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Iron-deficiency, Iron-deficiency Anemia & Contraception: **Bibliography**

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Contents

DOCUMENT OVERVIEW

This annotated bibliography was created to review existing evidence and better understand knowledge gaps related to the role of hormonal contraception in preventing and/or alleviating iron deficiency and iron-deficiency anemia. This bibliography serves as a collection of relevant literature related to hormonal contraception and iron deficiency/iron deficiency anemia in global settings and among diverse populations with the goal to aid in exploring potential areas for collaboration and to break down silos between family planning and nutrition fields (among others) in tackling anemia prevention.

This bibliography was developed beginning with a rapid literature review using PubMed, Global Health CINAHL, and Cochrane review databases. Additional sources were incorporated through handsearching.

The bibliography is organized into three key categories based on the overarching focus of the article: health topic (intervention or health issue), population of interest, and geographic location. Key themes within these broad categories have been identified and resources are categorized by these themes. The **hormonal contraceptives** section is organized by the primary focus of the literature, beginning with **general hormonal contraceptives** (often containing more than one type of contraceptive in the study), followed by articles primarily focused on **levonorgestrel-releasing intrauterine systems** (LNG-IUS), and finally **oral contraceptives**. This section is followed by literature focused on **abnormal bleeding -** its various intersections with hormonal contraceptives and associations with anemia. The next section includes literature with the primary focus of **nutrition and** intersections with anemia and hormonal contraceptives. The bibliography then transitions to literature organized by population and setting. Population focused sections are organized into two categories: **adolescents** and **athletes**. The next section of evidence is organized by setting, including low- and middle-income countries, Europe, and the United States. The final section is a list of relevant grey literature.

Articles are first organized within sections by sub-theme and then by author last name. Articles with particular relevance to our aims are highlighted in green for easy reference. Articles that fit into multiple themes have been cross-referenced in corresponding sections accordingly.

PRIMARY FOCUS: HORMONAL CONTRACEPTIVES

GENERAL HORMONAL CONTRACEPTIVES

1. **Aboagye, R. G., Okyere, J., Seidu, A. A., Ahinkorah, B. O., Budu, E., & Yaya, S. (2023). Relationship between history of hormonal contraceptive use and anaemia status among women in sub-Saharan Africa: A large population-based study. Plos one, 18(6), e0286392. https://doi.org/10.1371/journal.pone.0286392**

BACKGROUND: Anaemia among women has been reported to be a significant contributor to hemorrhage, exacerbated risk of stillbirths, miscarriages, and maternal mortalities. Hence, understanding the factors associated with anaemia is imperative to develop preventive strategies. We examined the association between history of hormonal contraceptive use and risk of anaemia among women in sub-Saharan Africa.

METHODS: We analyzed data from the recent Demographic and Health Surveys (DHS) of sixteen countries in sub-Saharan Africa. Countries with recent DHSs conducted from 2015 to 2020 were included in the study. A total of 88,474 women of reproductive age were included. We used percentages to summarize the prevalence of hormonal contraceptives and anaemia among women of reproductive age. We used multilevel binary logistic regression analysis to examine the association between hormonal contraceptives and anaemia. We presented the results using crude odds ratio (cOR) and adjusted odds ratios (aOR), with their respective 95 percent confidence intervals (95% CIs).

RESULTS: On the average, 16.2% of women are using hormonal contraceptives and this ranged from 7.2% in Burundi to 37.7% in Zimbabwe. The pooled prevalence of anaemia was 41%, ranging from 13.5% in Rwanda to 58.0% in Benin. Women who used hormonal contraceptives were less likely to be anaemic compared to those who were not using hormonal contraceptives (aOR = 0.56; 95%CI = 0.53, 0.59). At the country-level, hormonal contraceptive use was associated with a reduced likelihood of anaemia in 14 countries, except for Cameroon and Guinea.

CONCLUSION: The study underscores the importance of promoting the use of hormonal contraceptives in communities and regions that have a high burden of anaemia among women. Specifically, health promotion interventions aimed at promoting the use of hormonal contraceptives among women must be tailored to meet the needs of adolescents, multiparous women, those in the poorest wealth index, and women in union as these sub-populations were at significantly higher risk of anaemia in sub-Saharan Africa.

2. **Haider, Z., & D'Souza, R. (2009). Non-contraceptive benefits and risks of contraception. *Best Practice & Research: Clinical Obstetrics & Gynaecology*, *23*(2), 249–262. https://doi.org/10.1016/j.bpobgyn.2008.12.003**

Contraception is primarily used to prevent pregnancy. However, a user should be aware of both the possible non-contraceptive benefits she/he may experience and any potential risks to her/his health. These issues should be discussed as fully as possible, using current, evidence-based information prior to commencing a method. Some methods may be prescribed solely for their non-contraceptive benefits for a woman who does not require it for contraception. Potential risks to a woman's health may make certain methods unacceptable if concurrent medical problems or lifestyle issues exist. This chapter discusses the main non-contraceptive benefits and risks for each contraceptive method in turn.

3. **Haile, Z. T., Kingori, C., Teweldeberhan, A. K., & Chavan, B. (2017). The relationship between history of hormonal contraceptive use and iron status among women in Tanzania: A population-based study. *Sex Reprod Healthc*, *13*, 97–102. https://doi.org/10.1016/j.srhc.2017.07.003**

OBJECTIVES: Approximately 30% of the Tanzanian women in the reproductive age group are iron deficient. At population-level, there is a dearth of research on the relationship between hormonal contraceptive use and iron deficiency. The study objective was to examine the relationship between history of hormonal contraceptive use and iron status among women in Tanzania.

STUDY DESIGN: We conducted a cross-sectional study analysis including 4186 women who participated in the population-based 2010 Tanzania Demographic and Health Survey.

MAIN OUTCOME MEASURE: Iron status determined by iron deficiency, anemia, and iron deficiency anemia.

RESULTS: Almost 19.0% women reported history of hormonal contraceptive use. Nearly, 30.0%, 39.5%, and 14.3% women had iron deficiency, anemia and iron deficiency anemia respectively. History of hormonal contraceptive use was negatively associated with iron deficiency, anemia and iron deficiency anemia, independent of potential confounders. Compared to non-users, the multivariable-adjusted odds ratio OR (95% CI) among hormonal contraceptive users was 0.73 (0.56-0.94, p<0.05) for iron deficiency, 0.58 (0.46-0.72, p<0.001) for anemia, and 0.53 (0.37-0.74; p<0.001) for iron deficiency anemia. Longer duration of hormonal contraceptive use (>2years) had lesser odds of iron deficiency 0.63 (0.43-0.91, p for trend 0.005), anemia 0.51 (0.36-0.73, p for trend <0.001) and iron deficiency anemia 0.35 (0.19-0.65, p for trend <0.001).

CONCLUSION: Our finding has important implications for educating healthcare providers and women about additional nutritional benefits of the use of hormonal contraceptives.

4. **Rana, M. J., & Goli, S. (2017). THE RETURNS OF FAMILY PLANNING: MACRO-LEVEL ASSESSMENT OF THE EFFECT OF CONTRACEPTIVE USE ON WOMEN'S ANAEMIA AND CHILDHOOD UNDERNUTRITION. *J Biosoc Sci*, *49*(6), 773–791. https://doi.org/10.1017/s0021932016000717**

This study investigated the effect of family planning on the levels of women's anaemia and child undernutrition at the aggregate level using the compiled databases of the World Bank, UNICEF and the Economist Intelligence Unit. Correlation scatter matrix plots and multivariate OLS regression models were employed to assess the effect of family planning on women's anaemia and child nutritional status across countries. At the aggregate level, the bivariate correlation estimates found that the Contraceptive Prevalence Rate (CPR) was negatively associated with women's anaemia (r=-0.62, p<0.01), child underweight (r=-0.57, p<0.01) and child stunting (r=-0.63, p<0.01). The results of the OLS regression showed that the independent effect of CPR on women's anaemia (β=-0.35, p<0.01), child underweight (β=-0.13, p<0.01) and child stunting (β=-0.18, p<0.05) was negative, even after controlling for child marriage, female literacy, per capita GDP, poverty ratio, health expenditure and food security. The synthesis of these findings with the existing literature based on micro-data suggests pathways through which family planning influences the nutritional status of women and children. Family planning helps in avoiding shorter birth intervals, unintended pregnancy and unsafe abortion, which would otherwise result in nutrient depletion among mothers and further increase the risk of undernutrition in their children.

5. **Samuelson Bannow, B., McLintock, C., & James, P. (2021). Menstruation, anticoagulation, and contraception: VTE and uterine bleeding. *Res Pract Thromb Haemost*, *5*(5), e12570. https://doi.org/10.1002/rth2.12570**

   Abnormal or excessive menstrual bleeding affects one-third of reproductive-aged women. This number increases to 70% among women on direct oral anticoagulants (DOACs). While there is some variation in frequency of heavy menstrual bleeding (HMB) with different DOAC options, all menstruating individuals should receive counseling about the risk of HMB at the time of DOAC initiation. Management options include progestin-only therapies such as the levonorgestrel intrauterine system and etonogestrel subdermal implant or the progestin-only pill. Combined hormonal contraceptives and depot medroxyprogesterone acetate are associated with increased rates of thrombosis in nonanticoagulated women but may be continued, or even initiated, so long as therapeutic anticoagulation is ongoing. Procedural therapies, such as endometrial ablation, uterine artery embolization, or hysterectomy, are considerations for women who have completed childbearing and for whom more conservative measures are objectionable or ineffective. Given the high rates of HMB in women on DOACs, management strategies should be discussed even before heavy bleeding is diagnosed, particularly in women who experienced HMB prior to DOAC initiation. As iron deficiency with or without anemia is a common complication of HMB, complete blood count and ferritin levels should be monitored periodically, and iron deficiency should be treated with oral or intravenous iron supplementation.

Relevant Articles Cross-Referenced from Other Sections

Low-and-Middle-Income Countries

Ahmed, N., Mostafa, R., Abuelghar, W., Elbishry, G. (2018) Discontinuation Rates among Copper Intrauterine Device Users in Primary Healthcare Unit and University Clinic. Is There a Difference?. *The Egyptian Journal of Hospital Medicine*, 72(11), 5658-5665. https://ejhm.journals.ekb.eg/article_11543.html

Meertens, L., Solano, L., Sanchez, A. (2002). Hemoglobin, serum ferritin and zinc in women in reproductive ages: Its association with the use of contraceptives. *An. venezia. nourish,* 15(1), 5-10. https://search.bvsalud.org/gim/resource/en/lil-341005

Salehian, T., Delaram, M., Safdari, F., Alavi, A., Noor Bakhshian, M., Salehifard, A.Z. (2008). Comparison of Two Commonly Used IUDs in Pain and Menstrual Bleeding. *Journal of Shahrekord University of Medical Sciences*, 10 (3), 23-28. https://search.bvsalud.org/gim/resource/en/emr-88112

Samah Mohamed Ali Abd El- Azym, M. (2018). Levonorgestrel Releasing IUS (Metraplant E) in the Management of Copper IUD Related Heavy Painful Menstrual Loss. *The Egyptian Journal of Hospital Medicine*, 71(5), 3158-3165. https://applications.emro.who.int/imemrf/Egypt_J_Hosp_Med/Egypt_J_Hosp_Med_2018_71_5_3158_3165.pdf

LEVENORGESTREL-RELEASING INTRAUTERINE SYSTEMS (LNG IUS)

6. **Fraser, I. S. (2010). Non-contraceptive health benefits of intrauterine hormonal systems. *Contraception*, *82*(5), 396–403. https://doi.org/10.1016/j.contraception.2010.05.005**

   Non-contraceptive health benefits are now recognized as an important aspect of the overall impact of all hormonal contraceptives. The levonorgestrel-releasing intrauterine systems (LNG IUS) are particularly effective at producing a number of health benefits for women using the LNG IUS as a contraceptive (reduced menstrual bleeding; reduced dysmenorrhea and the potential for prevention of a number of gynecological conditions in the longer term, such as iron-deficiency anemia, endometrial hyperplasia, uterine fibroids, acute episodes of pelvic inflammatory disease, endometriosis and perhaps others). The LNG IUS also has the potential to specifically treat a range of pre-existing gynecological conditions such as heavy menstrual bleeding due to a wide range of underlying causes, endometrial hyperplasia, uterine fibroids, adenomyosis, and endometriosis. These health benefits should be recognized as a key component in the decision-making process for individual women in choosing a specific type of hormonal or other contraceptive. Investment in research into the very substantial health benefits of hormonal contraceptives, such as the LNG IUS, has generally been ignored in comparison with the massive investment into understanding the often subtle or rare complications of hormonal contraceptive use. Both are important, but there is a real need to define more accurately those women who will benefit most from these health benefits.

7. **Lowe, R. F., & Prata, N. (2013). Hemoglobin and serum ferritin levels in women using copper-releasing or levonorgestrel-releasing intrauterine devices: a systematic review. Contraception, 87(4), 486- 496. https://doi.org/10.1016/j.contraception.2012.09.025**

   BACKGROUND: The use of intrauterine devices as a contraceptive method has been steadily growing in developing countries. Anemia in reproductive-age women is a growing concern in those settings.

   STUDY DESIGN: A systematic review of studies with measured hemoglobin and serum ferritin at baseline and after 1 year of use of copper intrauterine devices (IUDs) or a levonorgestrel releasing intrauterine system (LNG IUS) was performed.

   RESULTS: Fourteen studies involving copper IUDs in nonanemic women and 4 studies in anemic women and 6 involving the LNG IUS met the criteria for the systematic review. Meta-analyses for hemoglobin changes showed significant decreases for users of copper IUDs and an increase for the LNG IUS, but with limited data. In general, ferritin levels followed the same pattern.

   CONCLUSION: Decreases in hemoglobin mean values in copper IUD users were not sufficient to induce anemia in previously nonanemic women. Women who are borderline anemic would likely benefit from using the LNG IUS

8. **Luukkainen, T. (2000). The levonorgestrel intrauterine system: therapeutic aspects. *Steroids*, *65*(10–11), 699–702. https://doi.org/10.1016/s0039-128x(00)00177-x**

   Use of the levonorgestrel-releasing intrauterine system (LNG IUS) is associated with a strong reduction in the number of days of bleeding and menstrual blood loss. This effect is based on the marked local action of the intrauterine release of levonorgestrel (LNG) on the endometrium. In suppressed endometrium the production of many highly active compounds ceases. On the other hand, LNG stimulates the synthesis of some regulatory proteins in the endometrium. Reduction of menstrual blood loss results in improvement

of the body iron balance and in an increase in hemoglobin concentration. The LNG IUS has been used in the prevention and treatment of iron deficiency anemia. Many studies have demonstrated that the LNG IUS is effective in the treatment of menorrhagia. Reduction of excessive blood loss is seen as soon as the first menstruation after insertion, and at 1 year the reduction is more than 90%. The therapeutic effect is maintained for more than 5 years after first placement of the LNG IUS in the uterine cavity. Correct insertion is essential, and complications and side effects are rare; fertility is preserved, and invasive procedures such as endometrial ablation or hysterectomy and hospitalization are avoided. The third major indication for therapeutic use is in protection of the endometrium in estrogen replacement therapy during peri- and postmenopausal years. A fundal position of the system in the uterine cavity results in reduction of bleeding, and an increasing number of women have no bleeding at all during use of the IUS. Acceptance and continuation of use of the LNG IUS in hormone replacement therapy (HRT) have been high.

9. **Cozza, G., Pinto, A., Giovanale, V., Bianchi, P., Guarino, A., Marziani, R., Frega, A., & Caserta, D. (2017). Comparative effectiveness and impact on health-related quality of life of hysterectomy vs. levonorgestrel intra-uterine system for abnormal uterine bleeding. *Eur Rev Med Pharmacol Sci*, *21*(9), 2255–2260. https://www.europeanreview.org/article/12708**

OBJECTIVE: To compare hysterectomy and levonorgestrel intra-uterine system (LNG-IUS) for the treatment of abnormal uterine bleeding (AUB) and iron deficiency anemia.

PATIENTS AND METHODS: Retrospective study evaluating quality of life, sexual function, satisfaction, and blood hemoglobin concentration improvement in 60 pre-menopausal women treated with hysterectomy or LNG-IUS. All analysis was performed with statistical software SPSS 21.0 (SPSS Inc., Chicago, IL, USA).

RESULTS: Despite superior control of bleeding and dysmenorrhea observed after hysterectomy, LNG-IUS showed similar impact on blood hemoglobin levels, quality of life, satisfaction and sexual function resulting more cost-effective.

CONCLUSIONS: In the absence of contraindications, LNG-IUS should always be the first therapeutic choice for chronic AUB. Surgical treatment must be considered as an "extrema ratio".

10. **Fraser, I. S. (2013). Added health benefits of the levonorgestrel contraceptive intrauterine system and other hormonal contraceptive delivery systems. *Contraception*, *87*(3), 273–279. https://doi.org/10.1016/j.contraception.2012.08.039**

BACKGROUND: It has been recognized for well over half a century that hormonal preparations designed as contraceptives are also capable of offering health benefits through the treatment and prevention of benign gynecological disease and even some systemic conditions. Increasing attention is now being paid to the extent and detail of such added health benefits, and it is becoming clear that the long-acting, low-dose, hormonal contraceptive delivery systems may offer particular advantages in this regard.

METHODS: Conventional databases were thoroughly searched, especially for publications from 2006 to 2012, which addressed non-contraceptive-related indications for therapy and prevention.

RESULTS: A considerable literature now exists to demonstrate the multiple and substantial noncontraceptive health benefits of long-acting progestogen-releasing systems, especially the levonorgestrel-releasing intrauterine system. These benefits mainly relate to disturbances of menstruation and related symptoms, such as heavy menstrual bleeding (due to many causes); iron deficiency; pelvic pain, especially around endometriosis; and endometrial hyperplasia. The long-acting

estrogen-progestogen systems may carry similar added health benefits to those of the combined oral contraceptives, but data are still lacking.

CONCLUSION: Added health benefits are now becoming an important part of the contraceptive choice equation, and the long-acting delivery systems are recognized as suitable primary therapies for a range of gynecological disorders.

11. **Ueda, Y., Kamiya, C. A., Horiuchi, C., Miyoshi, T., Hazama, R., Tsuritani, M., Iwanaga, N., Neki, R., Ikeda, T., & Yoshimatsu, J. (2019). Safety and efficacy of a 52-mg levonorgestrel-releasing intrauterine system in women with cardiovascular disease.** ***J Obstet Gynaecol Res*****,** ***45*****(2), 382–388. https://doi.org/10.1111/jog.13828**

AIM: We sought to examine the safety and efficacy of a 52-mg levonorgestrel-releasing intrauterine system (LNG-IUS), and to evaluate the changes in biomarkers of infection, anemia and cardiovascular conditions after LNG-IUS insertion in women with cardiovascular disease.

METHODS: We prospectively followed women with a cardiovascular disease in whom a 52-mg LNG-IUS was inserted between 2009 and 2015. The primary outcome was the frequency of cardiovascular and gynecologic side effects due to the LNG-IUS over the year after LNG-IUS insertion. The secondary outcomes were the changes in menstrual blood loss and biomarkers, e.g., white blood cell count and the levels of C-reactive protein, hemoglobin and brain natriuretic peptide. We also evaluated the 24-month continuation rate of LNG-IUS.

RESULTS: A total of 34 women were prospectively followed-up, including two women with pulmonary hypertension. No cardiovascular side effects were identified during the 1 year after LNG-IUS insertion, other than one case of mild vasovagal reaction at insertion. Neither the white blood cell count nor the C-reactive protein value increased after LNG-IUS insertion. The menstrual blood loss was decreased in most subjects and the median hemoglobin levels increased significantly within 1 year after insertion ($P < 0.001$ and $P = 0.002$). Moreover, brain natriuretic peptide levels tended to decrease in correspondence with the hemoglobin elevation ($P = 0.074$). The 24-month LNG-IUS continuation rate was 97% (95% confidence interval 85-100).

CONCLUSION: No clinically significant cardiovascular event was identified during the 1 year after 52-mg LNG-IUS insertion among women with cardiovascular disease. The 52-mg LNG-IUS may have specific favorable effects by decreasing the risk of iron deficiency anemia in these women.

12. **Wildemeersch, D., Andrade, A., & Goldstuck, N. (2016). Femilis® 60 Levonorgestrel-Releasing Intrauterine System--A Review of 10 Years of Clinical Experience.** ***Clinical Medicine Insights: Reproductive Health*****,** ***10*****, 19–27. https://doi.org/10.4137/CMRh.s40087**

OBJECTIVE: The aim of this study was to update the clinical experience with the Femilis® 60 levonorgestrel-releasing intrauterine system (LNG-IUS), now up to 10 years in parous and nulliparous women, particularly with regard to ease and safety of insertion, contraceptive performance, retention, acceptability, continuation of use, impact on menstrual blood loss (MBL), and duration of action.

STUDY DESIGN: Using the Femilis® 60 LNG-IUS releasing 20 µg of levonorgestrel/day, the following studies were conducted: an open, prospective noncomparative contraceptive study, an MBL study, a perimenopausal study, a study for the treatment of endometrial hyperplasia, and early cancer of the uterus, a residue study.

RESULTS: A total of 599 Femilis LNG-IUS were inserted in various clinical trials, the majority for contraceptive purposes. The total exposure in the first and second contraceptive studies, covering 558 parous and nulliparous women, was 32,717 woman-months. Femilis has high contraceptive effectiveness as only one pregnancy occurred. Expulsion of the LNG-IUS was rare with only two total and no partial expulsions (stem protruding through the cervical canal) occurred. Femilis was well tolerated, with continuation rates remaining high. Several MBL studies were conducted, totaling 80 heavy and normal menstrual bleeders, using the pictorial bleeding assessment chart method or the quantitative alkaline hematin technique. Virtually all women responded well with strongly reduced menstrual bleeding. Amenorrhea rates were high, up to 80% after three months, and ferritin levels simultaneously increased significantly. The Femilis LNG-IUS was tested in 104 symptomatic perimenopausal women for seamless transition to and through menopause, adding estrogen therapy when required. Patient tolerability appeared high as .80% requested a second and a third LNG-IUS. Twenty women presenting with nonatypical and atypical hyperplasia and one woman presenting with early endometrial carcinoma were treated with Femilis LNG-IUS. All histology specimens showed full regression, and patients remained in remission without signs of hyperplasia or cancer at yearly and ongoing follow-up examinations up to 10 years. Residual content of LNG was measured in 37 women having the Femilis LNG-IUS for up to 10 years. In 10 of the 102 women who had the Femilis 60 in situ for 10 years between 20% and 30% of the original 60 mg was recovered confirming the long duration of action of the Femilis 60 LNG-IUS.

CONCLUSION: These studies suggest that the Femilis 60 LNG-IUS releasing 20 µg of LNG/day is an effective, well-tolerated, and well-retained contraceptive both in parous and in nulliparous women. The design of the LNG-IUS, with flexible transverse arm(s) length of 28 mm, allows for a simplification of the insertion technique and training requirements facilitating the use by nonspecialist providers in either developed or developing countries. For nulliparous women, additional evaluation of devices with a 24 mm transverse arm(s), as it relates to tolerability, retention, and continuation of use, still needs to be undertaken.

Relevant Articles Cross-Referenced from Other Sections

Abnormal Bleeding

Tam, W. H., Yuen, P. M., Shan Ng, D. P., Leung, P. L., Lok, I. H., & Rogers, M. S. (2006). Health status function after treatment with thermal balloon endometrial ablation and levonorgestrel intrauterine system for idiopathic menorrhagia: a randomized study. *Gynecol Obstet Invest*, *62*(2), 84–88. https://doi.org/10.1159/000092660

Low-and-Middle-Income Countries

Samah Mohamed Ali Abd El- Azym, M. (2018). Levonorgestrel Releasing IUS (Metraplant E) in the Management of Copper IUD Related Heavy Painful Menstrual Loss. *The Egyptian Journal of Hospital Medicine*, 71(5), 3158-3165. https://platform.almanhal.com/Files/2/117427

ORAL CONTRACEPTIVES

13. Bellizzi, S., & Ali, M. M. (2018). Effect of oral contraception on anemia in 12 low- and middle-income countries. Contraception, 97(3), 236-242. https://doi.org/10.1016/j.contraception.2017.11.001

CONTEXT: In low- and middle-income countries, anemia is a major public health issue in women of reproductive age for a series of factors including iron deficiency. OBJECTIVE: To estimate prevalence of anemia and to assess the association of low level of hemoglobin versus duration of use of oral contraceptives (OC).

METHODS: Demographic and Health Surveys of 12 countries, conducted between 2005 and 2012, were analyzed. The status of anemia was separately evaluated for nonpregnant women using OC for at least 6 months, 1 year and 2 years, and for women using no method of contraception and/or using nonhormonal contraception.

RESULTS: The total study population comprised 201,720 women, with 40% diagnosed with anemia; around 1 out of 25 women was using oral contraception. The current and continuous use of oral contraception was of benefit against anemia, with the risk for anemia decreasing from odds ratio (OR) 0.68 [95% confidence interval (CI) 0.64–0.73] for use of at least 6 months to OR 0.56 (95% CI 0.52–0.61) for use of at least 1 year and to OR 0.50 (95% CI 0.46–0.54) for use of at least 2 years.

CONCLUSIONS: Findings reinforce evidence of the noncontraceptive benefit of long-term use of OC and provide valuable information for policy makers, family planning staff and clinicians working in low- and middle-income countries in efforts to control anemia.

14. **Casabellata, G., di Santolo, M., Banfi, G., Stel, G., Gonano, F., & Cauci, S. (2007). Evaluation of iron deficiency in young women in relation to oral contraceptive use. *Contraception*, *76*(3), 200–207. https://doi.org/10.1016/j.contraception.2007.04.016**

BACKGROUND: The purpose of this study was to identify the optimal measures for diagnosing iron deficiency (ID) in oral contraceptive (OC) users and nonusers, and to estimate ID frequency in relation to OC use.

STUDY DESIGN: Conventional biomarkers of iron status - serum ferritin, iron, transferrin (Tf) and transferrin saturation (TfS) - were compared with serum soluble Tf receptor (sTfR) and the sTfR/log ferritin ratio (sTfR-F index). Two hundred two healthy menstruating white Italian women (aged 24+/-4.8 years) were analyzed. Serum ferritin concentrations <12 microg/L were considered as ID.

RESULTS: ID was detected in 29.7% (60/202) of the study women. Fifty-nine women were OC users (59/202, 29.2%). OC use did not significantly affect ID prevalence (p=.24). However, OC use markedly increased Tf in OC users, who had an odds ratio (OR) of 9.3 (CI 3.8-22.7, p<.001) for elevated Tf >330 mg/dL. No other iron status measure was affected by OC. Of the markers for ID adjunctive to ferritin, an elevated sTfR-F index >or =1.5 showed the best performance. Specifically in OC users, the elevated sTfR-F index had better sensitivity (81.0% vs. 33.3%), specificity (94.7% vs. 92.1%), efficiency (89.8% vs. 71.2%), positive predictive value (89.5% vs. 70.0%) and negative predictive value (90.0% vs. 71.1%) than a TfS <15%. Additionally, the sTfR-F index allowed the identification of low iron stores in 4.5% (9/202) of women with ferritin > or =12 microg/L.

CONCLUSION: Among healthy OC users and non-OC users, the sTfR-F index had the highest performance for diagnosing ID compared with other serum markers adjunctive to ferritin measurements, whereas sTfR by itself had a low sensitivity. We showed that neither the sTfR nor sTfR-F index was affected by third-generation OC use. The sTfR measurement is useful in the diagnosis of ID, especially in women using OC, where Tf and TfS tests may be misleading.

15. **Cedars, M. I. (2002). Triphasic oral contraceptives: review and comparison of various regimens. *Fertil Steril*, *77*(1), 1–14. https://doi.org/10.1016/s0015-0282(01)02927-2**

OBJECTIVE: To review and compare the risk-benefit profile of triphasic oral contraceptives with that of low-dose monophasic oral contraceptives. DESIGN: Literature on currently marketed triphasics and monophasics.

PATIENT(S): Healthy women of reproductive age.

MAIN OUTCOME MEASURE(S): Comparison of the rationale for development, composition, mechanism, efficacy, menstrual cycle control, side effects, health benefits, and risk-benefit profile.

RESULT(S): All triphasics contain ethinyl estradiol (0.025-0.040 mg/d) and one of several progestins in doses (0.05-1.0 mg/d) related to their relative potencies, which are substantially lower overall (total dose) than those in monophasics. The triphasics are highly efficacious. In general, menstrual cycle control and side effects are similar in both types, but triphasics containing the newer progestins (desogestrel, gestodene, and norgestimate) have better cycle control and a reduced incidence of androgenic side effects compared with those with norethindrone or levonorgestrel. Both triphasics and monophasics have minimal effects on carbohydrate and lipid metabolism and hemostasis parameters, and therefore comparable low risks of coronary heart disease. The health benefits of triphasics and monophasics are similar and include decreased incidence of unwanted and ectopic pregnancies, ovarian cysts, endometrial and ovarian cancers, benign breast disease, and acute pelvic inflammatory disease; less menstrual blood loss and iron deficiency anemia; and lower frequency of irregular bleeding and menorrhagia.

CONCLUSION(S): The risk-benefit profiles of both triphasics and monophasics are favorable and similar.

16. **Dayal, M., & Barnhart, K. T. (2001). Noncontraceptive benefits and therapeutic uses of the oral contraceptive pill. *Semin Reprod Med*, *19*(4), 295–303. https://doi.org/10.1055/s-2001-18637**

The oral contraceptive pill is one of the most extensively studied medications ever prescribed. The health benefits are numerous and outweigh the risks of their use. Definitive evidence exists for protection against ovarian and endometrial cancers, benign breast disease, pelvic inflammatory disease requiring hospitalization, ectopic pregnancy, and iron-deficiency anemia. It has also been suggested that oral contraceptives may provide a benefit on bone mineral density, uterine fibroids, toxic shock syndrome, and colorectal cancer. Minimal supportive evidence exists for oral contraceptives protecting against the development of functional ovarian cysts and rheumatoid arthritis. Treatment of medical disorders with oral contraceptives is an "off-label" practice. Dysmenorrhea, irregular or excessive bleeding, acne, hirsutism, and endometriosis-associated pain are common targets for oral contraceptive therapy. Most patients are unaware of these health benefits and therapeutic uses of oral contraceptives, and they tend to overestimate their risk. Counseling and education are necessary to help women make well-informed health-care decisions and improve compliance.

17. **Fischer, J. A. J., Sasai, C. S., & Karakochuk, C. D. (2021). Iron-Containing Oral Contraceptives and Their Effect on Hemoglobin and Biomarkers of Iron Status: A Narrative Review. *Nutrients*, *13*(7). https://doi.org/10.3390/nu13072340**

Oral contraceptive use has been associated with decreased menstrual blood losses; thus, can independently reduce the risk of anemia and iron deficiency in women. Manufacturers have recently started to include supplemental iron in the non-hormonal placebo tablets of some contraceptives. The

aims of this narrative review are: (i) to describe the relationship between oral contraceptive use and both anemia and iron status in women; (ii) to describe the current formulations of iron-containing oral contraceptives (ICOC) available on the market; and (iii) to systematically review the existing literature on the effect of ICOC on biomarkers of anemia and iron status in women. We discovered 21 brands of ICOC, most commonly including 25 mg elemental iron as ferrous fumarate, for seven days, per monthly tablet package. Our search identified one randomized trial evaluating the effectiveness of ICOC use compared to two non-ICOC on increasing hemoglobin (Hb) and iron status biomarker concentrations in women; whereafter 12 months of contraception use, there were no significant differences in Hb concentration nor markers of iron status between the groups. ICOC has the potential to be a cost-effective solution to address both family planning needs and iron deficiency anemia. Yet, more rigorous trials evaluating the effectiveness of ICOC on improving markers of anemia and iron deficiency, as well as investigating the safety of its consumption among iron-replete populations, are warranted.

18. **Sim, M., Dawson, B., Landers, G., Swinkels, D. W., Wiegerinck, E., Yeap, B. B., Trinder, D., & Peeling, P. (2017). Interleukin-6 and Hepcidin Levels during Hormone-Deplete and Hormone-Replete Phases of an Oral Contraceptive Cycle: A Pilot Study. *Ann Nutr Metab*, *70*(2), 100–105. https://doi.org/10.1159/000465530**

BACKGROUND: In the past, elevated estradiol levels were reported to downregulate the iron regulatory hormone hepcidin, thereby potentially improving iron metabolism. As estrogen plays a role in regulating the menstrual cycle and can influence the cytokine interleukin-6 (IL-6; a hepcidin up-regulator), this investigation examined the effects of estradiol supplementation achieved by the use of a monophasic oral contraceptive pill (OCP) on IL-6, hepcidin levels and iron status during the hormone-deplete versus hormone-replete phases within an oral contraceptive cycle (OCC).

METHODS: Fifteen healthy female OCP users were recruited and provided a venous blood sample on 2 separate mornings during a 28-day period. These included (a) days 2-4 of the OCC, representing a hormone-free withdrawal period (WD); (b) days 12-14 of the OCC, representing the end of the first week of active hormone therapy (AHT).

RESULTS: IL-6 and hepcidin levels were not significantly different at WD and AHT. Serum ferritin was significantly higher ($p = 0.039$) during AHT as compared to WD.

CONCLUSIONS: Fluctuations in OCP hormones (estradiol and/or progestogen) had no effect on basal IL-6 and hepcidin levels in young women. Nevertheless, elevated ferritin levels recorded during AHT may indicate that OCP hormones can positively influence iron stores within an OCC despite unchanged hepcidin levels.

19. **Haile, Z. T., Teweldeberhan, A. K., & Chertok, I. R. (2016). Association between oral contraceptive use and markers of iron deficiency in a cross-sectional study of Tanzanian women. *Int J Gynaecol Obstet*, *132*(1), 50–54. https://doi.org/10.1016/j.ijgo.2015.06.040**

OBJECTIVE: To analyze the associations between oral contraceptive (OC) use and markers of iron deficiency, objectively measured using hemoglobin and soluble transferrin receptor.

METHODS: A secondary data analysis was performed of a population-based cross-sectional study using data from the 2010 Tanzania Demographic and Health Survey. Weighted percentages were calculated. Multivariable logistic regression was used to examine the associations between OC use and iron deficiency, anemia, and iron deficiency anemia.

RESULTS: Of the 4336 participants, only 7.3% reported a history of OC use. The prevalence rates of iron deficiency, anemia, and iron deficiency anemia were 30.3%, 40.9%, and 15.1%, respectively. Use of OCs was negatively associated with anemia and iron deficiency anemia, independent of potential confounders. Compared with OC nonusers, the multivariable-adjusted odds ratio among OC users was 0.44 (95% confidence interval 0.32-0.59; P<0.001) for anemia and 0.43 (95% confidence interval 0.27-0.68; P<0.001) for iron deficiency anemia. A longer duration of OC use was negatively associated with iron deficiency (P=0.003 for trend), anemia (P<0.001 for trend), and iron deficiency anemia (P<0.001 for trend).

CONCLUSION: The significant association between OC use and iron status has important implications for educating healthcare providers and women about additional nutritional benefits of the use of OCs.

20. **Jensen, J. T., & Speroff, L. (2000). Health benefits of oral contraceptives. *Obstet Gynecol Clin North Am*, *27*(4), 705–721. https://doi.org/10.1016/s0889-8545(05)70169-8**

A sizeable literature corroborates the multiple health benefits of oral contraceptive use. The first estrogen/progestin combination pills were marketed to treat a variety of menstrual disorders. Although currently used oral contraceptives no longer carry FDA-approved labeling for these indications, they remain important therapeutic options for a variety of gynecologic conditions. Well-established gynecologic benefits include a reduction in dysmenorrhea and menorrhagia, iron-deficiency anemia, ectopic pregnancy, and PID. Although older, higher-dose pills reduced the incidence of ovarian cysts, low-dose pills suppress follicular activity less consistently. Nevertheless, cycle-related symptoms, including functional cysts, dysmenorrhea, chronic pelvic pain, and ovulation pain (mittelschmerz), generally improve. Women with polycystic ovary syndrome note improvement in bleeding patterns and a reduction in acne and hirsutism. Symptoms from endometriosis also improve with oral contraceptive therapy. Current data suggest that oral contraceptive therapy increases bone density and that past use decreases fracture risk. Oral contraceptives also improve acne, a major health concern of young women. Oral contraceptives provide lasting reduction in the risk of two serious gynecologic malignancies--ovarian and endometrial cancer. The data with respect to ovarian cancer are compelling enough to recommend the use of oral contraceptives to women at high risk by virtue of family history, positive carrier status of the BRCA mutations, or nulliparity, even if contraception is not required. Health care providers must counsel women regarding these benefits to counteract deeply held public attitudes and misconceptions regarding oral contraceptive use. Messages should focus on topics of interest to particular groups of women. The fact that oral contraceptives increase bone mineral density and reduce ovarian cancer is of great interest to women in their forties and helps influence use and compliance in this group. In contrast, the beneficial effects of oral contraceptives on acne resonates with younger women. Getting the good news out about the benefits of oral contraceptives will enable more women to take advantage of their positive health effects.

21. **Weisberg, E., McGeehan, K., Hangan, J., & Fraser, I. S. (2017). Potentially effective therapy of heavy menstrual bleeding with an oestradiol-nomegestrol acetate oral contraceptive: a pilot study. *Pilot Feasibility Stud*, *3*, 18. https://doi.org/10.1186/s40814-017-0130-2**

BACKGROUND: Heavy menstrual bleeding (HMB) exceeding 80 mL per cycle leads to considerable adverse impact on a woman's iron metabolism, incidence of iron deficiency and anaemia, as well as her functioning in society. The objective of the study is to determine the potential efficacy of a Monophasic oestradiol-17β-nomegestrol acetate (E(2)/Nomac) combined oral contraceptive pill on measured

menstrual blood loss as a pilot study in 12 women with objectively demonstrated HMB (>80 mL per cycle). The pilot study aimed to recruit 20 women.

METHOD: Consented women completed the HMB questionnaire. The blood was taken for haemoglobin, transferrin, iron saturation, TIBC, serum iron and ferritin. Women were given verbal and written detailed instructions for MBL collection for three control cycles and four treatment cycles. RESULTS: Forty-three women were enrolled, but 31 were ineligible and withdrawn (mainly for failure to meet eligibility criteria). Twelve women entered the treatment phase and commenced the E(2)/nomegestrol acetate (NOMAC) 24/4 combined pill treatment on the first day of their fourth cycle. All women with complete MBL measurements had >50% reduction in MBL on treatment (exact 95% confidence interval for proportion with MBL reduction >50%: 69 to 100%). The mean percent reduction in MBL between pretreatment and during treatment was 76.9%, and the median was 79% with a range of 53.7 to 100%.

CONCLUSIONS: This pilot study indicates that the E(2)/NOMAC COC will provide a useful potential option for treating HMB in women with FIGO classification AUB-E (primary endometrial causes) but requires a larger placebo-controlled study for confirmation.

PRIMARY FOCUS: ABNORMAL UTERINE BLEEDING

22. **DeLoughery, E., & Bannow, B. S. (2022). Anticoagulant therapy for women: implications for menstruation, pregnancy, and lactation. *Hematology Am Soc Hematol Educ Program*, *2022*(1), 467–473. https://doi.org/10.1182/hematology.2022000401**

    Estrogen exposure, in the setting of pregnancy, the postpartum state, combined hormonal contraceptives (CHCs), or hormone therapy use, has been clearly associated with increased rates of venous thromboembolism (VTE). Although recurrence rates are low in these settings, up to 70% of anticoagulated menstruating individuals experience abnormal or heavy menstrual bleeding (HMB), which commonly results in iron deficiency with or without anemia. Patients taking rivaroxaban appear to experience higher rates of HMB compared with those on apixaban, dabigatran, or warfarin. HMB can often be diagnosed in a single visit with a good menstrual history assessing for factors with a known association with increased or heavy bleeding, such as changing pads or tampons more often than every 2 hours, clots larger than a quarter, and iron deficiency (ferritin <50 ng/mL). HMB can be managed with hormonal therapies, including those associated with VTE risk, such as CHCs and depot-medroxyprogesterone acetate (DMPA). In many cases, continuing CHCs or DMPA while a patient is therapeutically anticoagulated is reasonable, so long as the therapy is discontinued before anticoagulation is stopped. Modification of the anticoagulation regimen, such as decreasing to a prophylactic dose in the acute treatment period, is not currently recommended. For patients who are currently pregnant, low-molecular-weight heparin (LMWH) is still standard of care during pregnancy; routine monitoring of anti-factor Xa levels is not currently recommended. Warfarin or LMWH may be considered in the postpartum setting, but direct-acting oral anticoagulants are currently not recommended for lactating patients.

23. **Druckmann, R. (2010). Dysfunctional uterine bleeding: from adolescence to menopause. *Horm Mol Biol Clin Investig*, *3*(3), 461–467. https://doi.org/10.1515/hmbci.2010.043**

    Dysfunctional uterine bleeding (DUB) is defined as excessive or prolonged uterine bleeding in premenopausal women that is not caused by pelvic pathology, medications, systemic disease or pregnancy. It is a common condition that can lead not only to physical symptoms such as iron deficiency, anaemia, cramps and fatigue, but also has significant psychological and social effects that impair a

woman's quality of life. Progesterone is highly important in the regulation of menstrual bleeding and a progesterone-deficient anovulatory state is a common cause of DUB. There are a wide range of treatment options available including hormonal therapies (oral cyclical progestogens, depot progestogens, progestogen-releasing intrauterine devices, combined oral contraceptives, danazol, gonadotrophin-releasing hormone analogues and hormone replacement therapy), non-hormonal therapies (non-steroidal anti-inflammatory drugs and antifibrinolytic drugs) and surgery (hysterectomy and endometrial ablation). The choice of appropriate therapy should be based on factors such as the mechanism behind the DUB, which symptoms are most problematic, and the woman's need for fertility or contraception. However, there is currently a lack of clinical evidence to help support these decisions.

24. **Ragni, M. v, Machin, N., Malec, L. M., James, A. H., Kessler, C. M., Konkle, B. A., Kouides, P. A., Neff, A. T., Philipp, C. S., & Brambilla, D. J. (2016). Von Willebrand factor for menorrhagia: a survey and literature review.** ***Haemophilia*****,** ***22*****(3), 397–402. https://doi.org/10.1111/hae.12898**

    BACKGROUND: von Willebrand disease (VWD) is the most common congenital bleeding disorder. In women, menorrhagia is the most common bleeding symptom, and is disabling with iron deficiency anaemia, high health cost and poor quality of life. Current hormonal and non-hormonal therapies are limited by ineffectiveness and intolerance. Few data exist regarding von Willebrand factor (VWF), typically prescribed when other treatments fail. The lack of effective therapy for menorrhagia remains the greatest unmet healthcare need in women with VWD. Better therapies are needed to treat women with menorrhagia.

    METHODS: We conducted a survey of US haemophilia treatment centres (HTCs) and a literature review using medical subject heading (MeSH) search terms 'von Willebrand factor,' 'menorrhagia' and 'von Willebrand disease' to assess the use of VWF in menorrhagia. Analysis was by descriptive statistics.

    RESULTS: Of 83 surveys distributed to HTC MDs, 20 (24.1%) provided sufficient data for analysis. Of 1321 women with VWD seen during 2011-2014, 816 (61.8%) had menorrhagia, for which combined oral contraceptives, tranexamic acid and desmopressin were the most common first-line therapies for menorrhagia, whereas VWF was third-line therapy reported in 13 women (1.6%). Together with data from 88 women from six published studies, VWF safely reduced menorrhagia in 101 women at a dose of 33-100 IU kg(-1) on day 1-6 of menstrual cycle.

    CONCLUSIONS: This represents the largest VWD menorrhagia treatment experience to date. VWF safely and effectively reduces menorrhagia in women with VWD. A prospective clinical trial is planned to confirm these findings.

25. **Tam, W. H., Yuen, P. M., Shan Ng, D. P., Leung, P. L., Lok, I. H., & Rogers, M. S. (2006). Health status function after treatment with thermal balloon endometrial ablation and levonorgestrel intrauterine system for idiopathic menorrhagia: a randomized study.** ***Gynecol Obstet Invest*****,** ***62*****(2), 84–88. https://doi.org/10.1159/000092660**

    AIM: To compare patients' health status function after treatment with thermal balloon endometrial ablation (TBEA) and levonorgestrel intrauterine system (LNG-IUS) for idiopathic menorrhagia.

    METHODS: Forty-four patients were recruited into a randomized trial comparing their health status after treatment with TBEA or LNG-IUS for idiopathic menorrhagia.

RESULTS: At 1 year follow-up, the mean haemoglobin was significantly higher in women treated with TBEA (12.6 g/dl vs. 10.3 g/dl, p = 0.018). Iron deficiency occurred in 13.3% from the TBEA arm and in 50% from the LNG-IUS arm (p = 0.026). The women's mean Short Form 36 Questionnaire general health perception scores (54.9 vs. 40.5, p = 0.024) and mental health scores (49.5 vs. 38.3, p = 0.021) in TBEA arm were significantly higher than in the LNG-IUS arm. The mental health domain score was also significantly lower in the LNG-IUS arm (46.1 vs. 38.3, p = 0.041).

CONCLUSION: TBEA appears to offer better health status function at 1 year follow-up and to be more acceptable to our Chinese population in the treatment of idiopathic menorrhagia following failed medical treatment.

Relevant Articles Cross-Referenced from Other Sections

Levonorgestrel-Releasing Intrauterine Devices

Cozza, G., Pinto, A., Giovanale, V., Bianchi, P., Guarino, A., Marziani, R., Frega, A., & Caserta, D. (2017). Comparative effectiveness and impact on health-related quality of life of hysterectomy vs. levonorgestrel intra-uterine system for abnormal uterine bleeding. *Eur Rev Med Pharmacol Sci*, *21*(9), 2255–2260. https://www.europeanreview.org/article/12708

Oral Contraceptives

Weisberg, E., McGeehan, K., Hangan, J., & Fraser, I. S. (2017). Potentially effective therapy of heavy menstrual bleeding with an oestradiol-nomegestrol acetate oral contraceptive: a pilot study. *Pilot Feasibility Stud*, *3*, 18. https://doi.org/10.1186/s40814-017-0130-2

Adolescents

Alaqzam, T. S., Stanley, A. C., Simpson, P. M., Flood, V. H., & Menon, S. (2018). Treatment Modalities in Adolescents Who Present with Heavy Menstrual Bleeding. *J Pediatr Adolesc Gynecol*, *31*(5), 451–458. https://doi.org/10.1016/j.jpag.2018.02.130

Haq, B., Akram, H., & Rana, T. (2016). Medical intervention in adolescent menorrhagia. Annals of King Edward Medical University, 11(4). https://doi.org/10.21649/akemu.v11i4.1112

Low-and-Middle-Income Countries

Samah Mohamed Ali Abd El- Azym, M. (2018). Levonorgestrel Releasing IUS (Metraplant E) in the Management of Copper IUD Related Heavy Painful Menstrual Loss. *The Egyptian Journal of Hospital Medicine*, 71(5), 3158-3165. https://applications.emro.who.int/imemrf/Egypt_J_Hosp_Med/Egypt_J_Hosp_Med_2018_71_5_3158_3165.pdf

Relevant Grey Literature

ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 Feb 29 - . Identifier NCT00556400, Treatment of Menorrhagia in Women With Thrombocytopenia Using Platelets or Platelets and Hormones; 2007 Nov 9 [cited 2023 Aug 11]; [about 6 screens]. Available from: http://clinicaltrials.gov/ct/show/NCT00287391?order=1

PRIMARY FOCUS: NUTRITION

26. **Baines S, Powers J, Brown WJ. How does the health and well-being of young Australian vegetarian and semi-vegetarian women compare with non-vegetarians? Public Health Nutr. 2007 May;10(5):436-42. https://doi.org/10.1017/s1368980007217938**

    OBJECTIVE: To compare the sociodemographic characteristics, health status and health service use of vegetarians, semi-vegetarians and non-vegetarians.

    DESIGN: In cross-sectional data analyses of the Australian Longitudinal Study on Women's Health in 2000, 9113 women (aged 22-27 years) were defined as non-vegetarians if they reported including red meat in their diet, as semi-vegetarians if they excluded red meat and as vegetarians if they excluded meat, poultry and fish from their diet.

    RESULTS: The estimated prevalence was 3% and 10% for vegetarian and semi-vegetarian young women. Compared with non-vegetarians, vegetarians and semi-vegetarians were more likely to live in urban areas and to not be married. Vegetarians and semi-vegetarians had lower body mass index (mean (95% confidence interval): 22.2 (21.7-22.7) and 23.0 (22.7-23.3) kg m(-2)) than non-vegetarians (23.7 (23.6-23.8) kg m(-2)) and tended to exercise more. Semi-vegetarians and vegetarians had poorer mental health, with 21-22% reporting depression compared with 15% of non-vegetarians ($P < 0.001$). Low iron levels and menstrual symptoms were also more common in both vegetarian groups. Vegetarian and semi-vegetarian women were more likely to consult alternative health practitioners and semi-vegetarians reported taking more prescription and non-prescription medications. Compared with non-vegetarians, semi-vegetarians were less likely and vegetarians much less likely to be taking the oral contraceptive pill.

    CONCLUSION: The levels of physical activity and body mass indices of the vegetarian and semi-vegetarian women suggest they are healthier than non-vegetarians. However, the greater reports of menstrual problems and the poorer mental health of these young women may be of clinical significance.

27. **Patterson, A. J., Brown, W. J., & Roberts, D. C. K. (2001). Dietary and lifestyle factors influencing iron stores in Australian women: an examination of the role of bio-available dietary iron. *Australian Journal of Nutrition & Dietetics*, *58*(2), 107–113. https://www.academia.edu/download/45390778/Development_prevention_and_treatment_of_20160505-27710-pjzv7j.pdf**

    Research to date has not been able to adequately describe the relative impact of dietary and lifestyle variables on iron status. While total iron intake appears unrelated to iron status, bio-available dietary iron should correlate with iron stores, after adjustment for iron losses. Therefore, the objective of this study was to examine dietary and lifestyle variables that are important in the determination of iron status for Australian women of child-bearing age. Serum ferritin was measured in 52 iron-deficient and 24 iron-replete women. Dietary data were collected using seven-day weighed food records and bio-available dietary iron calculations were performed using the algorithms developed by Monsen et al., Monsen and Balintfy, and Tseng et al. Self-reported data on demographic characteristics, parity, breastfeeding, oral contraceptive pill, intrauterine device and hormone replacement therapy use, menstruation, smoking, alcohol intake, exercise, dieting, vitamin and mineral supplement use and blood donation were collected. Multiple linear regression was used to examine dietary and lifestyle factors associated with serum ferritin. Current oral contraceptive pill use and alcohol intake were positively associated ($P = 0.01$ and $P = 0.001$ respectively) and phytate intake was negatively associated ($P = 0.05$) with serum ferritin. Total iron, haem iron and bio-available dietary iron intakes were not associated with iron stores. Bio-available dietary iron

estimates were well below the recommended intakes for menstruating women, suggesting possible problems with either the algorithms or the assumptions built into the current Australian recommended dietary intakes. Further work to accurately determine bio-available dietary iron estimates for Australian women is needed.

POPULATION: ADOLESCENTS

28. **Alaqzam, T. S., Stanley, A. C., Simpson, P. M., Flood, V. H., & Menon, S. (2018). Treatment Modalities in Adolescents Who Present with Heavy Menstrual Bleeding.** ***J Pediatr Adolesc Gynecol*****,** ***31*****(5), 451–458. https://doi.org/10.1016/j.jpag.2018.02.130**

STUDY OBJECTIVE: On this study we sought to determine the relationship of bleeding disorders to iron deficiency anemia. Additionally, this study was undertaken to examine all current treatment modalities used in a menorrhagia clinic with respect to heavy menstrual bleeding management to identify the most effective options for menstrual management in the setting of an underlying bleeding disorder. DESIGN,

SETTING, PARTICIPANTS, INTERVENTIONS, AND MAIN OUTCOME MEASURES: We performed a retrospective chart review of adolescents younger than 21 years with heavy menstrual bleeding attending a multidisciplinary hematology-adolescent gynecology clinic. Information including demographic characteristics, bleeding diathesis, hematologic parameters, treatment, and the diagnosis was extracted from each chart. Subjects were grouped into 2 categories on the basis of the diagnosis of a bleeding disorder. Hemoglobin level, iron deficiency anemia, and need for transfusion were compared between a bleeding disorder and no bleeding disorder group. Subjects were grouped into categories depending on hormonal modality and treatment success of the groups were compared.

RESULTS: Seventy-three subjects were tested for a bleeding disorder. Of the subjects who completed testing, 34 (46%) were diagnosed with a bleeding disorder. Thirty-nine subjects (54%) had heavy menstrual bleeding because of other causes. There was no significant difference in hemoglobin between those with and without a bleeding disorder. Iron deficiency anemia was significantly higher in subjects without a bleeding disorder. In a comparison of hormone therapy success, the levonorgestrel intrauterine device (89%, 8 out of 9 subjects) had the highest rate of menstrual suppression followed by norethindrone acetate 5-10 mg/d (83%, 5 out of 6 subjects), and the transdermal patch (80%, 4 out of 5 subjects). All subjects using tranexamic acid as well as hormonal therapy had 100% achievement of menstrual suppression.

CONCLUSION: A high frequency of bleeding disorders was found in those tested. Subjects with a bleeding disorder were less likely to present with severe anemia requiring blood transfusion and less likely to have iron deficiency anemia. Although combined oral contraceptives were commonly used clinically for menstrual suppression, they were not found to be the most effective option.

29. **Carlsson, L. E., Hempel, S., & Greinacher, A. (2002). Iron deficiency anaemia in young women.** ***Eur J Haematol*****,** ***68*****(6), 341–344. https://doi.org/10.1034/j.1600-0609.2002.00679.x**

OBJECTIVES: The expression density of GPIaIIa, the primary platelet collagen receptor (integrin alpha2beta1), is linked to two polymorphisms (GPIa-807C/T and HPA-5a/b). During evolution a gene shift from the genotypes GPIa-807CC-HPA-5bb to the genotypes GPIa-807CT-HPA-5aa has taken place. The aim of the study was to assess whether iron deficiency anaemia (e.g. increased blood loss) in young women could be associated with a specific genotype, indicating a role as potential evolutionary selection factor.

STUDY DESIGN: Women between 18 and 40 yr of age presenting for their first blood donation were asked about alimentary habits and use of oral contraception. Haemoglobin and serum ferritin were measured and the GPIa-C807T and HPA-5 genotypes were determined. RESULTS: Two hundred women were included and grouped according to the WHO definition for iron deficiency anaemia (haemoglobin <121 g L(-1) and ferritin <15 microg L(-1)). Eight women fulfilled both WHO-criteria for iron deficiency anaemia, 145 women fulfilled none. No differences regarding age, use of oral contraceptives, alimentary habits, and HPA-5 were found between the groups. The GPIa-807CC genotype was strongly over-represented in the WHO-anaemic women as compared to the non-WHO-anaemic women (87.5% vs. 33.1%, P=0.003).

CONCLUSION: Iron deficiency anaemia in young women might have been the evolutionary disadvantage causing the gene shift from GPIa-807CC to 807CT.

30. **Haq, B., Akram, H., & Rana, T. (2016). Medical intervention in adolescent menorrhagia. *Annals of King Edward Medical University*, *11*(4). https://doi.org/10.21649/akemu.v11i4.1112**

Objectives: To find out causative factors of adolescent menorrhagia and success of various treatments. Design: Descriptive cross sectional study Place & duration of study: Lady Willingdon Hospital, Lahore from May 2004 to April 2005. Subject and methods: Fifty unmarried patients at 12-19 years with menorrhagia selected by non-probability convenience sampling. Blood loss was determined by duration of bleeding extending beyond seven days, passage of clots and presence of anaemia. Results: The most common cause of menorrhagia was DUB (92%) followed by bleeding and endocrinal disorder. Non-steroidal anti-inflammatory drug and antifibrinolytic agent produced 75% subjective improvement in complaints. However, combined oral contraceptive produced 66% improvement. Conclusion: NSAIDS and antifibrinolytic drugs were found to be effective in reducing menstrual loss and should be used as first line of treatment.

31. **Sekhar, D. L., Murray-Kolb, L. E., Kunselman, A. R., Weisman, C. S., & Paul, I. M. (2016). Differences in Risk Factors for Anemia Between Adolescent and Adult Women. *J Womens Health (Larchmt)*, *25*(5), 505–513. https://doi.org/10.1089/jwh.2015.5449h**

BACKGROUND: Iron deficiency anemia (IDA) affects 2%-5% of reproductive-age women. Screening is based on risk factors, such as a low-iron diet and menstruation. However, published IDA risk factors fail to consider age-related risks specific to adolescent women, potentially limiting identification of high-risk adolescents for objective testing. The goal of the study was to examine IDA risk factors in a nationally representative sample of younger (12-21 years) and older (22-49 years) reproductive-age women.

MATERIALS AND METHODS: Data were obtained from the National Health and Nutrition Examination Survey (NHANES) 2003-2010. IDA was defined using hemoglobin, ferritin, soluble transferrin receptor, standard NHANES laboratory measures. Sex-, age-, and race-specific hemoglobin values defined anemia. Iron deficiency was calculated using ferritin and soluble transferrin receptor in the body iron formula. Logistic regression assessed the association of potential risk factors (race, body mass index, poverty, iron intake, tobacco/nicotine exposure, physical activity, menses, and contraceptive use) with IDA in younger and older women.

RESULTS: The prevalence of IDA was 2.4% and 5.5% among younger and older women, respectively. Among younger women, contraceptive use was marginally protective from IDA (risk ratio 0.50, 95% confidence interval [CI] 0.25-1.00). Among older women, significant variables included Black race (risk

ratio 2.31, 95% CI 1.33-4.02) and increased years menstruating (≥25 years vs. <25 years; risk ratio 1.93, 95% CI 0.99-3.76).

CONCLUSIONS: Risk factors for IDA among older reproductive-age women do not apply to adolescent women. To better inform the timing and frequency of screening recommendations, further research must identify adolescent-specific IDA risk factors.

POPULATION: ATHLETES

32. Alfaro-Magallanes, V. M., Romero-Parra, N., Barba-Moreno, L., Rael, B., Benito, P. J., Díaz, Á. E., Cupeiro, R., & Peinado, A. B. (2023). Serum iron availability, but not iron stores, is lower in naturally menstruating than in oral contraceptive athletes. *European Journal of Sport Science*, *23*(2), 231–240. https://doi.org/10.1080/17461391.2021.2018503
https://www.tandfonline.com/doi/full/10.1080/17461391.2021.2018503

This study measured serum markers of iron status in naturally menstruating and oral contraceptive (OC) athletes during the main hormonal milieus of these two profiles to identify potential differences confounding the diagnosis of iron deficiency in female athletes. Resting blood samples were collected from 36 naturally menstruating athletes during the early-follicular phase (EFP), mid- late-follicular phase (MLFP) and mid-luteal phase (MLP) of the menstrual cycle. Simultaneously, blood samples were collected from 24 OC athletes during the withdrawal and active-pill phase of the OC cycle. Serum iron, ferritin, transferrin, transferrin saturation (TSAT), C-reactive protein (CRP), interleukin-6 and sex hormones were analyzed. Naturally menstruating athletes showed lower levels of TSAT, iron and transferrin than OC athletes when comparing the bleeding phase of both profiles ($p<0.05$) as well as when comparing all analyzed phases of the menstrual cycle to the active pill phase of the OC cycle ($p<0.05$). Interestingly, only lower transferrin was found during MLFP and MLP compared to the withdrawal phase of the OC cycle ($p>0.05$), with all other iron markers showing no differences ($p>0.05$). Intracycle variations were also found within both types of cycle, presenting reduced TSAT and iron during menstrual bleeding phases ($p<0.05$). In conclusion, in OC athletes, serum iron availability, but not serum ferritin, seems higher than in naturally menstruating ones. However, such differences are lost when comparing the MLFP and MLP of the menstrual cycle with the withdrawal phase of the OC cycle. This should be considered in the assessment of iron status in female athletes.

33. Clarke, A. C., Anson, J. M., Dziedzic, C. E., McDonald, W. A., & Pyne, D. B. (2018). Iron monitoring of male and female rugby sevens players over an international season. *J Sports Med Phys Fitness*, *58*(10), 1490–1496. https://doi.org/10.23736/s0022-4707.17.07363-7

BACKGROUND: Given the likely influence that high training loads, contact-induced hemolysis and female-specific requirements have on the incidence of iron deficiency, characterizing the direction and magnitude of fluctuations in iron status over an international season is important for managing player health and physical performance in rugby sevens.

METHODS: Australian national male (N.=27) and female (N.=23) rugby sevens players undertook blood tests at pre-season, mid-season, and end-season. Hemoglobin (Hb), hematocrit (Hct), ferritin, transferrin and transferrin saturation were quantified. Female athletes also reported oral contraceptive use and a subset (N.=7) provided 7-day food diaries to quantify iron intake.

RESULTS: Male players typically had a three-fold higher ferritin concentration than females. Pre-season ferritin concentrations in male (151±66 μg/L) and female (51±24 μg/L) players declined substantially (~20%) by mid-season but recovered by end-season. Over the season 23% of female players were

classified as iron deficient (ferritin <30 µg/L) and prescribed supplementation. The greatest incidence of iron deficiency in female players occurred mid-season (30%). Oral contraception and dietary iron intake had an unclear influence on female players' ferritin concentration, while age was largely positively correlated (r=0.66±~0.33).

CONCLUSIONS: Given the relatively low ferritin concentrations evident in female rugby sevens players, and the potential for a further decline midway through a season when physical load may be at its highest, 6-monthly hematological reviews are suggested in combination with dietary management. Annual screening may be beneficial for male players, with further monitoring only when clinically indicated.

ARTICLES BY SETTING

LOW- AND MIDDLE- INCOME COUNTRIES

EGYPT

34. **Ahmed, N., Mostafa, R., Abuelghar, W., Elbishry, G. (2018) Discontinuation Rates among Copper Intrauterine Device Users in Primary Healthcare Unit and University Clinic. Is There a Difference?. The Egyptian Journal of Hospital Medicine, 72(11), 5658-5665.** **https://ejhm.journals.ekb.eg/article_11543.html**

    BACKGROUND: in Egypt, despite the high percentage of women using IUD according to Demographic and Health Surveys (DHS) 2014 (52.9%) of total women using contraceptive methods, the discontinuation rates among Cu-IUD users (within 12 months of use) reaches 14.3% in 2014.

    AIM OF THE WORK: the aim of the study was to compare between primary health care unit and university family planning clinic in discontinuation rate among copper IUD users.

    PATIENTS AND METHOD: study design: prospective analytical observational study. Study setting: This study was conducted at Family planning Outpatient clinic of Ain Shams Maternity Hospital and El-Zahraa primary health care unit for a year. This study included 260 women whom attending family planning clinic for Cu- IUD insertion. Total 100 subjects was enrolled from each clinic. Rest of subjects was lost on follow up either after 6 months or 12 months. Some others refused to participate or gave wrong personal contacts.

    RESULTS: preliminary results of the study revealed that there is no statistically significant difference between discontinuation rate among Copper IUD users in university clinic and primary healthcare clinic (p-value = 0.095).

    CONCLUSION: in our Study, analysis of data revealed that age, parity and previous usage of IUD may affect discontinuation rate after 12 months of IUD use. The mean cause of IUD discontinuation was bleeding and anemia was present in 66.6% of patients complaining from bleeding.

35. **Samah Mohamed Ali Abd El- Azym, M. (2018). Levonorgestrel Releasing IUS (Metraplant E) in the Management of Copper IUD Related Heavy Painful Menstrual Loss. *The Egyptian Journal of Hospital Medicine*, 71(5), 3158-3165.** **https://platform.almanhal.com/Files/2/117427**

    BACKGROUND: the LNG-IUD was first introduced in Finland in 1990 and is currently marketed in most European countries and in the US since 2000. The Levonorgestrel IUD is approved for 5 years, but lasts up to 10 years and reduces the menstrual blood loss and pelvic infection rates.

AIM OF WORK: this study aimed to evaluate safety and efficacy of levonorgestrel releasing IUS (Metraplant-E) in the management of copper IUD related heavy painful menstrual loss. Among women of low socioeconomic status attended to family planning clinic at Abo-Elnomros Hospital (Abo-Elnomros is small village –Giza Government, Egypt. Patients and Methods: this was a prospective cohort study and it was performed in Abo- Elnomros hospital. Women who attended to the hospital (Family planning clinic) for IUD follow up and had complications (bleeding and dysmenohrea) for which copper IUD is removed.

RESULTS: all women in the present study reported a marked reduction in MBL, which started from the first menstrual period following insertion of Metraplant –E. Bleeding was reduced further over the next months until the 6th month except two cases . Amenorrhea occurred in 38 cases. The difference in menstrual bleeding was highly significant (P <0.0001). Hemoglobin level increased from a mean baseline value of 10.0 ± 1.3 at baseline controls to a mean level of 10.5 ± 1.2 after 6 months of Metraplant-E use. Differences in hemoglobin levels were highly significant P <0.0001.

CONCLUSION AND RECCOMENDATIONS: the copper IUD is the most commonly used method of reversible contraception worldwide and is used by an average of 23 percent of female contraceptive users. The copper IUD is associated with increased menstrual flow both in length of menses and in amount of blood loss. The most common reasons for the discontinuation of this method are menstrual bleeding and dysmenorrhea. Metraplant- E is effective in significantly reducing the amount of menstrual blood loss in women with heavy painful menstrual loss related to copper IUD. Strong endometrial suppression is the principal mechanism, explaining both the effect on menstrual blood loss and the contraceptive performance of the IUS. Proper treatment of the chronic endometritis prior to Metraplant-E insertion is recommended. Actively informing women about benefits, risks and common side effects of IUS appears to improve consideration and acceptance of the method.

ETHIOPIA

36. **Olani, D., & Shiferaw, Y. A. (2015). Correlates of anemia status among women of reproductive age in Ethiopia. *Ethiopian E-Journal for Research and Innovation Foresight*, *7*(2), 37–53. https://doi.org/https://www.nesglobal.org/eejrif4/index.php?journal=admin&page=article&op=view&path%5B%5D=162&path%5B%5D=325**

BACKGROUND: Anemia is a condition characterized by a low level of hemoglobin in the blood which seriously affects young children and women (1). It is a global public health problem affecting both developing and developed countries with major consequences for human health as well as social and economic development.

OBJECTIVE: To identify socio-economic, demographic and health correlates of anemia status among women of reproductive age in Ethiopia.

METHODS: Data from the Ethiopian Demographic and Health Survey conducted in 2011 was used for this study. Data of a total of 15,567 women of reproductive age were included in the analysis. The prevalence of anaemia was calculated and chi-square tests, odds ratios and binary logistic regression were used to identify the relationship between anemia and each independent variable.

RESULTS: The overall prevalence of anemia in the women aged 15-49 years was 19.9%. Total number of children born, BMI, region, educational level, wealth index, pregnancy, months of breast feeding and contraceptive use were significantly correlated with anemia. Utilizing maternity services, receiving iron

tablet and drug use for intestinal parasite have a significant effect in reducing the risk of anemia. The exposure of anemia increases with gestational age among pregnant women.

RECCOMENDATION: Women health intervention programs including access to maternal health care service, iron supplementation, drug use for intestinal parasite, improving mothers' access to education and family planning practice have been strongly recommended in order to reduce the risk of anemia among women.

37. **Haidar, J. (2010). Prevalence of anaemia, deficiencies of iron and folic acid and their determinants in Ethiopian women. *J Health Popul Nutr*, *28*(4), 359–368. https://doi.org/10.3329/jhpn.v28i4.6042**

A cross-sectional community-based study with analytic component was conducted among Ethiopian women during June-July 2005 to assess the magnitude of anaemia and deficiencies of iron and folic acid and to compare the factors responsible for anaemia among anaemic and non-anaemic cases. In total, 970 women, aged 15-19 years, were selected systematically for haematological and other important parameters. The overall prevalence of anaemia, iron deficiency, iron-deficiency anaemia, deficiency of folic acid, and parasitic infestations was 30.4%, 50.1%, 18.1%, 31.3%, and 13.7% respectively. Women who had more children aged less than five years but above two years, open-field toilet habits, chronic illnesses, and having intestinal parasites were positively associated with anaemia. Women who had no formal education and who did not use contraceptives were negatively associated with anaemia. The major determinants identified for anaemia were chronic illnesses [adjusted odds ratio (AOR) = 1.1, 95% confidence interval (CI) 1.15-1.55), deficiency of iron (AOR = 0.4, 95% CI 0.35-0.64), and deficiency of folic acid (AOR = 0.5, 95% CI 0.50-0.90). The odds for developing anaemia was 1.1 times more likely among women with chronic illnesses, 60% more likely in the iron-deficient and 40% more likely in the folic acid-deficient than their counterparts. One in every three women had anaemia and deficiency of folic acid while one in every two had iron deficiency, suggesting that deficiencies of both folic acid and iron constitute the major micronutrient deficiencies in Ethiopian women. The risk imposed by anaemia to the health of women ranging from impediment of daily activities and poor pregnancy outcome calls for effective public-health measures, such as improved nutrient supplementation, health education, and timely treatment of illnesses.

38. **Nagari, S. L., Egata, G., Mehadi, A., Hassen, T. A., Raru, T. B., Abdurke, M., ... & Roba, K. T. (2023). Anemia Among Women Using Family Planning at Public Health Facilities in Ambo Town, Central Ethiopia: Multi-Center Cross-Sectional Study. Journal of Blood Medicine, 83-97. https://doi.org/10.2147%2FJBM.S400191**

Background: Anemia affects more than a quarter of non-pregnant women over the globe, with Sub-Saharan Africa bearing a disproportionate share. Although the use of family planning is beneficial in reducing anemia, lack of scientific study on anemia among family planning users of reproductive-age women is notable, particularly in the study setting. The purpose of this study was to determine the extent of anemia and associated factors in women who used family planning.

Methods: A cross-sectional multi-centered study was conducted from March 3 to 29, 2019, among 443 non-pregnant reproductive age (15 to 49 years) women receiving family planning services in Ambo town. Sample size was calculated using Epi-info version 7 software. Participants were selected by systematic random sampling technique. Trained data collectors collected data using a structured pretested questionnaire, as well as venous blood and stool samples. Epi-Data and SPSS were used to enter and analyze data. The effect of independent variables on the outcome variable was determined by binary logistic regression analysis with adjusted odds ratio at 95% confidence interval and 5% margin of error. P-value <0.05 was used to declare statistical significance.

Results: This study revealed 28% (95% CI:23.9%, 32.3%) magnitude of anemia. Age of 25–35 years [AOR:2.84, 95% CI:1.74, 4.64], implantable family planning method [AOR: 0.34, 95% CI: 0.12, 0.96], no previous use of family planning [AOR:2.62, 95% CI: 1.62, 4.24], household food insecurity [AOR: 2.04, 95% CI: 1.06, 3.93], parasite infestations [AOR:2.01, 95% CI: 1.12, 3.63], and regular intake of coffee/tea within 30 minutes post meal [AOR:3.85, 95% CI:1.24, 11.92] were independently associated with anemia.

Conclusion: Anemia is a moderate public health concern among reproductive-age women receiving family planning services in the study area. There are missed opportunities to address the anemia burden during family planning services. This study emphasizes the importance of nutritional screening for early detection and targeted interventions for healthcare workers in reducing missed opportunities to prevent and control anemia in vulnerable populations.

INDIA

39. **Ganapathi, K. C., & Kumar, K. S. (2017). A cross-sectional study of anemia among women of reproductive age group (15-49 years) in a rural population of Tamil Nadu. *International Journal of Medical Science and Public Health*, *6*(3), 524–529. https://doi.org/https://www.ejmanager.com/fulltextpdf.php?mno=242490**

BACKGROUND: Iron deficiency is the most common nutritional disorder in the world, affecting particularly the women of reproductive age group in tropical and subtropical zones. In India, 20-40% of maternal deaths are due to anemia, and more than 50% of women do not have adequate iron stores for pregnancy.

OBJECTIVES: To estimate the prevalence of anemia among women in the reproductive age (15-49) in a rural population and to find out the association with selected variables.

MATERIALS AND METHODS: This was a population-based cross-sectional study conducted in a rural population served by primary health center, Ulundai in Kadambathur block of Thiruvallur district in Tamil Nadu among women in reproductive age group of 15-49 years from February 2007 to May 2007. Sample size was calculated to be 381 and participants were selected by simple random sampling. Data were collected using a pre-tested interview schedule.

RESULTS: Out of 400 women, 390 women were only willing to give blood sample giving a response rate of 97.5%. The overall prevalence of anemia among reproductive age group women 15-49 years was found to be 53.3%. Prevalence of anemia decreased with increase in age and was found to be statistically significant. Maternal occupation and menstrual and obstetric factors such as age at menarche, amount of menstrual bleeding, length of menstrual cycle, pelvic inflammatory disease, number of live births, contraception use, pregnancy, and iron and folic acid (IFA) use were found to have statistically significant association with anemia. Women who were underweight, taking vegetarian diet, using open field for defecation, and passed worms in stools were found to have statistically significant association with anemia. Similarly, age at menarche 13-14 years, normal menstrual bleeding, taking mixed diet, regular wearing of footwear, taking deworming tablets recently (<6 months), and using sanitary latrines were found to be at lower risk of anemia.

CONCLUSION: It is inferred from this study that sociodemographic, menstrual, obstetric, contraceptive, dietary, environmental, and behavioral factors were associated with anemia in reproductive age group. Hence, preventive measures such as IFA supplementation for adolescent girls and improving the environmental conditions have to be adopted to reduce the burden of the disease.

IRAN

40. **Asghari, S., Mohammadzadegan-Tabrizi, R., Rafraf, M., Sarbakhsh, P., & Babaie, J. (2020). Prevalence and predictors of iron-deficiency anemia: Women's health perspective at reproductive age in the suburb of dried Urmia Lake, Northwest of Iran. *J Educ Health Promot*, *9*, 332. https://doi.org/10.4103/jehp.jehp_166_20**

    BACKGROUND: Dried Urmia Lake in the northwest of Iran is a major regional source of sodium and toxic metal aerosols which may cause numerous health problems. The aim of this study was to evaluate iron-deficiency anemia (IDA) and some related risk factors among women of reproductive age in the suburb of dried Urmia Lake to provide the information about the problem to the health-care providers.

    METHODS: This cross-sectional study was conducted on 278 healthy nonpregnant, nonlactating women aged 18-45 years, living in the rural area of the Salmas city, closest to the Urmia Lake between February and June 2017. The study participants were selected using a stratified random sampling method with proportional allocation from seven villages. A general questionnaire was completed for each participant to collect sociodemographic information and a 3-day dietary recall questionnaire to obtain daily dietary intakes. IDA was defined as a hemoglobin (Hb) level of <12 g/dl and ferritin concentration of <15 μg/l. Spearman's correlation coefficient and Fisher's exact test were applied to determine sociodemographic factors associated with the serum Hb and ferritin levels.

    RESULTS: The prevalence of overall anemia (Hb <12 g/dl) was 7.9%. IDA was determined in 4.3% and iron deficiency (ID) in 19.1% (serum ferritin <15 μg/l) of the participants. There was a significant positive correlation between serum Hb concentrations and the mean daily intakes of protein and iron ($P < 0.001$). Similarly, a significant positive correlation was observed between serum ferritin levels and body mass index ($P < 0.001$). Significant inverse associations were found between Hb concentrations and the number of pregnancies and children ($P < 0.001$), as well as the number of family members ($P < 0.05$).

    CONCLUSIONS: Results indicated a mild prevalence of IDA and a relatively high rate of ID among studied participants. Educational programs are needed to improve nutritional habits as well as the use of contraceptives to promote women's health.

41. **Sadeghian, M., Fatourechi, A., Lesanpezeshki, M., & Ahmadnezhad, E. (2013). Prevalence of anemia and correlated factors in the reproductive age women in rural areas of tabas. *Journal of family & reproductive health*, 7(3), 139–144. http://www.ncbi.nlm.nih.gov/pmc/articles/pmc4064781/**

    OBJECTIVE: To find out the prevalence and relationship of anemia in reproductive age women in rural area of Tabas, center of Iran. Iron deficiency anemia is the most common nutritional problem, affecting about 41.8% of pregnant and 30.2% of non-pregnant women worldwide.

    MATAERIALS AND METHODS: A cross-sectional study was conducted on the random sample of 382 reproductive age women in rural areas of Tabas in March 2010. Independent sample t-test, one way analysis of variance (ANOVA) and logistic regression were applied for the data analysis.

    RESULTS: The obtained data revealed a total response rate of 13.8% for prevalence of anemia, while 14.5% and 5.9% belonged to non-pregnant and pregnant participants, respectively. Low socioeconomic

status (odds ratio 3.35) and high parity index (odds ratio 2.31) were associated with higher prevalence of anemia.

CONCLUSION: Although this study was conducted in a rural area of Tabas, where their average incomes were lower than average income of major cities in Iran, the prevalence of anemia was lower than the rate reported in previous studies carried out in other locations of Iran, even in high risk (pregnant women) groups.

42. **Salehian, T., Delaram, M., Safdari, F., Alavi, A., Noor Bakhshian, M., Salehifard, A.Z. (2008). Comparison of Two Commonly Used IUDs in Pain and Menstrual Bleeding. *Journal of Shahrekord University of Medical Sciences*, 10 (3), 23-28. https://search.bvsalud.org/gim/resource/en/emr-88112**

The intrauterine device [IUD] is the most widely used reversible method of contraception in the world. One of the most common side effects of intrauterine device is increasing of menstrual blood loss, which may cause discontinuation and iron - deficiency anemia. BY considering the effects of IUD type on menstrual bleeding this study was conducted to compare the side effects of T Cu 380A and Cu safe300 IUDs including bleeding, pain on during 3-month period in clients referring to family planning center of Shahrekord Hajar hospital. This study was a randomized single-blind clinical trial, during which 70 candidates applied for IUD were randomly placed in two groups of IUD T Cu 380A and Cu safe300. The major side effects were recorded in the following 1, 2, 3 months. The comparisons were made using t-test, Mann-Whitney, Chi-Square and Wilcoxon tests by SPSS soft ware. Menstrual bleeding and dysmenorrheal was more commonly occurred during the 3 month of implantation in both groups but bleeding and pain was significantly lower in Cu safe300 group than the other group. With regard in this study showed menstrual blood loss and dysmenorrheal in the 3 months after IUD insertion a in Cu safe300 users were less than T Cu380A users therefore recommending to be possible this kind IUD to distribute in the health center.

JORDAN

43. **Arabyat, R., Arabyat, G., Al-Taani, G. (2019). Prevalence and risk factors of anaemia among ever-married women in Jordan. *East Mediterranean Health Journal*, 25(8), 543–552. https://doi.org/10.26719/emhj.18.074**

BACKGROUND: Anaemia is associated with poor health outcomes and is considered a serious public health problem particularly in low- and middle-income countries. Specific subgroups are at higher risk of anaemia, such as women of reproductive age.

AIMS: This study examined the prevalence and risk factors of anaemia among ever-married women in Jordan using a secondary analysis of the Jordan Population and Family Health Survey.

METHODS: This is a secondary analysis of data from a nationally representative sample of ever-married women aged 15–49 years that were tested for haemoglobin levels in the 2012 JPFHS. Anaemia was categorized according to the WHO criteria. Univariate and multivariate logistic regression analyses were used to investigate risk factors associated with anaemia.

RESULTS: The prevalence of any anaemia was 37.3%; specifically, 20% had mild anaemia (haemoglobin 11.0–11.9 g/dl), 16.3% had moderate anaemia (hemoglobin 8.0–10.9 g/dl) and 1% had severe anaemia (haemoglobin < 8.0 g/dl). Factors that were associated with anaemia in the multivariate regression

included urban women (P = 0.01), living in the north (P = 0.014) or south regions (P = 0.013) of Jordan, having multiple children (P < 0.001), being pregnant (P < 0.01), and using IUD as a contraceptive method (P < 0.001).

CONCLUSIONS: A high prevalence of anaemia among ever-married women of reproductive age in Jordan was noticed. The results emphasize the importance of urgent public health interventions to prevent anaemia in Jordan, particularly among high-risk subgroups.

KAZAKHSTAN

44. Dangour, A. D., Hill, H. L., & Ismail, S. J. (2001). Haemoglobin status of adult non-pregnant Kazakh women living in Kzyl-Orda region, Kazakhstan. *Eur J Clin Nutr*, *55*(12), 1068–1075. https://doi.org/10.1038/sj.ejcn.1601267

OBJECTIVE: To estimate the prevalence of anaemia among adult non-pregnant women in the Kzyl-Orda region of Kazakhstan, and to determine the association between haemoglobin concentration and anthropometric, socioeconomic, reproductive and dietary factors.

DESIGN: A cross-sectional study using a randomly selected sample. Subjects were interviewed, and finger-prick blood samples and anthropometric measurements were collected. Associations between haemoglobin concentration and anthropometric and questionnaire data were evaluated by sequential linear regression analysis.

SETTING: Health centres in Kazalinsk, Djalagash and Zhanakorgan districts of Kzyl-Orda region, Kazakhstan.

SUBJECTS: Three-thousand six-hundred and twenty-five non-pregnant women aged 18-45 y randomly selected from health centre records. RESULTS: Iron deficiency anaemia, as reflected by low haemoglobin levels (Hb<12 g/dl), was detected in 40.2% of the total sample. There was a significant curvilinear relationship between haemoglobin concentration and age, with the nadir of the curve in the 30-40 y age-group. Haemoglobin concentration was found to be positively associated with body mass index (BMI) and socioeconomic factors. Significant negative associations were found between haemoglobin concentration and duration of menses, use of the intra-uterine contraceptive device and the consumption of tea.

CONCLUSIONS: This study demonstrates that iron deficiency anaemia is present at considerable levels among adult women living in Kzyl-Orda region, Kazakhstan, and provides important baseline information for future research and public health interventions.

SOUTH AFRICA

45. Jordaan, E. M., Berg, V. L. van den, Rooyen, F. C. van, & Walsh, C. M. (2020). Anaemia prevalence and dietary diversity among women in the rural Free State, South Africa. *Health SA Gesondheid*, *25*. https://doi.org/10.4102/hsag.v25i0.1421

BACKGROUND: Anaemia, a global public health problem that particularly affects women, holds major consequences for human health. Aim: Determining dietary diversity, prevalence of anaemia and contraception use. Setting: Rural women, 25-49 years, in the Free State Province, South Africa.

METHODS: In a cross-sectional descriptive quantitative study, dietary diversity was determined with a 24-h recall; biochemical markers of anaemia, iron deficiency and inflammation were measured; and contraceptive use was recorded.

RESULTS: Of 134 women (median age 41 years), 51.5% had medium, and 44.8% had low dietary diversity. Overall, 76.9% consumed flesh meats and fish, but only 25.4% ate dark green leafy vegetables. Anaemia was present in 4.6%; 1.5% presented with iron deficiency; and 0.7% presented with iron deficiency anaemia, evidenced by low ferritin levels. However, 45.0% had elevated C-reactive protein (CRP). Overall, 7.5% presented with elevated homocysteine levels, but only 3.8% had low red cell folate levels. More than half (54.1%) reported menstruating regularly and 71.6% used injectable contraceptives. Significant associations were found between median mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) and dietary diversity score.

CONCLUSIONS: Although the prevalence of anaemia is low in this population, elevated CRP in almost half indicates that inflammation may mask iron deficiency. The older median age of the sample and approximately half of the women not menstruating regularly may also contribute to the low anaemia prevalence. Attention should be given to the women's diets as almost half consume diets of low diversity, and not all consume foods rich in haemopoietic nutrients.

46. **Silubonde, T. M., Smuts, C. M., Ware, L. J., Chidumwa, G., Malan, L., & Norris, S. A. (2023). Determinants of anaemia among women of reproductive age in South Africa: A Healthy Life Trajectories Initiative (HeLTI). *PLoS One*, *18*(3), e0283645. https://doi.org/10.1371/journal.pone.0283645**

Anaemia continues to be a persistent concern among South African women of reproductive age (WRA), yet population specific information on its determinants remains sparse. We used baseline data from the Healthy Lives Trajectory Initiative a randomised trial (n = 480) to quantify factors associated with anaemia in Soweto, South Africa aged 18-25 years. We used multivariable logistic regression to describe associations with anaemia and used structural equation modelling to assess a theoretical model, which tested three categories socioeconomic status (household asset score, education level), nutritional factors (food security, leafy green vegetable and chicken and beef consumption, iron status and vitamin A status) and biodemographic factors (parity, age at start of menarche, HIV status, contraception use, anthropometry, and inflammation status). The multiple logistic regression showed that ID (OR: 2.62, 95% CI: 1.72, 3.98), iron deficiency erythropoiesis (IDE) (OR: 1.62, 95% CI: 1.07, 2.46), and elevated CRP (OR: 1.69, 95% CI: 1.04, 2.76), increased the odds of being anaemic. SEM analysis revealed Hb was directly and positively associated with adjusted ferritin (0.0031 per mg/dL; p≤0.001), and CRP (0.015 per mg/dL; p≤0.05), and directly and negatively associated with soluble transferrin receptor sTfR (-0.042 per mg/dL; p≤0.001). While contraception use had both a direct (0.34; p≤0.05) and indirect (0.11; p≤0.01) positive association with Hb. Additionally, chicken and beef consumption had a positive indirect association with Hb concentrations (0.15; p≤0.05) through adjusted ferritin. Iron deficiency was the main anaemia risk factor in this low resource setting. However, anaemia of inflammation is present. Therefore, we suggest that in our setting, WRA anaemia control programs that include interventions to reduce ID and inflammation should be tested.

47. **Soepnel, L. M., Mabetha, K., Draper, C. E., Silubonde, T. M., Smuts, C. M., Pettifor, J. M., & Norris, S. A. (2023). A Cross-Sectional Study of the Associations between Biomarkers of Vitamin D, Iron Status, and Hemoglobin in South African Women of Reproductive Age: the Healthy Life Trajectories Initiative, South Africa. *Curr Dev Nutr*, *7*(5), 100072. https://doi.org/10.1016/j.cdnut.2023.100072**

BACKGROUND: Vitamin D deficiency and anemia impact the health of women of reproductive age. Evidence suggests an inverse relationship between serum vitamin D (25-hydroxyvitamin D [25(OH)D]) and

anemia/iron deficiency, but less is known about these associations in women of reproductive age, in particular in a setting with a combined burden of micronutrient deficiency, food insecurity, and obesity.

OBJECTIVE: We aimed to assess the associations between 25(OH)D and biomarkers of iron and anemia in a cohort of women of reproductive age from Soweto, South Africa. The prevalence of vitamin D deficiency was also assessed.

METHODS: In this cross-sectional substudy of the Healthy Life Trajectories Initiative (HeLTI) South Africa pilot trial, 25(OH)D, iron markers (ferritin and soluble transferrin receptor [sTFR]), and altitude-adjusted hemoglobin (Hb) were measured in 493 women aged 18 to 25 years. Associations between iron deficiency/anemia and vitamin D status were evaluated using multivariable logistic regression, adjusting for confounders including fat mass index (FMI). Structural equation modeling (SEM) was performed to evaluate direct and indirect pathways between 25(OH)D, iron and anemia markers, and covariates.

RESULTS: Of 493 participants, 136 (27.6%) had vitamin D insufficiency (25(OH)D ≥12-20 ng/mL), whereas 28 (5.6%) had vitamin D deficiency (<12 ng/mL). Anemia and iron deficiency were not significantly associated with vitamin D category (25(OH)D<20 ng/mL compared with ≥20 ng/mL) in multivariable logistic regression analyses. In SEM, log-transformed 25(OH)D was not significantly associated with Hb, ferritin, or sTFR, but it was significantly associated with season of data collection, hormonal contraceptive use, and FMI (total effects: B = 0.17, 95% CI: 0.104, 0.236, P < 0.001; B: 0.10, 95% CI: 0.041, 0.154, P < 0.001; B: -0.01, 95%CI: -0.016, -0.003, P = 0.003, respectively).

CONCLUSION: No significant association between vitamin D (25(OH)D), anemia (Hb), and iron markers was found. The inverse relationship between FMI and vitamin D status emphasizes the overlap between adiposity and micronutrient deficiencies in young South African women, exacerbating their risk of disease development.

TANZANIA

48. **Massawe, S. N., Urassa, E. N., Nyström, L., & Lindmark, G. (2002). Anaemia in women of reproductive age in Dar-es-Salaam, Tanzania. *East African Medical Journal*, *79*(9), 461–466. https://doi.org/10.4314/eamj.v79i9.9117**

BAACKGROUND: Anaemia is among the greatest health problems in reproductive age women in developing countries. Objectives: To estimate the prevalence of anaemia among non-pregnant parous women, and to investigate the main underlying cause for the anaemia.

SETTING: A sub-urban Maternal and Child Health Clinic (MCH) in Dar es Salaam.

DESIGN: Cross-sectional.

METHODS: Consecutive parous non-pregnant women who had brought their children for vaccination and/or had come for family planning to Mbagala MCH clinic were invited to participate in the study. Obstetric and social history was recorded, and their height and weight were checked. Haemoglobin was measured using HemoCue hemoglobinometer. Anaemic women were further investigated to determine the cause of anaemia by haematological and biochemical tests.

RESULTS: Five hundred and four parous non-pregnant women were screened, 49% were anaemic (Hb<12 g/dl) and 1.6% severely anaemic (Hb<7 g/dl). Anaemia was not related to socio-demographic and

obstetric history characteristics, but decreased significantly with increasing Body Mass Index (BMI) (p=0.042). The prevalence of anaemia was significantly lower in women using hormonal contraceptives, compared to non-users (36% vs 54%) (p=0.04). Eighty-seven percent of the anaemic women were iron deficient and 8.7% had elevated serum C-reactive protein indicating undiagnosed infections.

CONCLUSION: Nutritional deficiencies in women have to be corrected before and between pregnancies and all contacts women have with the health system should be utilised for anaemia control interventions, in addition to long-term community approaches. To improve maternal health calls for a broader agenda and a change of approach in the MCH-clinics.

VENEZUELA

49. Meertens, L., Solano, L., Sanchez, A. (2002). Hemoglobina, ferritina y zinc sérico de mujeres en edad reproductiva. Su asociación con el uso de anticonceptivos [Hemoglobin, serum ferritin and zinc in women in reproductive ages: Its association with the use of contraceptives]. *An. venezia. nourish,* 15(1), 5-10. https://search.bvsalud.org/gim/resource/en/lil-341005

Las mujeres en edad reproductiva constituyen uno de los grupos de población vulnerables a las deficiencias específicas de nutrientes tales como anemia por deficiencia de hierro y deficiencia de zinc, asociada al uso de anticonceptivos orales. El objetivo de este estudio fue determinar los niveles de hemoglobina, ferritina y zinc sérico de mujeres en edad reproductiva y su asociación al uso de anticonceptivos. La muestra estuvo constituida por 60 mujeres de 15 a 45 años de edad, aparentemente sanas, que asistían a control de planificación familiar. Se determinó hemoglobina por método automatizado, ferritina por enzimoinmunoanálisis y zinc por espectrofotometría de absorción atómica y se evaluó estado nutricional según índice de Masa Corporal (IMC), así como el uso de anticonceptivos. La hemoglobina fue de 12,98ñ1,4g/dl, ferritina 30,77ñ18,78 ng/ml, zinc 77,12ñ11,87µg/dl. 15 por ciento de las mujeres estuvieron desnutridas, 13,3 por ciento presentó sobrepeso y 13,3 por ciento obesidad. El 13,3 por ciento de las mujeres evaluadas presentaron deficiencia de hierro, un 21,7 por ciento entaban anémicas y 41,8 por ciento presentaron hipozincemia. No existió asociación entre deficiencia de hierro y zinc con el método anticonceptivo. Estos resultados constituyen una base para estudios de intervención en grupos vulnerables.

TRANSLATION: Women of reproductive age constitute one of the population groups vulnerable to specific nutrient deficiencies such as iron deficiency anemia and zinc deficiency associated with oral contraceptive use. The aim of this study was to determine hemoglobin, ferritin and serum zinc levels in women of reproductive age and their association with contraceptive use. The sample consisted of 60 women between 15 and 45 years of age, apparently healthy, who attended family planning counseling. Hemoglobin was determined by automated method, ferritin by enzyme immunoassay and zinc by atomic absorption spectrophotometry and nutritional status was evaluated according to Body Mass Index (BMI), as well as the use of contraceptives. Hemoglobin was 12.98ñ1.4g/dl, ferritin 30.77ñ18.78 ng/ml, zinc 77.12ñ11.87µg/dl. Fifteen percent of the women were undernourished, 13.3 percent were overweight and 13.3 percent were obese. Iron deficiency was found in 13.3 percent of the women evaluated, 21.7 percent were anemic and 41.8 percent had hypozincemia. There was no association between iron and zinc deficiency and contraceptive method. These results constitute a basis for intervention studies in vulnerable groups.

Relevant Articles Cross-Referenced from Other Sections

General Hormonal Contraceptives

Haile, Z. T., Kingori, C., Teweldeberhan, A. K., & Chavan, B. (2017). The relationship between history of hormonal contraceptive use and iron status among women in Tanzania: A population-based study. *Sex Reprod Healthc*, *13*, 97–102. https://doi.org/10.1016/j.srhc.2017.07.003

Oral Contraceptives

Bellizzi, S., & Ali, M. M. (2018). Effect of oral contraception on anemia in 12 low- and middle-income countries. Contraception, 97(3), 236-242. https://doi.org/10.1016/j.contraception.2017.11.001

Haile, Z. T., Teweldeberhan, A. K., & Chertok, I. R. (2016). Association between oral contraceptive use and markers of iron deficiency in a cross-sectional study of Tanzanian women. *Int J Gynaecol Obstet*, *132*(1), 50–54. https://doi.org/10.1016/j.ijgo.2015.06.040

Low-and-Middle-Income Countries

Arabyat, R., Arabyat, G., Al-Taani, G. (2019). Prevalence and risk factors of anaemia among ever-married women in Jordan. *East Mediterranean Health Journal*, 25(8), 543–552. https://doi.org/10.26719/emhj.18.074

Sadeghian, M., Fatourechi, A., Lesanpezeshki, M., & Ahmadnezhad, E. (2013). Prevalence of anemia and correlated factors in the reproductive age women in rural areas of tabas. *Journal of family & reproductive health*, 7(3), 139–144. https://applications.emro.who.int/imemrf/J_Fam_Reprod_Health/J_Fam_Reprod_Health_2013_7_3_139_144.pdf

Relevant Grey Literature

ClinicalTrials.gov [Internet]. National Library of Medicine (US). 2000 Feb 29 - . Identifier NCT05233956, Levonorgestrel Intrauterine System Effects on Hemoglobin and Serum Ferritin Among Anemic Women in Kenya (LISA); 2021 Jan 31 [cited 2023 Aug 11]; [about 5 screens]. Available from: https://beta.clinicaltrials.gov/study/NCT05233956?cond=Anemia&term=Contraception&rank=2&a=1

Min, K. K., Win, H. H., MacQuarrie, K. (2019). Regional Disparities and Determinants of Anemia and Modern Contraceptive Use among Women in Myanmar. Further Analysis of the Myanmar Demographic and Health Survey 2015-16. *DHS Further Analysis Reports*, 126. https://dec.usaid.gov/dec/content/Detail.aspx?vID=47&ctID=ODVhZjk4NWQtM2YyMi00YjRmLTkxNjktZTcxMjM2NDBmY2Uy&rID=NTc1Nzgz

AUSTRALIA

Relevant Articles Cross-Referenced from Other Sections

Nutrition

Baines S, Powers J, Brown WJ. How does the health and well-being of young Australian vegetarian and semi-vegetarian women compare with non-vegetarians? Public Health Nutr. 2007 May;10(5):436-42. **https://doi.org/10.1017/s1368980007217938**

Patterson, A. J., Brown, W. J., & Roberts, D. C. K. (2001). Dietary and lifestyle factors influencing iron stores in Australian women: an examination of the role of bio-available dietary iron. *Australian Journal of Nutrition & Dietetics*, *58*(2), 107–113. https://www.academia.edu/download/45390778/Development_prevention_and_treatment_of_20160505-27710-pjzv7j.pdf

Athletes

Clarke, A. C., Anson, J. M., Dziedzic, C. E., McDonald, W. A., & Pyne, D. B. (2018). Iron monitoring of male and female rugby sevens players over an international season. *J Sports Med Phys Fitness*, *58*(10), 1490–1496. https://doi.org/10.23736/s0022-4707.17.07363-7

EUROPE

50. Hercberg, S., Preziosi, P., & Galan, P. (2001). Iron deficiency in Europe. *Public Health Nutr*, *4*(2b), 537–545. https://doi.org/10.1079/phn2001139

In Europe, iron deficiency is considered to be one of the main nutritional deficiency disorders affecting large fractions of the population, particularly such physiological groups as children, menstruating women and pregnant women. Some factors such as type of contraception in women, blood donation or minor pathological blood loss (haemorrhoids, gynaecological bleeding...) considerably increase the difficulty of covering iron needs. Moreover, women, especially adolescents consuming low-energy diets, vegetarians and vegans are at high risk of iron deficiency. Although there is no evidence that an absence of iron stores has any adverse consequences, it does indicate that iron nutrition is borderline, since any further reduction in body iron is associated with a decrease in the level of functional compounds such as haemoglobin. The prevalence of iron-deficient anaemia has slightly decreased in infants and menstruating women. Some positive factors may have contributed to reducing the prevalence of iron-deficiency anaemia in some groups of population: the use of iron-fortified formulas and iron-fortified cereals; the use of oral contraceptives and increased enrichment of iron in several countries; and the use of iron supplements during pregnancy in some European countries. It is possible to prevent and control iron deficiency by counseling individuals and families about sound iron nutrition during infancy and beyond, and about iron supplementation during pregnancy, by screening persons on the basis of their risk for iron deficiency, and by treating and following up persons with presumptive iron deficiency. This may help to reduce manifestations of iron deficiency and thus improve public health. Evidence linking iron status with risk of cardiovascular disease or cancer is unconvincing and does not justify changes in food fortification or medical practice, particularly because the benefits of assuring adequate iron intake during growth and development are well established. But stronger evidence is needed before rejecting the hypothesis that greater iron stores increase the incidence of CVD or cancer. At present, currently available data do not support radical changes in dietary recommendations. They include all means for increasing the content of dietary factors enhancing iron absorption or reducing the content of factors inhibiting iron absorption. Increased knowledge and

increased information about factors may be important tools in the prevention of iron deficiency in Europe.

BELGIUM

51. **Pynaert, I., de Bacquer, D., Matthys, C., Delanghe, J., Temmerman, M., de Backer, G., & de Henauw, S. (2009). Determinants of ferritin and soluble transferrin receptors as iron status parameters in young adult women. *Public Health Nutrition*, *12*(10), 1775–1782. https://doi.org/10.1017/S1368980008004369**

OBJECTIVE: To investigate associations between nutritional and non-nutritional variables and Fe status parameters, i.e. serum ferritin and soluble transferrin receptors (sTfR).

DESIGN: Cross-sectional design. Fe status parameters were determined on a fasting venous blood sample. Nutritional variables were assessed using a 2-d food record and non-nutritional variables by a general questionnaire. A general linear model was used to investigate associations between the variables and Fe status parameters.

SETTING: Region of Ghent, Dutch-speaking part of Belgium.

SUBJECTS: Random sample of 788 women (aged 18-39 years).

RESULTS: Median (interquartile range) ferritin and sTfR were 26.3 (15.9, 48.9) ng/ml and 1.11 (0.95, 1.30) mg/l, respectively. BMI and alcohol intake were positively associated and tea intake was negatively associated with serum ferritin. Women who used a non-hormonal intra-uterine device, who gave blood within the past year or who had been pregnant within the past year had lower serum ferritin values than their counterparts. Significant determinants of sTfR were smoking habit and pregnancy, with higher values for non-smokers and women who had been pregnant within the past year.

CONCLUSIONS: The present study indicates that contraceptive use, time since last blood donation, time since last pregnancy, BMI, alcohol and tea intake are determinants of Fe stores, whereas smoking habit and time since last pregnancy are determinants of tissue Fe needs. When developing strategies to improve Fe status, special attention should be given to women who use a non-hormonal intra-uterine device, gave blood within the past year and had been pregnant within the past year.

UNITED STATES

52. **Frith-Terhune, A. L., Cogswell, M. E., Khan, L. K., Will, J. C., & Ramakrishnan, U. (2000). Iron deficiency anemia: higher prevalence in Mexican American than in non-Hispanic white females in the third National Health and Nutrition Examination Survey, 1988-1994. Am J Clin Nutr, 72(4), 963–968. https://doi.org/10.1093/ajcn/72.4.963**

BACKGROUND: Mexican American females have a higher prevalence of iron deficiency than do non-Hispanic white females. OBJECTIVE: The objective was to estimate the prevalence of iron deficiency anemia and examine potential reasons for this difference between Mexican American (n = 1194) and non-Hispanic white (n = 1183) females aged 12-39 y.

DESIGN: We used data from the third National Health and Nutrition Examination Survey (1988-1994). Iron deficiency anemia was defined as abnormal results from >/=2 of 3 tests (erythrocyte protoporphyrin, transferrin saturation, and serum ferritin) and a low hemoglobin concentration. We used multiple logistic

regression to adjust for factors that were more prevalent in Mexican American females and significantly associated with iron deficiency anemia.

RESULTS: The prevalence of iron deficiency anemia was 6.2 +/- 0.8% (f1.gif" BORDER="0"> +/- SE) in Mexican American females and 2.3 +/- 0.4% in non-Hispanic white females. Mean dietary iron intake, mean serum vitamin C concentrations, and the proportion of females using oral contraceptives were similar in the 2 groups. Age <20 y and education were not associated with iron deficiency anemia. After adjustment for poverty level, parity, and iron supplement use, the prevalence of iron deficiency anemia was 2.3 times higher in Mexican American than in non-Hispanic white females (95% CI: 1.4, 3.9). In those with a poverty income ratio (based on household income) >3.0, however, the prevalence of iron deficiency anemia was 2.6 +/- 0.9% in Mexican American and 1.9 +/- 0.6% in non-Hispanic white females (NS).

CONCLUSION: Although much of the ethnic disparity in iron deficiency anemia remains unexplained, factors associated with household income may be involved.

53. **Spencer, B. R., Guo, Y., Cable, R. G., Kiss, J. E., Busch, M. P., Page, G. P., Endres-Dighe, S. M., Kleinman, S., Glynn, S. A., Mast, A. E., & Endres-Dighe, S. M. (2019). Iron status and risk factors for iron depletion in a racially/ethnically diverse blood donor population. *Transfusion*, *59*(10), 3146–3156. https://doi.org/10.1111/trf.15448**

BACKGROUND: The optimal approach for reducing iron depletion (ID) in blood donors may vary depending on biologic or behavioral differences across donors.

STUDY DESIGN AND METHODS: More than 12,600 successful whole blood donors were enrolled from four US blood centers for ferritin testing. The study population was enriched for racial/ethnic minorities (1605 African American, 1616 Asian, 1023 Hispanic). Subjects completed questionnaires on ID risk factors. Logistic regression identified predictors of absent iron stores (AIS; ferritin <12 ng/mL) and low ferritin (LF; ferritin <26 ng/mL).

RESULTS: Across all subjects, 19% had AIS and 42% had LF, with a sharp increase in risk observed with increasing donation intensity and among women a large decrease in risk in those more than 50 years old. When other factors were controlled for, African American and Asian donors showed 20% to 25% decreased risk for AIS compared to non-Hispanic Caucasian donors, while Hispanic donors had 25% higher risk. Daily iron supplementation reduced risk for LF and AIS by 30% to 40%, respectively, while the benefit from less frequent use was lower (7%-19% protection). Regular antacid use was associated with at least 20% increment to risk. Use of oral contraceptives or estrogen in females reduced risk by 16% to 22%, while males who reported supplemental testosterone use had a 50% to 125% greater risk for LF and AIS.

CONCLUSIONS: This study confirms high prevalence of LF and AIS in US donors and the principal risk factors of age, sex, and donation frequency. Additional demographic and behavioral risk factors of secondary importance might allow for refinement of ID mitigation strategies.

GREY LITERATURE

54. **ClinicalTrials.gov [Internet]. National Library of Medicine (US). 2000 Feb 29 - . Identifier NCT05233956, Levonorgestrel Intrauterine System Effects on Hemoglobin and Serum Ferritin Among Anemic Women in Kenya (LISA); 2021 Jan 31 [cited 2023 Aug 11]; [about 5 screens]. Available from: https://beta.clinicaltrials.gov/study/NCT05233956?cond=Anemia&term=Contraception&rank=2&a=1**

Estimated Completion: 2026-02

Women with mild/moderate anemia who are seeking contraception will be randomized to a levonorgestrel (LNG) intrauterine system (IUS) or an LNG/ethinyl estradiol (EE)/ferrous fumarate combined oral contraceptive (COC) regimen and followed prospectively for 18 months. Approximately 600 participants will be enrolled. The primary hypothesis is that the mean change in hemoglobin concentration will be significantly higher in the group assigned to the LNG IUS compared to the group assigned to COCs.

55. **ClinicalTrials.gov [Internet]. Madrid (Spain): National Library of Medicine (US). 2000 Feb 29 - . Identifier NCT04458662, Iron and Muscular Damage: Female Metabolism and Menstrual Cycle During Exercise (IronFEMME); 2020 Jul 02 [cited 2023 Aug 11]; [about 6 screens]. Available from: https://clinicaltrials.gov/study/NCT04458662**

This project is an observational controlled randomized counterbalance study. One hundred and three physically active and healthy women were selected to participate in the IronFEMME Study, of which 57 were eumenorrheic, 30 were oral contraceptive users (OCP) and 16 were postmenopausal women. The project consisted on two sections carrying out at the same time: Iron metabolism (Study I) and Muscle damage (Study II). For the study I, the exercise protocol consisted on an interval running test (8 bouts of 3 min at 85% of the maximal aerobic speed), whereas the study II protocol was based on an eccentric-based resistance exercise protocol (10 sets of 10 repetitions of plate-loaded barbell parallel back squats at 60% of their 1RM with 2 min of rest between sets). In both studies, eumenorrheic participants were evaluated at three specific moments of the menstrual cycle: Early-follicular phase, late-follicular phase and mid-luteal phase; OCP performed the trial at two moments: Withdrawal phase and active pill phase. Lastly, postmenopausal women were tested only once, since their hormonal status does not fluctuate. The three-step method was used to verify the menstrual cycle phase: calendar counting, blood analyses confirmation and urine-based ovulation kits. Blood samples were obtained to measure sexual hormones (e.g., 17β-Estradiol, Progesterone), iron metabolism parameters (e.g., Hepcidin, Iron, Ferritin, Transferrin) and muscle damage related markers (e.g., Creatine Kinase, Myoglobin, Lactate Dehydrogenase).

56. **ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 Feb 29 - . Identifier NCT00556400, Treatment of Menorrhagia in Women With Thrombocytopenia Using Platelets or Platelets and Hormones; 2007 Nov 9 [cited 2023 Aug 11]; [about 6 screens]. Available from: http://clinicaltrials.gov/ct/show/NCT00287391?order=1**

This study will explore the role of oral contraceptive pills in managing uterine bleeding in women who have low blood platelet counts as a result of aplastic anemia. Oral contraceptive pills have been shown to be effective in managing uterine bleeding in healthy women, but the effects have not been thoroughly studied in women who have low platelet counts. The purpose of the study is to determine whether oral contraceptive pills are a useful complement to platelet transfusions in women with aplastic anemia and uterine bleeding.

Volunteers for this study must be women between 12 and 55 years of age who have been diagnosed with aplastic anemia (with a platelet count of less than 50,000/microliter) and currently have active uterine bleeding. Candidates must not be pregnant or breastfeeding, must have a uterus and at least one functioning ovary, and must be willing to use nonhormonal methods of birth control (such as condoms or a diaphragm) for the duration of the study. On the first visit, candidates will be screened with a complete

medical history (including obstetric and gynecological history) and will undergo a physical examination, a pelvic exam and a pelvic ultrasound. Blood and urine samples will also be taken on this first visit.

The study will last approximately two weeks. Participants will be asked to monitor their medication doses and severity of bleeding during the course of the study. After the first visit, participants will be separated into two randomized groups and will receive either one tablet of oral contraceptive or a placebo twice daily, to be taken 12 hours apart at the same times each day. Participants will also receive platelet transfusions as needed to ensure that their platelet counts remain over 20,000/microliter. After seven days, researchers will assess participants' uterine bleeding and all participants will be given oral contraceptives in the second week of the study. Participants whose bleeding has decreased will receive only one tablet; participants who still have moderate to severe uterine bleeding will receive two tablets. A final assessment will be performed on day 14 of the study.

57. **Min, K. K., Win, H. H., MacQuarrie, K. (2019). Regional Disparities and Determinants of Anemia and Modern Contraceptive Use among Women in Myanmar. Further Analysis of the Myanmar Demographic and Health Survey 2015-16. *DHS Further Analysis Reports*, 126. https://dec.usaid.gov/dec/content/Detail.aspx?vID=47&ctID=ODVhZjk4NWQtM2YyMi00YjRmLTkxNjktZTcxMjM2NDBmY2Uy&rID=NTc1Nzgz**

Geographic disparities are an important consideration in the health equity of a country. Understanding regional disparities, the determinants of anemia, and the use of modern contraception by women of reproductive age would help to reduce the anemic burden, unwanted pregnancy, and related deaths. The aim of this study is to determine regional disparities and determinants of anemic health outcomes and use of modern contraception methods by women of reproductive age in Myanmar. The study is a secondary analysis that used cross-sectional data from the 2015-16 Myanmar Demographic and Health Survey. The unit of analysis for the anemic outcome is based on weighted samples of 12,489 eligible women of reproductive age (age 15-49). Analysis of modern contraception use was restricted to a weighted sample of 12,419 women age 15-49 who were not currently pregnant. The findings show that there are regional disparities in anemia and use of modern contraception within geographical zones, and that the disparities across States and Regions in Myanmar were especially large. Rakhine State in the Coastal zone was the most vulnerable region for anemic disparities (55.4%), while women of Chin State (17.5%) in the Hilly zone and Rakhine State (23%) in the Coastal zone were the least likely to use modern contraception. The determinants for anemia were biological and factors related to pregnancy, and not socioeconomic factors. Determinants of the use of modern contraception methods were region, age, education, marital status, wealth, and number of children. Regional disparities in anemia health outcomes and the low use of modern contraception methods remain major public health problems in Myanmar. The study recommends qualitative research that would explore food patterns and nutrient contents of households in the assessment of anemia status and cultural perspectives on family planning methods among communities in the different geographic areas. Providing iron tablets for women of reproductive age and all pregnant women would be the easiest, most effective way to prevent anemia in women. Investments in family planning and maternal and child health care services that focus on vulnerable areas in Myanmar would be a better solution for narrowing the geographic disparities in Myanmar.

58. **World Health Organization. (2023). Accelerating anaemia reduction: a comprehensive framework for action. https://www.who.int/publications/i/item/9789240074033**

This document is an output of a WHO cross-programme initiative aiming to improve the prevention, diagnosis and management of anaemia and thereby accelerate reduction in its prevalence.

It comes at an important time, midway through the era of the Sustainable Development Goals, when progress in reducing anaemia has stagnated. This framework is based on the core principles of primary health care: meeting people's health needs through comprehensive promotive, protective, curative, and rehabilitative care along the life course; systematically addressing the broader determinants of health; and empowering individuals, families, and communities to optimize their health

Iron deficiency is the most common and commonly recognized cause of anaemia and, to date, most work on addressing anaemia has been focused on the prevention and treatment of iron deficiency. However, anaemia is a complex condition with multiple causes – including other nutritional deficiencies, infections, inflammation, gynaecological and obstetric conditions, and inherited red blood cell disorders — requiring a multisectoral approach, building on existing interventions, to make progress against the global target.

This document will be complemented by operational guidance and a monitoring framework that will elaborate on how to strengthen multisectoral responses and implement actions in a coordinated and comprehensive way.

By leveraging the evidence, actions and resources in this document, we can further accelerate anaemia reduction. We must all work together to ensure that women, adolescent girls and children affected by anaemia receive the care and support they need and deserve.

59. **World Health Organization. (2022).** ***Family Planning - A global handbook for providers.*** **https://www.who.int/publications/i/item/9780999203705**

    This handbook offers clinic-based health care professionals in low- and middle-income countries the latest guidance on providing contraceptive methods. Anemia is mentioned in the following sections of the book: Chapter 4: Progestin-Only Injectables, Chapter 10 – Copper-Bearing Intrauterine Device, Job Aids – Comparing IUDs.

60. **Zhu, Y., Kolaja, C. A., Stamas, N., Matsuno, R. K., & Rull, R. P. (2022). Menstrual suppression among U.S. female service members in the millennium cohort study.** ***MSMR*****,** ***29*****(9), 19–22. https://www.health.mil/News/Articles/2022/09/01/Brief-MSMR**

    In order to evaluate the prevalence of menstruation suppression at two time intervals, this research investigates the demographic and military characteristics of female service members who took part in the Millennium Cohort Study. These findings show that between 2008 and 2013, the number of female U.S. service members who suppressed their periods increased. Despite the fact that menstruation suppression was embraced unequally by some subgroups of female service personnel, this increase was visible across demographic and military categories. At the time of this research, only 2 other studies had looked at the prevalence of menstruation suppression among female military members. Powell-Dunford found that in a convenience sample (n=154) at Walter Reed Medical Center, 7% (4%, 95% CI) of female Army personnel suppressed their menstrual cycle at some point during field training or deployment. Another study found that 21% of female soldiers used oral contraceptives constantly while they were deployed. Having access to menstrual suppression while deployment ensures menstrual control and can reduce the danger of iron deficiency anemia and the need for evacuation from the theater due to heavy bleeding or pregnancy**.** Pre-deployment medical exams and a 180-day supply of maintenance medicine are mandated by CENTCOM

MOD 14 (Modification 14 to USCENTCOM Individual Protection and Individual/Unit Deployment Policy), however it makes no mention of menstruation management or the use of contraception. Discussing menstrual suppression tactics at pre-deployment appointments can also be too late because many of them cause irregular bleeding in the early months of adoption. This study has a notable shortcoming in that survey-derived data may not fully reflect the prevalence of menstruation suppression among all female military personnel. Because there is no validated test for menstrual suppression, the prevalence estimates in this study are tentative and may not include those who chose shorter menstrual suppression cycles or who started it less than a year before the survey was conducted. Because deployment lengths may vary, with many lasting less than a year, this study may not have included female service members who use menstruation suppression exclusively while deployed. However, the large sample size, inclusion of all service branches, and both deployed and non-deployed personnel allowed for a distinct and more accurate examination of menstrual suppression.