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Use of the Electronic Health Record to Assess Prevalence of Anemia and Iron Deficiency in Pregnancy

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Abstract

Background: In the United States, the prevalence of anemia, iron deficiency (ID), and irondeficiency anemia (IDA) during pregnancy remains largely unknown as data at the national or state level are limited or nonexistent, respectively.

Objectives: In an effort to identify opportunities to improve maternal health surveillance, we assessed the feasibility of anemia, ID, and IDA surveillance among first-trimester pregnancies using electronic health records (EHRs).

Methods: We identified pregnancies among Kaiser Permanente Northwest members aged 18 y during 2005–2016 with first-trimester prenatal care (n = 41,991). Earliest laboratory test results for hemoglobin or hematocrit and ferritin were selected. We describe the proportion of pregnancies screened for and the prevalence of anemia, ID, and IDA; the concordance of anemia status by hemoglobin compared with hematocrit; and the proportion of pregnancies with laboratory-confirmed anemia that also had an International Classification of Diseases diagnostic code related to anemia.

Results: Identified pregnancies included women who were 73.1% non-Hispanic (NH) white, 11.5% Hispanic, 8.5% NH Asian/Pacific Islander, and 2.9% NH black. Hemoglobin and hematocrit results were available for 92.7% (n = 38,923) pregnancies. Anemia prevalence was 2.7% (n = 1045) based on hemoglobin <11.0 g/dL or hematocrit <33%; 45.2% of anemia cases had both low hemoglobin and low hematocrit. Among pregnancies with anemia, 18.9% (n = 197)

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Supplemental Table 1 is available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/jn.

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had a ferritin result; of those, 48.2% had ID (ferritin <15 μ g/L). In pregnancies without anemia, 3.4% (*n* = 1275) had a ferritin result; of those, 23.5% had ID. Based on 1472 pregnancies with both anemia and ID assessed, prevalence of ID and IDA was 26.8% and 6.5%, respectively; estimates likely represent selective screening.

Conclusions: EHR data have potential to monitor anemia prevalence and trends in health systems where prenatal anemia screening is nearly universal. However, if iron assessment is not routine, then representative estimates of ID or IDA are unattainable.

Keywords

pregnancy; anemia; iron deficiency; iron deficiency anemia; surveillance

Introduction

Anemia, iron deficiency (ID), and iron-deficiency anemia (IDA, presence of both) during pregnancy are prevalent global health concerns associated with adverse maternal and child health outcomes, including low birth weight, preterm birth, perinatal hemorrhage and mortality, and intellectual disabilities in offspring (1–7). In the United States, the prevalence of anemia, ID, and IDA during pregnancy and their contributions to health outcomes remain largely unknown as data at the national or state level are limited or nonexistent, respectively. The need to improve maternal health surveillance overall is well recognized and a current national priority (8–10).

National prevalence estimates for anemia, ID, and IDA are obtained from NHANES. However, data must be aggregated across ~10 y to produce reliable estimates because the number of pregnant women participating each year is small. Data from the 2003–2012 NHANES observed anemia prevalence of 8.8% among pregnant women (n = 776) with notable disparities by race-ethnicity [range: 3.1% among non-Hispanic (NH) white to 24.2% among NH black] (11). According to the 1999–2010 NHANES, ID and IDA prevalence among pregnant women (n = 1283) was 16.3% and 2.6%, respectively, also with notable disparities by race-ethnicity (ID was highest among NH black women, 27.8%) and by stage of pregnancy (ID was highest in the third trimester, 27.5%) (12). In 2013, NHANES stopped collecting information on the trimester of pregnancy, so trimester-specific cut-points for anemia can no longer be applied; hence, trimester-specific estimates are no longer available. The lack of timely surveillance data, particularly among high-risk groups that are also representative, hinders efforts to identify signals of concern, target interventions, evaluate programs, and guide policy. Thus, there is a need to identify alternative data sources for surveillance of anemia, ID, and IDA during pregnancy.

The American College of Obstetrics and Gynecologists (ACOG) recommends pregnant women be screened for anemia, and those with anemia may be evaluated for ID (4). Electronic health records (EHRs) that capture laboratory test results and/or diagnosis data have the potential to support public health surveillance needs. In an effort to explore whether use of EHRs is feasible for surveillance of anemia, ID, and IDA, we analyzed EHR data to *1*) describe the availability of laboratory results for anemia and ID; *2*) estimate the prevalence of anemia, ID, and IDA; and *3*) assess the use of International Classification of

Diseases (ICD) diagnosis codes for laboratory-confirmed anemia. The causes of anemia and

reasons for screening may be condition specific and vary across trimesters. We focused on first-trimester pregnancies to better understand data availability and nuances of using the EHR for this purpose.

Methods

We conducted a retrospective cohort study of all pregnancies to Kaiser Permanente Northwest (KPNW) members aged 18 y who began pregnancy on or after January 1,2005,and ended the pregnancy episode by December 31, 2016 (n = 78,533). KPNW is a nonprofit integrated delivery system caring for >610,000 medical plan members in western Oregon and southwest Washington. KPNW's members represent ~24% of the area's population and are demographically representative of the coverage area. Seventy-four percent of KPNW members receive benefits as part of a group membership, primarily through employers, whereas the rest are individual subscribers. This study was approved by the KPNW Institutional Review Board.

Data were extracted from the KPNW EHR system and Oregon and Washington birth certificates to obtain maternal smoking, parity, and multiple gestation information. Validated algorithms to identify pregnancies and link medical records to birth certificates have been described elsewhere (13). Pregnancies were eligible for analysis if *1*) prenatal care started during the first trimester (14 wk; n = 30,742 pregnancies excluded) and *2*) the woman was continuously enrolled in KPNW for first 20 wk or for the entire pregnancy if the pregnancy ended before 20 wk (n = 5,800 pregnancies excluded). Although we focused on the first trimester, we required enrollment for 20 wk to ensure observation time for ordering and diagnostic testing of iron status (n = 41,991 pregnancies).

Laboratory tests and definitions of anemia, ID, and IDA

From EHR clinical and research laboratory databases, we identified the earliest laboratory result during the first trimester (<14 wk) for hemoglobin (Hgb) or hematocrit (Hct). The first occurrence of either result set the "anemia screening date," and laboratory results for Hgb and Hct were selected from this date. We selected the earliest laboratory result for mean corpuscular volume (MCV) within the first 14 wk of pregnancy and selected indicators of iron status, including ferritin, serum iron, and total iron binding capacity (TIBC), within the first 20 wk. Ferritin was considered the preferred indicator to assess ID as it is the most specific test correlating to body iron stores (14,15); however, we also characterized the availability of serum iron and TIBC as they are used in clinical practice. Ferritin is an acute-phase reactant whose concentrations rise in the presence of infection or inflammation (15) and during pregnancy (16, 17). We assessed whether laboratory results were available for C-reactive protein (CRP; biomarker of inflammation) within the first 20 wk in an effort to account for inflammation when interpreting ferritin concentration (15).Few pregnancies (<0.1%) had a CRP laboratory result, particularly in combination with a ferritin result, so this measure was not further explored.

Anemia is defined as an Hgb concentration below normal values for age, sex, and physiologic state (e.g., pregnancy) (5). Because US clinical recommendations describe

anemia using both Hgb and Hct (4, 18), we estimated laboratory-confirmed anemia in 4 ways: *I*) Hgb <11.0 g/dL or Hct <33%, *2*) Hgb <11.0 g/dL and Hct <33%, *3*) Hgb<11.0g/dL, and *4*) Hct <33%. Althoughnottheprimaryobjective of our study, we also describe high Hgb, which we defined as >15 g/dL. Hgb was assessed with and without adjustment for any smoking during pregnancy and elevation based on ZIP code of residence using the recommended adjustments (5). Hgb 10.0–10.9 g/dL was considered mild anemia, 7.0–9.9 g/dL moderate, and <7.0 g/dL severe (5). Due to few cases of severe anemia, moderate and severe were examined as 1 category. Hct percentage is ~3 times the Hgb concentration (18, 19); thus, for comparison purposes, Hct <30% was considered moderate/ severe anemia. Microcytic and macrocytic anemia were defined as anemia based on abnormal Hgb or Hct plus an MCV <80 fL or an MCV >100 fL, respectively (4). ID was defined as ferritin <15 µg/L as referenced by the CDC and WHO (15, 18); we also report ferritin <10 µg/L as this was the laboratory reference value for KPNW and also referenced by ACOG (4). If a ferritin result was unavailable, we considered TIBC >400 µg/dL or serum iron <40 µg/dL indicative of ID (4). IDA was defined as the presence of both anemia and ID.

The availability of laboratory data from EHRs may be limited for some health systems. Therefore, we estimated the proportion of laboratory-confirmed anemia cases with a documented diagnosis code(s) for anemia or anemia-related conditions to assess the general feasibility of using only diagnosis codes to estimate prevalence. We reviewed all ICD, Clinical Modification, Ninth Revision (ICD-9-CM) and ICD, Clinical Modification, Tenth Revision (ICD-10-CM) diagnosis codes for anemia or anemia-related conditions and created 19 ICD-10-CM–based groupings (with the ICD-9-CM equivalent). A listing of ICD-10-CM and equivalent ICD-9-CM group codes assessed can be found in Supplemental Table 1. We extracted codes recorded in the EHR within the first 20 wk of gestation.

Other variables

From EHR clinical and administrative databases, we obtained mother's age at pregnancy onset, Medicaid coverage, and prepregnancy BMI (in kg/m²),using either self-reported prepregnancy weight or, if unavailable, the closest measured weight to pregnancy onset between 6 mo prior to or 42 d after onset, as well as the median of all heights >18 y of age. Race and ethnicity, smoking status (any smoking reported during the pregnancy), parity, and multiple gestation were obtained preferentially from the birth certificate. If the pregnancy was not linked to a birth certificate or if data were missing in the birth certificate file, we obtained data from the EHR. Elevation in meters above sea level at place of residence was determined by averaging the minimum and maximum altitude for each US ZIP code zone using a geographic information system (Esri ArcGIS Desktop 10.5). Elevation was acquired using a 10-m digital elevation model from the USGS 3D Elevation Program (3DEP). ZIP code boundaries were from TIGER/Line 2018 Zip Code Tabulation Areas from the US Census Bureau (https://catalog.data.gov/dataset/tiger-line-shapefile-2018-2010-nation-u-s-2010-census-5-digit-zip-code-tabulation-area-zcta5-na).

Statistical analyses

We examined the proportion of pregnancies screened for anemia during the first trimester and characteristics of Hgb or Hct results, including distribution of laboratory values and

prevalence of anemia overall and by severity. We also examined concordance of anemia status by Hgb compared with Hct. We compared the characteristics of those who were screened with those who were not screened, as well as those with laboratory-confirmed anemia compared with no anemia, among those with laboratory results. To determine if the distribution of anemia screening or anemia prevalence differed by characteristic, we used generalized estimating equations to account for correlations introduced by including >1 pregnancy to the same woman. To assess feasibility of using ICD diagnostic codes only to estimate prevalence instead of laboratory results, we assessed the proportion of pregnancies with laboratory-confirmed anemia that also had an ICD diagnostic code related to anemia diagnosis or other inherited or acquired reason for anemia. We described the proportion of pregnancies screened for ID and the proportion with ID and IDA. Statistical significance was set at P < 0.05. Statistical analyses were run in Statistical Analysis Software version 9.4 (SAS Institute).

Results

The study sample included 41,991 pregnancies to 31,824 unique women. Among the 41,991 pregnancies, 92.7% (n = 38,925) had a laboratory result for Hgb or Hct in the EHR. For all but 2 pregnancies, Hgb and Hct were assessed on the same date; both pregnancies had normal laboratory results. For simplicity, these 2 pregnancies were excluded from further analyses. Median first prenatal visit was at 8.6 wk [quartiles 1– 3 (Q_{1-3}): 7.7–9.7], and median first Hgb and Hct laboratory results were at 9.0 wk (Q_{1-3} : 7.4–10.4). Hgb concentrations ranged from 4.5 to 19.0 g/dL, with a median value of 12.9 g/dL (Q_{1-3} : 12.3–13.5). Hct concentrations ranged from 17% to 55%, with a median value of 38% (Q_{1-3} : 36–40%).Hematocrit was 2.9–3.0 times higher than hemoglobin at the first, second, and third quartiles and the minimum and maximum values (data not shown). The total number of Hgb/Hct tests per pregnancy in the first trimester ranged from 1 to 20 (Q_{1-3} : 1–1).

The characteristics of pregnancies screened for anemia differed from pregnancies not screened (Table 1). Anemia screening tended to be lower among women who were younger (18–24 y) or older (35 y), were NH black, covered by Medicaid, or had obesity. Screening was lowest among pregnant women missing data on smoking, parity, or multiple gestation status; most (>97%) women missing at least 1 of these variables had a pregnancy that did not end with a live birth (data not shown). Among pregnancies not screened, a higher proportion ended in the first trimester (37.1%) compared with pregnancies screened for anemia (8.5%; P < 0.0001).

Overall, anemia prevalence was low. The prevalence of anemia based on having abnormal Hgb or abnormal Hct (n = 1045) was 2.7%. Anemia based on both abnormal Hgb and abnormal Hct (n = 472) was 1.2%, abnormal Hgb only (n = 701) was 1.8%, and abnormal Hct only (n = 816) was 2.1%. The prevalence of anemia by Hgb only was 1.9% (n = 739) when Hgb was adjusted for smoking and elevation. Just over 5% of pregnancies required an adjustment for smoking, and 25 pregnancies resided in an area >1000 m above sea level. The prevalence of anemia (abnormal Hgb or abnormal Hct) in the first trimester differed by all maternal characteristics examined, except smoking status (Table 1). Anemia prevalence was higher among women who were underweight, were NH black, were NH Asian/Pacific

Islander, covered by Medicaid, and had parity 2 or a pregnancy with multiple fetuses. Most notable, the prevalence of anemia (10.9%) among NH black women was 2–5 times higher than the prevalence observed in other groups (range: 2.0–4.3%). Patterns were similar for moderate/severe anemia (data not shown).

Less than 1% (n = 271) of pregnancies had an Hgb >15.0 g/dL. After Hgb was adjusted for smoking and elevation, this reduced to n = 255, but the proportion of pregnancies with Hgb >15.0 g/dL compared with Hgb 15 g/dL remained highest for those with missing data on smoking status (2.4%) compared with nonsmokers (0.7%) and smokers (0.6%) (P = 0.06, data not shown), suggesting that smoking may still explain some of the elevated Hgb. The proportion of pregnancies with Hgb >15.0 g/dL compared with Hgb >15.0 g/dL significantly differed only by maternal race and ethnicity (P < 0.0001) and multiple gestation status (P = 0.03). For both characteristics, the proportion with Hgb >15.0 g/dL was highest among the group classified as multiple/other/missing, thus limiting ability to make any meaningful interpretations (data not shown).

Among pregnancies with a laboratory result for Hgb and Hct, 99.9% also had MCV measured on the same day. For 30 pregnancies, the first MCV laboratory result available was measured a mean \pm SD 37 \pm 20 d after the first Hgb and Hct test. MCV laboratory result was unavailable for 14 pregnancies. One-third of anemia cases were classified as microcytic anemia; the remaining had normal MCV values. There were no cases of macrocytic anemia (data not shown).

Most anemia was classified as mild (Table 2). Only 3 pregnancies were classified with severe anemia based on Hgb (data not shown). Overall, the concordance in anemia status based on Hgb or Hct was 98.5%, but this was driven by the large number of normal test results. Among 1045 pregnancies identified with anemia by either abnormal Hgb or Hct, the concordance in diagnosis across the 2 tests was 45.2%. Agreement according to anemia severity (mild and moderate/severe) was 36.8% (Table 2).

Availability of ferritin results was low (n = 1472). Among pregnancies with anemia (n = 1045), 18.9% had a ferritin measure compared with 3.4% among pregnancies without anemia (n = 37,878) at the first laboratory test (Table 3). Among the pregnancies with anemia, ferritin was assessed among 15.2% of those with mild anemia and 39.7% of those with moderate/severe anemia. The proportion with ferritin assessed differed by race-ethnicity. Among pregnancies with anemia, ferritin was assessed at a higher rate among NH black (23.1%) and NH Asian/Pacific Islander (23.5%) compared with Hispanic (15.3%) and NH white (10.4%) women (data not shown). Among pregnancies without Hgb or Hct results, <2% had a ferritin result (data not shown). Ferritin was assessed at a median of 9.0 wk (Q_{1-3} : 5–12 wk).Median ferritin concentrations and ID status by anemia status are described in Table 3. Of the 1472 pregnancies with ferritin and anemia assessed, prevalence of ID and IDA was 26.8% (395/1472) and 6.5% (95/1472), respectively. Of the 197 pregnancies with laboratory-confirmed anemia and with ferritin assessed, 43.0% of those with mild anemia (n = 62) had ID (data not shown). There were 184 pregnancies with laboratory results for TIBC

or serum iron but not ferritin. Including laboratory results using ferritin, TIBC, or serum iron, prevalence of ID and IDA was 27.4% (453/1656) and 7.1% (118/1656), respectively.

Of the 1045 pregnancies with laboratory-confirmed anemia, only 30.6% (n = 320) had any anemia-related diagnosis code recorded in the EHR within the first 20 wk of pregnancy. Of the 320 pregnancies with any anemia-related diagnosis code recorded, 28.4% (n = 91) included at least 1 code related to a hereditary enzyme deficiency or blood disorder (Supplemental Table 1 footnote). Among the 37,878 pregnancies in which the first Hgb/Hct result examined was negative for anemia, there were 1013 (2.7%) with an anemia-related diagnosis code recorded in the first 20 wk.

Discussion

This study sought to assess the feasibility of using EHR data for the surveillance of anemia, ID, and IDA among pregnant women in the first trimester within the context of a large, integrated health care delivery system. Overall, screening for anemia within the first 14 wk of pregnancy was high (~92%), with most records having a measure of Hgb and Hct. Although there were disparities in anemia screening across several characteristics, a higher proportion of women not screened also had a pregnancy that ended in the first trimester, a finding that may be explained by early pregnancy loss prior to the collection of routine prenatal laboratory values. Anemia prevalence was low in our study but consistent with the first-trimester prevalence estimate observed in the 1999–2006 NHANES (2.7%; 95% CI: 0.0,5.5) (20). Anemia prevalence was not higher among women with obesity as might be expected based on the reported association between obesity and ID (21). Anemia prevalence was >5 times higher among NH black women compared with NH white women, a disparity also consistent with observations from NHANES (11, 20). Among women pregnant with multiple gestation, anemia prevalence was twice as high as that among women with a singleton gestation and may be related to both an increased rate of plasma volume expansion and an increased utilization of iron stores (22). These findings illustrate a need for improved surveillance to better identify and understand high-risk groups in whom targeted interventions may improve maternal and child health.

Less than one-third of records with laboratory-confirmed anemia had an anemia-related diagnosis code recorded. We were unable to determine whether the anemia was considered clinically insignificant or simply not documented in diagnosis codes. We also observed notable discordance in classification of anemia defined by low hemoglobin, low hematocrit, or both. Provider preference in use of a specific indicator may influence anemia recognition and documentation. Overall findings suggest that the EHR may be a viable data source for surveillance of anemia if laboratory testing result data are available and a consistent case definition is used; ICD diagnosis codes alone are insufficient based on this study, but this should be confirmed in other EHR sources.

In contrast to anemia, this EHR did not appear to be a viable source for surveillance of ID or IDA during early pregnancy. Laboratory-based screening for ID within the first 20 wk of pregnancy was low, even among women with laboratory-confirmed anemia. We abstracted the earliest iron status test result within the first 20 wk under the assumption that iron tests

would be conducted after anemia was identified. However, we found the median gestational age and interquartile range among those screened for anemia and ID were nearly identical, suggesting that some pregnant women, albeit few, were assessed for ID earlier or at the same time as anemia. Among women with iron status and anemia status assessed, the prevalence of ID and IDA was ~27% and 7%, respectively. These estimates are higher than NHANES prevalence estimates (12) and may represent selective measurement of iron status in the context of medical care. Notably, compared with other race and ethnicity groups, a higher proportion of NH black and NH Asian/Pacific Islander women with anemia had ferritin assessed. This may be due to the possible differences in the positive predictive value of anemia screening for ID among race/ethnic groups (18) and evaluation to rule out IDA before proceeding to a hemoglobin electrophoresis to assess for sickle cell or thalassemia. Among the subset of women with laboratory-diagnosed anemia and with ferritin assessed, nearly half (48.2%) were iron deficient, presumably correctable with iron treatment. We were unable to determine if supplemental iron was advised or dispensed as iron supplements are typically obtained over the counter, and these data are not routinely recorded in the EHR. ID can exist without anemia because declines in hemoglobin concentrations occur only in the late stages of ID (5, 18). Current obstetric practice guidelines do not recommend universal iron screening at the onset of prenatal care, and few women with anemia had iron status evaluated. Together, these factors hamper the feasibility of using EHR data for ID and IDA surveillance.

Our findings demonstrate that the use of EHR for anemia surveillance among pregnant women has potential but requires several considerations if surveillance is to be standardized and scaled to monitor temporal and geographic trends. Population selection describing who is being assessed by the EHR must clearly be identified; often, pregnant women not included are hardest to study, and understanding selection biases is essential. An estimated one-fourth of pregnancies do not end in a live birth (23, 24), and ~15% of women do not begin first-trimester prenatal care (25). We chose to identify all pregnancies regardless of birth outcome and then restrict to pregnancies that sought first-trimester prenatal care. Maternal characteristics, such as race and ethnicity, smoking, and parity, are important to ascertain but may be limited in EHRs (26, 27). We obtained these measures preferentially from the birth certificate, but this linkage may be impractical for many EHR systems. Clear and consistent guidance on which laboratory result(s) to use is also critical. We selected the first laboratory test result during the first trimester, which generally coincided with the first prenatal visit ~9 wk of gestation. Pregnant women can have repeated Hgb/Hct test results if being followed for threatened or spontaneous abortion, ectopic pregnancy, or hospitalization (condition related or unrelated to pregnancy), where routine complete blood counts may be collected serially when bleeding is of concern (e.g., every 6 h or every day). Selecting the first test result in the first trimester is the earliest test available for a pregnancy being monitored for any bleeding process. Concurrent reporting of gestational age of laboratory assessment is warranted.

In addition, a standard case definition of anemia and IDA is required. ACOG guidelines define anemia using either Hgb or Hct (4), and NHANES reports only Hgb (11, 12). Nearly all pregnancies had both Hgb and Hct measured simultaneously, yet the concordance for identifying anemia was <50%.Hct classified more women with mild anemia, whereas

the proportion of women classified with moderate/severe anemia was higher using Hgb. Although there is a relation between Hgb and Hct (3:1 on average), these tests do not measure the same physiologic construct. Hgb is a direct measure of the iron-containing protein in RBCs. Hct is the proportion of whole blood occupied by RBCs, where RBC volume is affected differently by nutritional deficiencies, disease processes, and genetic blood disorders (4, 18). At the individual level, small variations in the relation between Hgb and Hct may lead to discordance of anemia for measures close to cut-points defining anemia. It remains unclear whether health outcomes are better predicted when anemia and severity are classified by Hgb, Hct, or both. In the context of clinical settings, the alignment of anemia identification with standards of clinical care may be necessary until there is more evidence to recommend a certain test. Furthermore, although Hgb and Hct are the primary screening tests for identifying anemia, neither are specific for ID (28). Ferritin is considered the best diagnostic test clinically available for ID (29), but among pregnancies with any iron indices assessed, we found at least 10% had an iron indicator other than ferritin. Issues surrounding selection of laboratory test type and threshold for diagnosis would also apply to surveillance of ID and IDA should ferritin or other iron status indices be routinely measured.

Although most women unscreened may be explained by early pregnancy loss, it is possible that some women categorized as unscreened live in areas where laboratory tests are performed at non-Kaiser Permanente laboratories, may have had laboratory tests conducted just prior to conception, received pregnancy care outside the KPNW network (e.g., dual insurance coverage), or chose not to have laboratory tests conducted; thus, screening rates may be slightly underestimated. We only examined anemia-related diagnosis codes recorded during the first 20 wk of gestation. It is possible that diagnosis codes related to inherited enzyme deficiencies or blood disorders were available prior to this window, but examining historical ICD codes was beyond the scope of this analysis. Iron status data were too sparse to determine whether the measurement of these indices varied by maternal or clinical characteristics. The recommended iron indicator, ferritin, is a positive acute-phase protein; thus, in the presence of inflammation (e.g., due to obesity, infection, or physiologic changes in pregnancy), ferritin concentrations may be elevated, resulting in an underdiagnosis of ID. Using a higher ferritin threshold to identify ID or adjusting ferritin for the influence of inflammation may be warranted, although the use of these methods among pregnant populations is not well studied (15, 30, 31). Although not unexpected, the paucity of CRP laboratory results hindered ability to identify inflammation and the degree to which prevalence of ID and IDA may be underestimated. This study examined availability of EHR data within 1 integrated-care health system in the Pacific Northwest; thus, findings may not be generalizable to other health systems or US populations of pregnant women. These findings will need to be confirmed as screening practices may differ across systems (32). Similarly, we focused on the first trimester as a starting place to assess EHR use for anemia, ID, and IDA surveillance. Additional studies are needed to explore whether use of HER is feasible among second-and trimester-pregnancies as methods such as inclusion criteria and selection of laboratory test result may differ.

The purpose of screening for and treatment of anemia, ID, and IDA among pregnant women is to improve maternal and infant health outcomes. However, in 2015, the US Preventative Services Task Force (USPSTF) concluded that there was insufficient evidence to make a

recommendation about the effectiveness of IDA screening among asymptomatic pregnant women (8), a deviation from their 2006 statement recommending routine screening (33). The change was driven by methodologic updates to better identify evidence applicable to the current US population (8). Consequently, practice guidelines vary across medical specialty organizations (4, 34). Upon reviewing the evidence, the USPSTF identified several data gaps preventing researchers from assessing the balance of benefits and harms of IDA screening. Most germane here: I) few data are available to estimate the current prevalence of IDA among pregnant women, 2) rates of screening for IDA and iron supplementation among pregnant women are not well documented, and 3) evidence is insufficient to recommend a specific screening test. Filling these data gaps was the impetus to explore whether use of EHR is feasible and potentially scalable for surveillance of anemia, ID, and IDA.

We found that using laboratory results may be necessary if surveillance systems rely on EHR data because anemia ICD diagnoses are not reliably documented in the EHR in the first trimester. The lack of systematic assessment of iron status, however, precludes use of these EHR data for first-trimester ID or IDA surveillance. Therefore, the evidence gap to update clinical preventive services recommendations for anemia and IDA, as indicated by the USPSTF, may remain if surveillance relies only on EHR. Conversely, surveillance using the EHR may depend on having clinical guidelines.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations used:

ACOG	American College of Obstetrics and Gynecologists
CRP	C-reactive protein
EHR	electronic health record
ICD	International Classification of Diseases
ICD-9-CM	International Classification of Diseases, Clinical Modification, Ninth Revision
ICD-10-CM	International Classification of Diseases, Clinical Modification, Tenth Revision
ID	iron deficiency
IDA	iron-deficiency anemia

Hct	hematocrit
Hgb	hemoglobin
KPNW	Kaiser Permanente Northwest
MCV	mean corpuscular volume
NH	non-Hispanic
Q	quartile
TIBC	total iron binding capacity
USPSTF	US Preventative Services Task Force

References

- Stevens GA, Finucane MM, De-Regil LM, Paciorek CJ, Flaxman SR, Branca F, Pena-Rosas JP, Bhutta ZA, Ezzati M; Nutrition Impact Model Study Group. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. Lancet Glob Health 2013;1:e16–25. [PubMed: 25103581]
- Albacar G, Sans T, Martin-Santos R, Garcia-Esteve L, Guillamat R, Sanjuan J, Canellas F, Gratacos M, Cavalle P, Arija V, et al. An association between plasma ferritin concentrations measured 48 h after delivery and postpartum depression. J Affect Disord 2011;131:136–42. [PubMed: 21130499]
- Allen LH. Anemia and iron deficiency: effects on pregnancy outcome. Am J Clin Nutr 2000;71:1280S–4S. [PubMed: 10799402]
- 4. American College of Obstetricians Gynecologists. ACOG Practice Bulletin No. 95: anemia in pregnancy (reaffirmed in 2015). Obstet Gynecol 2008;112:201–7. [PubMed: 18591330]
- WHO. Nutritional anaemias: tools for effective prevention and control[Internet]. 2017 [cited 2021 Jun 22]. Report No.: 978–92-4–151306-7.Availablefrom:https://apps.who.int/iris/bitstream/handle/ 10665/259425/9789241513067-eng.pdf.
- Georgieff MK. Long-term brain and behavioral consequences of early iron deficiency. Nutr Rev 2011;69(Suppl 1):S43–8. [PubMed: 22043882]
- Radlowski EC, Johnson RW. Perinatal iron deficiency and neurocognitive development. Front Hum Neurosci 2013;7:585. [PubMed: 24065908]
- Siu AL; U.S. Preventive Services Task Force (USPSTF). Screening for iron deficiency anemia and iron supplementation in pregnant women to improve maternal health and birth outcomes: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2015;163: 529–36. [PubMed: 26344176]
- 9. US Department of Health & Human Services, Office of the Surgeon General. The surgeon general's call to action to improve maternal health [Internet]. 2020 [cited 2021 Jun 22]. Available from: https://www.hhs.gov/sites/default/files/call-to-action-maternal-health.pdf.
- USepartment of Health & Human Services. Healthy Women, healthy pregnancies, healthy futures: action plan to improve maternal health in America [Internet]. 2020 [cited 2021 Jun 22]. Available from: https://aspe.hhs.gov/system/files/aspe-files/264076/healthy-women-healthypregnancies-healthy-future-action-plan_0.pdf.
- 11. Le CH. The prevalence of anemia and moderate-severe anemia in the US population (NHANES 2003–2012). PLoS One 2016;11:e0166635.
- Gupta PM, Hamner HC, Suchdev PS, Flores-Ayala R, Mei Z. Iron status of toddlers, nonpregnant females, and pregnant females in the United States. Am J Clin Nutr 2017;106:1640S–6S. [PubMed: 29070559]

- Hornbrook MC, Whitlock EP, Berg CJ, Callaghan WM, Bachman DJ, Gold R, Bruce FC, Dietz PM, Williams SB. Development of an algorithm to identify pregnancy episodes in an integrated health care delivery system. Health Serv Res 2007;42:908–27. [PubMed: 17362224]
- United Nations Children's Fund, United Nations University, World Health Organization. Irondeficiency anaemia. Assessment, prevention, and control: a guide for programme managers [Internet]. Geneva (Switzerland): World Health Organization; 2001 [cited 2021 Jun 22]. Report No. WHO/NHD/01.3. Available from: http://apps.who.int/iris/bitstream/10665/66914/1/ WHO_NHD_01.3.pdf?ua=1.
- WHO. WHO guideline on ferritin concentrations to assess iron statusin individuals and populations [Internet]. Geneva (Swizterland): WHO; 2020 [cited 2021 Jun 22]. Available from: http://www.who.int/vmnis/indicators/haemoglobin.pdf.
- Mei Z, Li H, Serdula MK, Flores-Ayala RC, Wang L, Liu JM, Grummer-Strawn LM. C-reactive protein increases with gestational age during pregnancy among Chinese women. Am J Hum Biol 2016;28: 574–9. [PubMed: 26865074]
- Raio L, Bersinger NA, Malek A, Schneider H, Messerli FH, Hurter H, Rimoldi SF, Baumann MU. Ultra-high sensitive C-reactive protein during normal pregnancy and in preeclampsia: a pilot study. J Hypertens 2019;37:1012–7. [PubMed: 30882594]
- Centers for Disease Control and Prevention. Recommendations to prevent and control iron deficiency in the United States. MMWR Recomm Rep 1998;47:1–29.
- Bain BJ, Bates I, Laffan MA, (editors). Dacie and Lewis practical haematology. 12th ed. Elsevier; 2017. ISBN: 9780702066962.
- Mei Z, Cogswell ME, Looker AC, Pfeiffer CM, Cusick SE, Lacher DA, Grummer-Strawn LM. Assessment of iron status in US pregnant women from the National Health and Nutrition Examination Survey (NHANES), 1999–2006. Am J Clin Nutr 2011;93:1312–20. [PubMed: 21430118]
- Zhao L, Zhang X, Shen Y, Fang X, Wang Y, Wang F. Obesity and iron deficiency: a quantitative meta-analysis. Obes Rev 2015;16:1081–93. [PubMed: 26395622]
- 22. Shinar S, Shapira U, Maslovitz S. Redefining normal hemoglobin and anemia in singleton and twin pregnancies. Int J Gynaecol Obstet 2018;142:42–7. [PubMed: 29637566]
- Wilcox AJ, Weinberg CR, O'Connor JF, Baird DD, Schlatterer JP, Canfield RE, Armstrong EG, Nisula BC. Incidence of early loss of pregnancy. N Engl J Med 1988;319:189–94. [PubMed: 3393170]
- 24. Zinaman MJ, Clegg ED, Brown CC, O'Connor J, Selevan SG. Estimates of human fertility and pregnancy loss. Fertil Steril 1996;65: 503–9. [PubMed: 8774277]
- 25. Pregnancy Risk Assessment Monitoring System (PRAMS). Prevalence of selected maternal and child health indicators for all PRAMS sites, 2016–2017 [Internet]. Atlanta (GA): Centers for Disease Control and Prevention; 2018 [cited 2021 Jun 22]. Available from: https://www.cdc.gov/ prams/prams-data/mch-indicators/states/pdf/2018/All-PRAMS-Sites-2016-2017_508.pdf.
- Polubriaginof FCG, Ryan P, Salmasian H, Shapiro AW, Perotte A, Safford MM, Hripcsak G, Smith S, Tatonetti NP, Vawdrey DK. Challenges with quality of race and ethnicity data in observational databases. J Am Med Inform Assoc 2019;26:730–6. [PubMed: 31365089]
- 27. Polubriaginof F, Salmasian H, Albert DA, Vawdrey DK. Challenges with collecting smoking status in electronic health records. AMIA Annu Symp Proc 2017;2017:1392–400. [PubMed: 29854208]
- Mei Z, Parvanta I, Cogswell ME, Gunter EW, Grummer-Strawn LM. Erythrocyte protoporphyrin or hemoglobin: which is a better screening test for iron deficiency in children and women? Am J Clin Nutr 2003;77:1229–33. [PubMed: 12716676]
- 29. WHO. Assessing the iron status of populations: report of a Joint World Health Organization/ Centers for Disease Control and Prevention Technical Consultation on the Assessment of Iron Status at the Population Level [Internet]. Geneva (Switzerland): WHO; 2004 [cited 2021 Jun 22].Available from: https://www.who.int/nutrition/publications/micronutrients/ anaemia_iron_deficiency/9789241596107.pdf.
- Daru J, Colman K, Stanworth SJ, De La Salle B, Wood EM, Pasricha SR. Serum ferritin as an indicator of iron status: what do we need to know? Am J Clin Nutr 2017;106:1634S–9S. [PubMed: 29070560]

- 31. Namaste SM, Rohner F, Huang J, Bhushan NL, Flores-Ayala R, Kupka R, Mei Z, Rawat R, Williams AM, Raiten DJ, et al. Adjusting ferritin concentrations for inflammation: biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. Am J Clin Nutr 2017;106:359S–71S. [PubMed: 28615259]
- Marcewicz LH, Anderson BL, Byams VR, Grant AM, Schulkin J.Screening and treatment for iron deficiency anemia in women: results of a survey of obstetrician-gynecologists. Matern Child Health J 2017;21:1627–33. [PubMed: 28251440]
- U.S. Preventive Services Task Force. Screening for iron deficiency anemia—including iron supplementation for children and pregnant women: recommendation statement [Internet].
 2006 [cited 2021 Jun 22]. Available from: https://www.uspreventiveservicestaskforce.org/uspstf/ recommendation/iron-deficiency-anemia-screening.
- 34. American Academy of Family Physicians. Summary of recommendations for clinical preventive services [Internet]. 2017 [cited 2021 Jun 22]. Available from: https://www.aafp.org/dam/AAFP/ documents/patient_care/clinical_recommendations/cps-recommendations.pdf.

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TABLE 1

Description of eligible pregnancies, the proportion screened for anemia, and anemia status by sociodemographic characteristics, Kaiser Permanente Northwest, 2005–2016

	Eligible popu	ilation, $n = 41,991$	Screened	I for anemia, $n = 38,923$	Have	anemia, <i>n</i> = 1045
Characteristic	u	Column %	Row %	P value for screening	Row %	<i>P</i> value for anemia ²
Age, y				<0.0001		0.0003
18–24	8285	19.7	91.0		2.8	
25-29	12,666	30.2	94.0		2.3	
30–34	13,139	31.3	93.7		2.6	
35	7901	18.8	90.5		3.4	
BMI status				<0.0001		0.005
Underweight	891	2.1	93.7		4.4	
Normal	18,709	44.6	93.3		2.9	
Overweight	10,306	24.5	92.5		2.4	
Obese	2066	23.6	91.9		2.5	
Unknown	2178	5.2	91.7		3.2	
Race/ethnicity				<0.0001		<0.0001
Hispanic	4844	11.5	92.0		3.5	
NH white	30,683	73.1	93.0		2.0	
NH black	1207	2.9	89.3		10.9	
NH Asian/Pacific Islander	3576	8.5	93.3		4.3	
Multiple/other/unknown	1681	4.0	90.6		3.3	
Medicaid coverage				<0.0001		<0.0001
Yes	2221	5.3	88.9		4.8	
No	39,770	94.7	92.9		2.6	
Smoking status				<0.0001		0.25
Yes	2305	5.5	90.0		3.3	
No	39,451	94.0	93.1		2.7	
Unknown	235	0.6	53.6		1.6	
Parity				<0.0001		<0.0001
0	17,124	40.8	92.6		2.3	

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	Eligible popu	lation, $n = 41,991$	Screened	for anemia, $n = 38,923$	Have	anemia, $n = 1045$
Characteristic	u	Column %	Row %	P value for screening	Row %	P value for anemia
1	13,624	32.5	93.3		2.5	
2	8745	20.8	91.5		3.8	
Unknown	2498	6.0	74.2		2.6	
Multiple gestation				<0.0001		0.0006
No	36,485	86.9	94.8		2.7	
Yes	752	1.8	94.3		6.1	
Unknown	4754	11.3	76.4		2.4	

characteristic and account for correlations introduced by including >1 pregnancy to the same woman. Screened for anemia was determined by the availability of a hemoglobin or hematocrit laboratory value $^{\prime}$ Generalized estimating equations (GEEs) were used to assess whether the proportions between eligible pregnancies screened (n = 38,923) and not screened (n = 3068) for anemia differed by maternal in the electronic health record during the first trimester.

²GEEs were used to assess whether the proportions among pregnancies with (n = 1045) or without anemia (n = 37, 878) differed by maternal characteristic and account for correlations introduced by including >1 pregnancy to the same woman. Anemia defined as hemoglobin <11.0 g/dL or hematocrit <33% (4).

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TABLE 2

Concordance in anemia severity based on hemoglobin and hematocrit among first-trimester pregnancies, Kaiser Permanente Northwest, 2005–2016¹

		Hematocrit, n		
Hemoglobin	No anemia (33%)	Mild (30–32.9%)	Moderate/severe (<30%)	Total, n (%)
No anemia (11.0 g/dL)	37,878	344	0	38,222 (98.2)
Mild (10–10.9 g/dL)	222	323	13	558(1.4)
Moderate/severe (<10 g/dL)	7	74	62	143 (0.4)
Total, n (%)	38,107 (97.9)	741 (1.9)	75(0.2)	38,923
Concordance criteria			n ²	%
Anemia by Hgb (<11 g/dL) or Hct (<3:	3%)		38,923	98.5
Anemia by Hgb (<11 g/dL) and Hct (<	33%) among pregnancies with anem	ia	1045	45.2
Anemia severity by Hgb or Hct			38,923	98.3
Anemia severity by Hgb and Hct amon	g pregnancies with anemia		1045	36.8

Wild, moderate, and severe classifications based on the Hgb definitions (5, 18) and the 3:1 ratio for Hgb/Hct (18, 19). For comparison to Hct, Hgb was not adjusted for smoking or elevation. Hct, hematocrit; Hgb, hemoglobin.

² Denominator 38,923 includes all pregnancies with both laboratory tests. Denominator 1045 excludes pregnancies identified as not anemic by both Hgb and Hct.

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TABLE 3

Availability and distribution of ferritin results and iron-deficiency status among pregnancies screened for anemia status in the first trimester, Kaiser Permanente Northwest, 2005–2016

	An	and those with anemia, $I_n = 1045$]	Among those without anemia, $I = 37,878$
Characteristic	% u	or median (IQR) [minimum-maximum	<i>u</i> [t	% or median (IQR) [minimum-maximum]
Ferritin result available, %	197	18.9	1,275	3.4
TIBC result available, %	183	17.5	869	2.3
Serum iron result available, %	183	17.5	872	2.3
Ferritin, µg/L	197	15 (6–58) [1–2761] ²	1,275	27 (15–47) [2–475]
TIBC, $\mu g/L$	183	379 (326-437)	869	346 (315–386)
		[213–646]		[111–579]
Serum iron, µg/L	183	53 (28–93) [10–184]	872	78 (54–106) [10–252]
ID among those with ferritin assessed $(n = 1472)$: U	= 197		n = 1275
Ferritin $<10 \ \mu g/L$	79	40.1	140	11.0
Ferritin <15 µg/L	95	48.2	300	23.5
ID among those with TIBC assessed $(n = 1052)$: U	= 183		<i>n</i> = 869
TIBC >400 $\mu g/L$	76	41.5	165	19.0
ID among those with serum iron assessed $(n = 1055)$: U	= 183		n = 872
Serum iron <40 µg/L	67	36.6	91	10.4
ID among those with ferritin, TIBC, or serum iron assessed($n = 1656$)	: U	= 231		n = 1425
Any iron test abnormal (ferritin, TIBC, or serum iron)	132	57.1	418	29.3
Ferritin <15 µg/L, if ferritin not available, then abnormal TIBC or serum iron (preferential to ferritin)	118	51.1	335	23.5

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I Anemia defined as hemoglobin <11 g/dL (not adjusted for smoking or elevation) or hematocrit <33% based on first test result in the first 14 wk of gestation. Iron indicators based on first test result through 20 wk of gestation to ensure observation time for ordering and diagnostic testing of iron status.

²One ferritin result (>2000 µg/L) was a clear outlier. Review of record indicated patient diagnosed with genetic blood disorders and hemochromatosis with iron overload, and thus the value is considered biologically plausible and retained.