

**PATTERNS OF FERRIC CARBOXYMALTOSE USE,
DEMOGRAPHIC CHARACTERISTICS AND
DEPARTMENTAL PREFERENCES**

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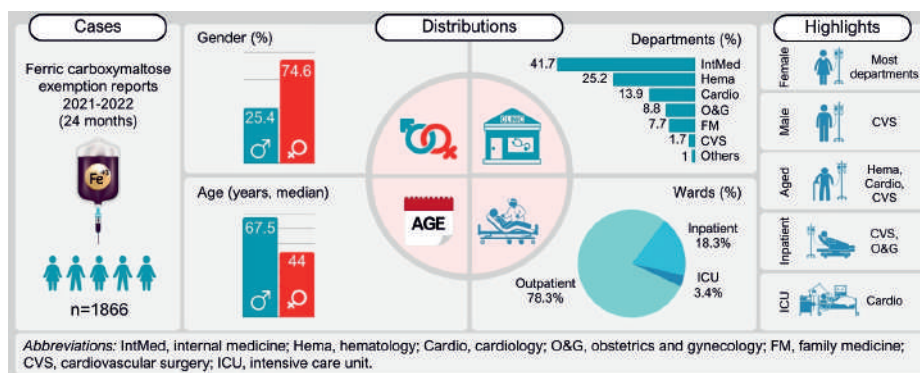
Abstract

Ferric carboxymaltose (FCM), a common intravenous iron therapy for iron deficiency anemia, is useful but may cause side effects depending on age, gender, and hospital unit. This study examines the use trends of FCM across several medical departments, emphasizing demographic and ward-specific differences. Patients who received FCM treatment at a training and research hospital were analyzed retrospectively and cross-sectionally throughout a 24-month period from January 2021 to December 2022. Accordingly, the drug exemption reports were assessed to determine which departments favoured ferric carboxymaltose in which clinical conditions for patients above 18 years of age. The sample consisted of 1866 patients. The median age was 49 years (18–97). Women accounted for 74.6% of cases, with a median age of 44 years, while men represented 25.4% ($\chi^2 = 452$, $df = 1$, $p < 0.001$), with a higher median age of 67.5 years ($U = 161327$, $p < 0.001$). The departments that most commonly granted FCM drug exemption reports were internal medicine (41.7%), hematology (25.2%), and cardiology (13.9%) ($\chi^2 = 1665$, $df = 6$, $p < 0.001$). Administration locations were 78.3% outpatient clinics, 18.3% normal wards, and 3.4% intensive care units (ICU) ($\chi^2 = 1759$, $df = 2$, $p < 0.001$). In contrast to other departments, cardiovascular surgery treated predominantly male patients (80.6%). Obstetrics and gynecology and cardiovascular surgery predominantly administered FCM to inpatients. The cardiology department administered 71.8% of FCM treatments in ICUs. Ferric carboxymaltose exhibits department-specific variations based on gender and its administration

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to outpatients or inpatients, offering significant insights for all administrative procedures related to this medicine.

Key words: iron deficiency, ferric carboxymaltose, hospital admission, medical departments



Graphical abstract. Patient demographics and hospital ward differences in ferric carboxymaltose (FCM) preference between January 2021 and December 2022 (24 months) were investigated. The sample ($n = 1866$) predominantly comprises women, and the age distribution indicates that men are older than women. Internal medicine (41.7%) and hematology (25.2%) prescribed FCM most often. The majority of the medications were administered in an outpatient setting (78.3%). These findings showed that the cardiovascular surgery (CVS) department had mostly male patients; hematology, cardiology, and CVS departments had mostly elderly patients; and obstetrics and gynecology department and CVS departments mostly prescribed the relevant drug to inpatients; and cardiology was prominent in ICU patients.

Introduction. Iron deficiency (ID), the most prevalent micronutrient deficiency, affects one-third of the world's population, and iron deficiency anemia (IDA) is responsible for approximately half of all anemias [1]. The IDA continues to rank among the top ten conditions in the Global Burden of Disease and is associated with substantial economic losses [2].

The treatment of ID/IDA primarily targets the underlying cause, while physicians replace iron either orally or parenterally. Due to their low cost and simplicity of use, oral iron therapies are frequently the first choice for the short- or long-term treatment of iron deficiency. Nevertheless, the listing of indications for intravenous iron administration is increasing as a result of factors such as intolerance, inadequate effectiveness, and adverse reactions. Another factor contributing to the growing demand for intravenous iron replacement therapy for iron deficiency is the third generation of intravenous iron preparations, which are now much more dependable [3].

In this context, ferric carboxymaltose (FCM) is one of the new generations of intravenous iron compounds. Since iron deficiency anemia is a disease that

affects numerous medical specialties, many medical departments have begun to favour FCM for its rapid and effective treatment, and it is also recommended by guidelines. Moreover, the reduced occurrence of side effects linked to FCM improves patient adherence and safety, establishing it as a favoured option in healthcare [4].

However, FCM administration is not without risks. Specifically, it has been linked to hypophosphatemia, a condition marked by diminished phosphate levels in the blood, which may arise from the drug's method of action influencing phosphate metabolism [5]. The recently identified side effect of methemoglobinemia associated with ferric carboxymaltose raises questions about its prevalence and clinical significance [6, 7]. On the other hand, a further concern associated with iron replacement therapy is iron overload. This situation differs based on age and gender. The elderly face an elevated risk of iron overload due to various causes, including diminished regulatory mechanisms, the prevalence of chronic diseases, and a higher vulnerability to iron accumulation. As is the case with this demographic data, males are often at a higher risk of iron overload than women are [8]. Lastly, the potential risk of oxidative stress linked to iron therapy is especially significant for intensive care patients, making the prevention of iron overload crucial for these patients [9].

Therefore, it is evident that various sub-information, including the quantity and frequency of drug use, the units and departments administering the drug, and the demographic features of the patients, would be crucial for health and hospital management.

This study aimed to investigate the distribution of medical departments in the preference for ferric carboxymaltose and the hospital services or wards where this preference is administered. Additionally, a department-by-department analysis of the gender and age distribution of patients undergoing FCM was planned.

Materials and Methods. *Ethical approval.* This study was conducted in accordance with the Declaration of Helsinki of 1975 (as revised in 2013), and the protocol was reviewed and approved by the Ethics Committee of Ordu University (protocol code: 2023/187 and date of approval 07.07.2023).

Study design and patient selection. For the purpose of this investigation, the exemption reports that were written for the availability of the relevant medicine were to ascertain the departments' preferences regarding ferric carboxymaltose. In Turkey, public hospitals provide ferric carboxymaltose either free of charge or at a minimal cost, but only with a drug exemption report issued by a specialist physician. Therefore, the number of departments that prefer FCM was attempted to be determined using this reporting system. Data spanning two years, from January 2021 to December 2022 (24 months), were gathered for this purpose. Patients above 18 years of age who applied to the Ministry of Health Ordu University Training and Research Hospital and for whom a ferric carboxymaltose drug exemption report was issued constituted the study population.

Data type. The data set was compiled by reviewing the Health Information Management System (HIMS) over a two-year period, focusing on patients who met the study's inclusion criteria. The data types included the relevant departments implementing FCM, the outpatient/inpatient treatment status, the patients' age and gender.

Statistical analysis. Microsoft Excel was used to record the whole data. The data were transferred from Microsoft Excel to Jamovi (version 2.3.28) for statistical analysis [10]. Descriptive statistics, contingency tables, chi-square test, and independent sample *t*-tests were utilized as statistical approaches. Descriptive data were presented as median, minimum, and maximum values, whereas categorical variables were presented as numbers (*n*) and percentages. The level of statistical significance was set at $p < 0.05$ for all analyses.

Results. A total of 1866 cases were recorded, with a median age of 49 years (range: 18 to 97 years) as a result of the analysis. There were 1392 (74.6%) female patients and 474 (25.4%) male patients ($\chi^2 = 452$, $df = 1$, $p < 0.001$). The median age of women was 44 years (18–97) and the median age of men was 67.5 years (18–94) ($U = 161327$, $p < 0.001$).

The information on six major medical departments that administer FCM as well as a few departments that administer this drug infrequently was gathered. Departments that administer FCM infrequently were categorized as “Others”. The departments classified as ‘Others’ issued the following number of drug exemption reports: infectious diseases (5), urology (4), orthopedics (2), emergency (2), pulmonology (2), and neurology (1). As a result, seven distinct department groups were identified, and the data distribution was analyzed accordingly.

The medical departments issuing FCM exemption reports were distributed as follows, and their distributions were statistically significant ($\chi^2 = 1665$, $df = 6$, $p < 0.001$): internal medicine 41.7% ($n = 777$), hematology 25.2% ($n = 470$), cardiology 13.9% ($n = 260$), obstetrics and gynecology (O&G) 8.8% ($n = 165$), family medicine 7.7% ($n = 143$), cardiovascular surgery 1.7% ($n = 31$) and the others 1% ($n = 20$).

There was a considerable gender gap between departments on the composition of FCM exemption reports ($\chi^2 = 172$, $df = 6$, $p < 0.001$). The most notable difference in gender was observed in the CVS department, while FCM was predominantly favoured for male patients (80.6%). In this regard, the department with the highest proportion of male patients following CVS was the hematology department, with a rate of 39.1% for this grouping. Without taking into account the O&G department, the family medicine department exhibited the highest preference for female patients at 86.7%. The gender distribution of departments issuing FCM exemption reports is shown in Table 1.

Analyzing the distribution by age, the Kruskal–Wallis test revealed a statistically significant difference between the groups ($\chi^2 = 247$, $df = 6$, $p < 0.001$). According to the median values in this sub-analysis, the O&G department had the

T a b l e 1

Gender distribution of departments issuing FCM exemption reports

Departments		Gender		Total
		Women	Men	
Internal Medicine	<i>n</i>	611	166	777
	%	78.6	21.4	100.0
Hematology	<i>n</i>	286	184	470
	%	60.9	39.1	100.0
Cardiology	<i>n</i>	186	74	260
	%	71.5	28.5	100.0
Obstetrics and Gynecology	<i>n</i>	165	0	165
	%	100.0	0.0	100.0
Family Medicine	<i>n</i>	124	19	143
	%	86.7	13.3	100.0
Cardiovascular Surgery	<i>n</i>	6	25	31
	%	19.4	80.6	100.0
Others	<i>n</i>	14	6	20
	%	70.0	30.0	100.0
Total	<i>n</i>	1392	474	1866
	%	74.6	25.4	100.0

The percentages are calculated based on the total number of the related row.

youngest patient group, with 38 years of age (18–97), while the cardiology department had the oldest age group, with 64 years of age (18–97). This sub-analysis reveals a prominent detail: departments were essentially categorized into two categories based on median age. Consequently, the internal medicine, obstetrics and gynecology, and family medicine departments administered FCM to the younger population (46 years and younger), whereas the hematology, cardiology, cardiovascular surgery, and other departments administered FCM to the older patient population (61 years and over). The age distribution by department is displayed in Table 2.

The distribution of whether FCM was administered to patients by outpatient, inpatient, or intensive care unit departments was also evaluated (Table 3). When analyzing the places where the drug was administered, 78.3% were administered in outpatient clinics, 18.4% in normal wards, and 3.4% in intensive care units ($\chi^2 = 1759$, $df = 2$, $p < 0.001$). The distribution of this drug administration by departments revealed that the majority of departments manage it in outpatient settings, while CVS (90.3%) and O&G (75.8%) departments primarily administer FCM treatment to inpatients. When compared to other departments, the cardiology department was found to administer FCM in intensive care units more frequently than any other department. This is an intriguing observation. Despite the fact that the percentage of FCM administration in the intensive care unit of

T a b l e 2

Age distribution of patients according to departments

Departments	<i>n</i>	Median	Min	Max
Internal Medicine	777	46	18	94
Hematology	470	62.0	18	97
Cardiology	260	64.0	18	97
Obstetrics and Gynecology	165	38	18	90
Family Medicine	143	41	18	94
Cardiovascular Surgery	31	62	19	83
Others	20	61.5	19	84
Total	1866	49.0	18	97

T a b l e 3

Distribution of FCM administrations by outpatient, inpatient wards, or intensive care unit

Departments	Administration location				Total
		Outpatient	Normal ward	ICU	
Internal Medicine	<i>n</i>	636	137	4	777
	%	81.9	17.6	0.5	100.0
Hematology	<i>n</i>	443	25	2	470
	%	94.3	5.3	0.4	100.0
Cardiology	<i>n</i>	204	10	46	260
	%	78.5	3.8	17.7	100.0
Obstetrics & Gynecology	<i>n</i>	31	125	9	165
	%	18.8	75.8	5.5	100.0
Family Medicine	<i>n</i>	139	4	0	143
	%	97.2	2.8	0.0	100.0
Cardiovascular Surgery	<i>n</i>	0	28	3	31
	%	0.0	90.3	9.7	100.0
Others	<i>n</i>	8	12	0	20
	%	40.0	60.0	0.0	100.0
Total	<i>n</i>	1461	341	64	1866
	%	78.3	18.3	3.4	100.0

Abbreviations: FCM, ferric carboxymaltose; ICU, intensive care unit; *n*, number.

The percentages are calculated based on the total number of the related row.

the cardiology department was 17.7%, cardiology was responsible for 71.8% of the patients who received FCM in intensive care units across all departments.

Discussion. Internal Medicine is the department that performs FCM for iron deficiency and/or iron deficiency anemia most frequently because it is responsible for the majority of initial management of chronic diseases and initial diagnosis of ID/IDA in non-chronic patients [11]. Again, in some countries, internists also conduct FCM administrations for heart failure [12]. Thus, it is not

surprising that internists have developed substantially more FCM administrations than hematology and other subspecialties.

In terms of age and gender, the findings typically reveal that younger female patients predominate because in developed countries, ID/IDA is most prevalent among women due to menstrual bleeding [13]. In contrast, the hematology, cardiology, and cardiovascular surgery departments had median patient ages that were relatively higher than those of the other departments in the study. This is because these departments' patient populations are more likely to include elderly people with chronic illnesses. Specifically, the FCM administered by cardiology focuses on the patient population with heart failure, which is already a group of elderly individuals [14].

The high median age observed in men in the study can be attributed to the prevalence of gastrointestinal diseases, which are the leading cause of iron deficiency (ID) and iron deficiency anemia (IDA) in this gender group [15]. These conditions tend to increase with age, along with heart failure, which is more common among older individuals and particularly prevalent in men [16].

The outpatient treatment of FCM is more prevalent than inpatient treatment, according to the findings of the study. The reason for this is that FCM is well tolerated by patients and is more successful in outpatient contexts [17]. Even intravenous iron administration at home is currently discussed and advised [18]. In obstetrics and gynecology and cardiovascular surgery, the high rate of inpatient FCM administration suggests pre- and postoperative applications. Similarly, the high frequency of FCM administration in the intensive care unit observed in cardiology suggests that heart failure patients are predominantly followed in the intensive care unit during decompensation periods, during which FCM is administered.

It was discovered that surgical departments other than the department of cardiovascular surgery preferred FCM either not at all or in extremely small quantities. In addition to the possibility that the exemption report for the relevant drug was issued by other departments, as highlighted in the previous paragraph, FCM may be underutilized in surgical departments. Current literature suggests treating IDA with intravenous iron during the preoperative period. However, it is unclear whether its use is preferable to other blood transfusions [19]. This may partially influence surgeons' FCM preferences. However, many general medical departments and primary care practices may lack the resources necessary to diagnose and treat anemia [20].

This study demonstrated that medical departments vary in their prescription of FCM based on patient demographics and specific hospital areas where the drug is administered. Given that the potential side effects of the medicine in certain patient populations are theoretically anticipated, additional research is required to determine the extent to which these risks occur. Consequently, all medical departments will possess the knowledge to manage patients more effectively while

administering this medication to the appropriate groups and in the pertinent hospital regions.

Limitations. Several limitations are associated with the study. The first is that the departments' predicted preference for FCM was evaluated by issuing an exemption report. Although uncommon, some patients may purchase this medication with their own funds. Consequently, this information was excluded from the analysis. Nephrology and gastroenterology departments, which have the potential to frequently use intravenous iron therapy, are not available in our facility; consequently, no observations can be made regarding these two branches. Lastly, it was not possible to locate an article that compared and/or contrasted the findings of this study with similar and/or distinct findings.

Conclusion. This study highlights the essential function of FCM in the management of ID/IDA, revealing significant changes based on gender, age, and departmental usage patterns. The majority of patients for whom medical departments prefer ferric carboxymaltose (FCM) are female. High age values were notable among males receiving FCM. The most preferred department for ferric carboxymaltose was the department of internal medicine. Department-specific variations in the administration of the drug to outpatients and hospitalized patients were also identified. These results provide essential data for the management of all processes (demand, supply, inventory, etc.) associated with ferric carboxymaltose. More importantly, it necessitates increased vigilance in departments characterized by advanced age, male demographics, and inpatient profiles, where the risk of adverse consequences, particularly iron overload, is elevated.

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