Sep 15;108(6):2013-9. doi: 10.1182/blood-2006-03-008953. Epub 2006 May 25.. https://doi.org/10.1182/blood-2006-03-008953

PMid:16728700

32. Woo YR, Kim JS, Lim JH, Hwang S, Kim M, Bae JM, Park YM, Min CK, Kim DW, Park HJ. Prevalence and clinicopathologic characteristics of multiple myeloma with cutaneous involvement: A case series from Korea. J Am Acad Dermatol. 2018 Mar;78(3):471-478.e4. doi: 10.1016/j.jaad.2017.08.054. Epub 2017 Nov 6. https://doi.org/10.1016/j.jaad.2017.08.054

PMid:29107338