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A SURVEY-BASED STUDY TO UNDERSTAND THE PRACTICE PROFILE OF INDIAN GYNAECOLOGISTS ON IRON SUPPLEMENTATION IN WOMEN WITH IRON-DEFICIENCY ANAEMIA

Obstetrics & Gynaecology

Dr Alok Sharma MBBS, MD (OBG), MICOG, FICOG, DHA, Civil Hospital, Sunder Nagar, Mandi, Himachal Pradesh

Ms Devika Chitnis* Senior Manager, Medical Affairs, Cipla Ltd, 289, Bellasis road, Mumbai Central east, Mumbai, India. *Corresponding Author

ABSTRACT

Aim: To understand the practice profile and prescribing patterns of iron supplements in women from menarche to menopause. **Materials and Methods:** The study was carried out among 334 gynaecologists practicing across various zones of India. Participants were invited to complete a digital link survey on prescribing iron supplements to patients with iron deficiency and IDA. Data were analyzed using suitable statistical tests. **Results:** Around 49.7% of the gynaecologists reported the prevalence of anaemia to be 21–40%, whereas 11.1% reported it to be >60%. 84.1% preferred assessing haemoglobin to diagnose IDA. However, 56.6% favoured ruling out any haematological condition before commencing an iron supplement. Ferrous ascorbate was the most prescribed salt form of iron (87%), in combination with L-methylfolate (72.8%). 80.5% gynaecologists did not prescribe an oral iron supplement in the first trimester, and 46.4% reported that 75% of their patients were compliant with the prescribed iron supplements. 61.4% of gynaecologists reported constipation as the most common side effect encountered by patients with oral iron supplements. For majority (48.8%), iron sucrose was the most preferred IV iron salt and its recommended dose in pregnancy was 100-200mg (63.66%). **Conclusion:** These findings provide a clear understanding of the prescribing patterns of oral and IV iron supplements, including the better outcomes associated with the sustained-release formulation and the use of L-methylfolate, leading to reduced non-compliance and improving anaemic conditions in Indian women.

KEYWORDS

Ferrous ascorbate, Iron deficiency anaemia (IDA), IV iron, L-methylfolate, Sustained-release formulations

INTRODUCTION

Anaemia is one of the prime health concerns in developing nations like India.[1] Iron deficiency anaemia (IDA) is the most common type of anaemia caused by insufficient iron stores within the body for the process of erythropoiesis.[2] Worldwide, it affects around 500 million females of reproductive age, and around 75% of anaemia cases in pregnant women are suggested to be due to IDA.[4, 5] Symptoms suggesting IDA include fatigue and shortness of breath on exertion. Extended hospital stays and adverse events are also commonly associated with IDA.[6] As per World Health Organization (WHO), 20% of maternal deaths are attributed to IDA.[7]

Ministry of Health and Family Welfare (MOHFW) report suggests around 65% of females in India are affected with IDA during the postpartum period.[8] Postpartum anaemia may lead to several mental health-related problems.[9] The 2019/2021 National Family Health Survey 5 (NFHS-5) revealed that the prevalence of anaemia among Indian women is 57%, compared to 53% reported in NFHS-4 (2015/16).[10]

During pre-operative procedures, women are at higher risk of developing anaemia than men and therefore, at risk of higher blood transfusion rates.[11] Thus, timely diagnosis is important for identifying the root cause and managing IDA with adequate iron supplementation.[6] This survey was conducted to understand the practice and prescribing patterns of the iron supplements in women from menarche to menopause amongst the gynaecologists.

MATERIALS AND METHODS

In this survey-based study, a 28-item self-administered questionnaire was distributed digitally among gynaecologists across different zones of India, prescribing iron supplements to patients with iron deficiency and IDA. The survey was conducted from July 2021 to November 2021. Ethics committee approval was taken and consent was obtained from all the participants before initiating the survey. Anonymity and confidentiality were maintained throughout the survey.

Results of the categorical variables were presented in the form of frequencies and percentages. The responses were presented descriptively in tables, and graphical representations were used to visualise where necessary. All statistical analysis was performed using SPSS Software Version 27.0.

RESULTS

Out of 334 participants, the majority of them were MD professionals (56.58%), from the age group of 41-50 years (34.4%), practicing in private consulting settings (46.7%) and nursing homes (40.1%). Respondents were predominantly from the north zone (35.9%), followed by south (22.8%), west (21.3%), and east (20.1%) zones (Table 1).

Table 1: Summary Statistics for Doctor Profile

Characteristics (N=334)	Counts (%)
Age	
<30 years	9 (2.7%)
31-40 years	106 (31.7%)
41-50 years	115 (34.4%)
51-60 years	74 (22.2%)
>60 years	30 (9%)
Practice Type	
Corporate Hospital	22 (6.6%)
Government Hospital/Academic Institutes	22 (6.6%)
Nursing Home	134 (40.1%)
Private Consulting Practice	156 (46.7%)
Qualification	
MBBS	82 (24.6%)
DGO	25 (7.5%)
DNB	38 (11.32%)
MD/MS Obstetrics and Gynaecology	189 (56.58%)
Zone wise division of states	
West	71 (21.3%)
South	76 (22.8%)
North	120 (35.9%)
East	67 (20.1%)

Prevalence:

In the survey, 49.7% gynaecologists reported the prevalence of anaemia in their clinical practice to be 21–40%, 29% of them stated it to be 41–60%; while 11.1% reported it to be > 60% and 10.2% reported < 20%. In pregnant and non-pregnant women, with a mean age of 39.49 and 38.61 years respectively, mild anaemia was discovered to be more prevalent than moderate or severe anaemia. More than half of the gynaecologists (64.1%) found that anaemia was most prevalent in women aged 26 to 35 years.

Diagnostic criteria:

To diagnose IDA, majority of the gynaecologists (84.1%) preferred assessing haemoglobin levels, while 57.5% favoured serum ferritin. Iron-binding capacity and serum iron were preferred by 35.3% and 32.3% of the gynaecologists. Most gynaecologists (56.6%) favoured

ruling out any haematological conditions and the presence of other nutritional deficiencies before commencing an iron supplement. Many of them also preferred to rule out the existence of any parasitic infections (49.1%) or anaemia of chronic disease (43.1%) (Table 2). Regarding non-pregnant conditions, 88.6% gynaecologists reported prescribing iron supplementation in women with dysfunctional or abnormal uterine bleeding. In addition, 52.1%, 51.8%, and 32.6% reported prescribing iron supplementation in cases of abortion, fibroids, and any polyps respectively (Table 2).

Table 2: Prescription preferences of oral iron supplements

Characteristics (N=334)	Counts (%)
Conditions to rule out before starting an iron supplementation	
Parasitic infections (e.g. malaria, hookworm, roundworm)	164 (49.1%)
Other haematological conditions (e.g. thalassemia)	189 (56.6%)
Anaemia of chronic disease	144 (43.1%)
Other nutritional deficiencies (Vit B9/B12, etc.)	189 (56.6%)
Non-pregnant conditions in which iron supplementation prescribed	
Endometriosis / adenomyosis	78 (23.4%)
Fibroids	173 (51.8%)
Any polyps	109 (32.6%)
Dysfunctional uterine bleeding / Abnormal uterine bleeding	296 (88.6%)
PCOS	40 (12%)
Infertility	40 (12%)
Menopause	48 (14.4%)
Abortion	174 (52.1%)
Other	9 (2.7%)
Prescribing Vit B9 supplementation with iron	
Folic acid	91 (27.2%)
L-methylfolate	243 (72.8%)
Most preferred formulation of oral iron	
Tablets	278 (83.2%)
Capsules	51 (15.3%)
Syrup	5 (1.5%)
Most preferred technology of delivering iron salts	
Immediate release	23 (6.9%)
Sustained-release	236 (70.7%)
Liposomal	75 (22.5%)
Oral iron supplements prescribed in the first trimester of pregnancy	
Yes	65 (19.5%)
No	269 (80.5%)
Oral iron supplements prescribed in preconception period	
Yes	183 (54.8%)
No	151 (45.2%)
Duration of prescribing oral iron supplements during postpartum	
<3 months	105 (31.4%)
3-6 months	186 (55.7%)
6-9 months	26 (7.8%)
9-12 months	16 (4.8%)
Not prescribed	1 (0.3%)

PCOS: Polycystic ovary syndrome

Iron supplements: efficacy and tolerability:

Majority of the gynaecologists reported that the most prescribed salt of iron was ferrous ascorbate (87%), while ferrous sulphate (13%) was the least prescribed salt of iron (Fig 1). 45% of gynaecologists preferred prescribing iron supplements in combination with folic acid. In comparison, 55% prescribed it in combination with multivitamins/multi-minerals/amino acids or other adjuncts as per the dietary requirement of the patient. Most gynaecologists (72.8%) reported L-methylfolate as the most common form of Vitamin B9 prescribed along with the iron, while only 27.2% preferred folic acid. As tablets render consistent absorption, 83.2% of gynaecologists preferred an oral iron supplement in tablet form. In addition, 70.7% of gynaecologists preferred a "sustained-release" technology to improve patient compliance while prescribing the iron salts, whereas 22.5% preferred "liposomal" (Table 2).

Ferrous ascorbate is the most preferred iron salt as ascorbate has the most efficient iron absorption-enhancing effect due to its ability to reduce ferric to ferrous iron. L-methylfolate is a newer alternative to conventional folic acid supplements and effectively improves folate status. A sustained-release formulation maintains a constant level of medication in the body for a more extended period. With this pretext, participants were asked about their experience on ferrous ascorbate sustained-release formulation. The sustained-release formulation of ferrous ascorbate, along with L-methylfolate, was reported to be more effective than immediate-release oral iron supplements by a significant segment of gynaecologists (97%), and 99.4% reported better tolerability. A rise of 1–2g/dl of haemoglobin within a month was reported by 69.2% of gynaecologists, while 23.4% gynaecologists encountered a rise of > 2g/dl with the sustained-release formulation of ferrous ascorbate and L-methylfolate.

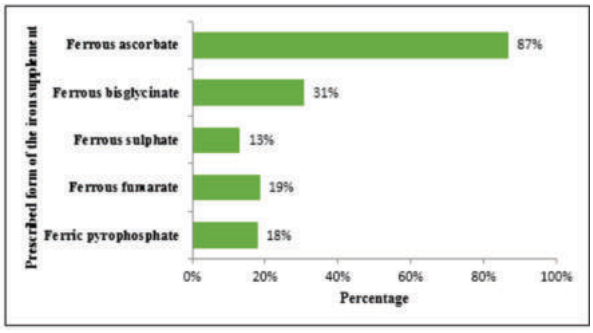

Figure 1: The prescribed form of the iron supplement

Iron supplements: Compliance:

46.4 % gynaecologists reported that 75% of their patients were compliant with the prescribed iron supplements. Patients continued taking iron supplements for 3–6 months as per 43.1% of gynaecologists and for 2–3 months as per 41.3% of gynaecologists.

Iron supplements in pregnancy:

In general practice, iron supplementation is prescribed in the second trimester due to the progressive increase of iron absorption in the second and third trimesters. Maternal absorption of iron is markedly reduced in the first trimester. In the survey, about 80.5% gynaecologists did not prescribe an oral iron supplement in the first trimester of pregnancy. About 54.8% favoured prescribing an oral iron supplement during the preconception period. More than half of the gynaecologists (55.7%) reported prescribing an oral iron supplement for about 3–6 months during the postpartum period as the prevalence of anaemia is high due to postpartum haemorrhage (Table 2).

Side effects:

Gynaecologists reported constipation (61.4%), nausea/vomiting (60.8%), black stools (58.7%), and gastritis (54.2%) as the common side effects encountered with oral iron supplements. Non-adherence to an oral iron supplement was mostly attributed to intolerability (78.1%), non-compliance (43.1%), and cost (22.8%).

IV iron:

Intolerability or insufficient response with oral iron necessitates the use of IV iron. For the majority of the gynaecologists (48.8%), iron sucrose was the most preferred IV iron salt, followed by ferric carboxymaltose (32.5%) and iron isomaltoside (15.1%). Furthermore, 63.66% reported that the most common dose for iron sucrose in pregnancy was 100-200 mg, while that of ferric carboxymaltose was 500-1000 mg as reported by 47.15% of gynaecologists.

The 3 most common indications for prescribing IV iron infusion were moderate to severe IDA in the late second or third trimester (75.1%), followed by failure to the oral iron therapy (59%) and non-compliance or intolerance to oral iron supplements (57.2%) (Fig 2). 60.8% gynaecologists reported administering a test dose of IV iron to their patients to avoid the risk of anaphylactic reactions during infusion. While majority of the gynaecologists (82.6%) never prescribed IV iron in the first trimester of pregnancy, 17.4% reported prescribing it during early pregnancy even though it is not recommended to be used in first trimester.

Challenges and Counselling:

The major challenge faced with prescribing IV iron formulation such as ferric carboxymaltose and iron isomaltoside was cost, as stated by 81.7% and 58.4% of the gynaecologists, whereas 61.4% reported dose frequency as the principal challenge encountered with iron sucrose. According to 79.3% gynaecologists, the primary objective of

counselling the patients was to make them understand the importance of taking iron, while the secondary objectives were aimed at counselling about other aspects of iron supplements like interactions (with food and other nutritional supplements), consequences of non-compliance and side effects.

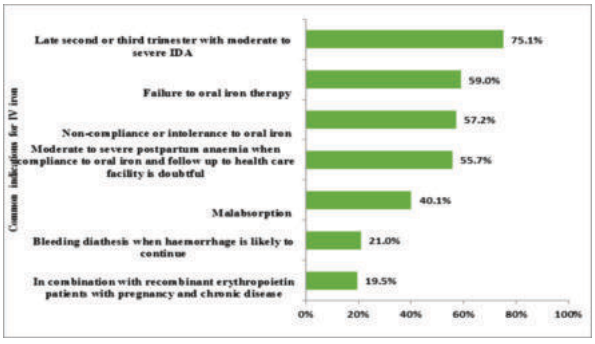

Figure 2: Common indications in which IV iron is administered

DISCUSSION

Iron deficiency is recognised as the most prevalent micronutrient deficiency in > 20% of females during their reproductive age around the globe.[12] Particularly, IDA remains the top cause of anaemia with a substantial effect on infants and women, increasing maternal morbidity and mortality. Thus, there is a strong emphasis from WHO to reduce anaemia by 50% among women of reproductive age by 2025.[13]

In our survey, most gynaecologists reported the prevalence of anaemia in Indian fertile women between 21–40%, while some reported between 41–60%, which is consistent with the previously published data.[14,15] Although, as per the survey by NFHS-5, 66.4% of the women in India were reported to be anaemic in 2019.[16] The present survey showed that mild anaemia was more prevalent than moderate or severe anaemia, consistent with earlier findings.[17] In contrast, reports indicate that mild and moderate forms of anaemias were equally prevalent (24.8% each) and much higher than the severe (1.3%) form of anaemia.[15]

Furthermore, a high prevalence of severe anaemia (1.6%) is reported among pregnant women aged < 25 years from India.[18] A prospective study suggested an association between socio-demographic factors and IDA development in Indian women, with the age group 25–30 years most affected by IDA.[19] These findings coincide partly with our results, as majority of the gynaecologists reported that 26–35 years was a ubiquitous age group of women affected by IDA.

In this study, most of the gynaecologists reported haemoglobin levels followed by serum ferritin as the most common diagnostic criteria to rule out IDA. As per the National Health Portal, India, haemoglobin levels and vitamin B12 levels are recommended as diagnostic criteria for IDA.[20] In the United States, the measurement of ferritin level was the most accepted diagnostic test (92.9%), followed by total iron-binding capacity and transferrin saturation (85.5%) among primary care physicians.[21] However, it is crucial to note that the haemoglobin levels may not be as adequate as serum ferritin in diagnosing IDA, but there is a significant correlation between haemoglobin and serum ferritin levels. Measurement of blood haemoglobin levels provides a more practical approach to monitoring the efficacy of the remedies to intervene IDA.[22]

Ascorbic acid counters the oxidation of ferrous iron, thereby aiding the absorption of iron. Thus, it is most commonly used in clinical practice for promoting iron absorption.[23] Ferrous ascorbate has the benefit of delivering both ferrous iron and ascorbate in the same compound.[23] In the present survey, ferrous ascorbate was the most preferred salt prescribed by around 87% gynaecologists. Supporting our results, a multicentric study from India reported that ferrous ascorbate was the most commonly prescribed iron salt (69.2%) among rural anaemic women, resulting in a significant increase in Hb concentration in the successive months.[24] Another study evaluating the efficacy and tolerability of various iron salts in pregnant women showed a significant rise in haemoglobin levels with ferrous ascorbate at 90 days from baseline (11.3 ± 0.51 vs 8.61 ± 0.56) with fewer side effects.[25]

More than half of gynaecologists in our survey prescribed oral iron supplements during preconception and postpartum. In a randomised controlled trial, the impact of preconception micronutrient supplementation on anaemia and iron status during pregnancy and postpartum were evaluated.[26] A modest increase in prenatal plasma ferritin with preconception iron-folic acid (IFA) supplementation was reported. Moreover, plasma ferritin was high in cord blood and significantly high in 3 months postpartum if IFA was taken for 26 weeks during the preconception period.[26]

Iron supplements incorporated in multivitamin preparations are low in doses and not adequate to rectify iron deficiency. Additionally, these preparations may contain other minerals that may interfere with iron absorption.[27] In this study, most gynaecologists opted for iron with folic acid. Folic acid is a vital component of the periconceptional care of women in the reproductive age group.[28] Evidence suggests that L-methylfolate helps prevent neural tube defects during fertilisation, making it a better option than regular folic acid.[29] Our survey findings are in accordance with this statement, as most gynaecologists preferred L-methylfolate over folic acid.

Sustained-release formulations are favoured instead of immediate-release formulations if the drug is prone to cause side effects in the gastrointestinal (GI) tract.[30] In this survey, gynaecologists preferred prescribing oral iron in sustained-release formulation instead of immediate-release for the same reason. Results from a prospective study concluded that ferrous sulphate is a potent iron salt in improving the IDA status in pregnant women, however associated with higher rates of non-compliance (42%) due to its severe GI side effects. The authors suggested the usage of newer iron supplementations with better GI effects to alter the non-compliance rates.[31] In our survey, gynaecologists reported better compliance rates in their patients as most of them were prescribing ferrous ascorbate sustained-release formulation with better efficacy and tolerability, thus better drug adherence.

In developed and developing nations, the common indications for parenteral infusion of iron supplements are intolerance, adverse GI effects, not responding to oral iron, and complete non-compliance, which coincide with our survey outcomes.[26] In our survey, the most common reason for non-adherence was intolerability (side-effects) among the non-compliant population, similar to the study mentioned above. Constipation, nausea/vomiting, black stools, and gastritis were reported as the most common side-effects of iron supplementation by our study respondents. Evidence suggests similar side-effects in oral iron supplementation.[32]

Iron carboxymaltose is the drug of choice for parenteral use.[33] However, Iron sucrose is the most commonly used IV iron therapy worldwide, with clinical experience encircling 25 million patient-years.[34] The Federation of Obstetric and Gynaecological Societies of India (FOGSI) also recommend iron sucrose as it is cost-effective and readily available compared to other options.[35] Half of the gynaecologists followed the recommended option by the Government of India for prescribing iron sucrose to their patients. According to WHO, effective communication is required to improve the acceptability and compliance to the iron supplements prescribed.[36] A similar outcome was reported in our survey where the importance of taking iron was the most prominent aspect of counselling patients for taking an oral iron supplement.

It is wise to point out certain limitations of the study, including the administration of survey questionnaires digitally and the possibility of obtaining unconscious responses or survey fatigue among the participating population. The number of participants was insufficient to establish any generalised result, thus necessitating more such studies on a larger scale to postulate an effective conclusion.

CONCLUSION

IDA continues to be a primary concern among Indian women of reproductive age. Several guidelines have been formulated on a national level to lower the burden of IDA, however, these measures seem to be ineffective to show proven results. This survey provided a better understanding of the prescribing pattern of iron supplements among gynaecologists from different zones of India, including the better outcomes associated with sustained-release formulation and the use of L-methylfolate in reducing non-compliance rates, thus providing a standardized approach with the goal of improving patient care and clinical outcomes.

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