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Prevalence and association of iron deficiency with anemia among patients with heart failure in the USA: NHANES 2017-2018

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ABSTRACT

Background: Heart failure (HF) is a major debilitating disease. HF patients with iron deficiency(ID) have poorer outcomes and treatment significantly improves outcomes. We set out to update the national prevalence of ID in the USA and its association with anemia using data from NHANES 2017–2018.

Methods: Diagnosis of HF was self-reported. ID was defined as serum ferritin levels <100 ng/mL or a ferritin level between 100 and 299 ng/mL with transferrin saturation <20%. Anemia was defined as a hemoglobin level of <13 g/dl and <12 g/dl for men and women, respectively. Differences in prevalence of ID across various groups were assessed using Chi-squared test for categorical variables and equality of means for continuous variables with p-values <0.05 considered statistically significant.

Results: A total of 187 persons ≥20 years, corresponding to a 5.57million had HF. The prevalence of ID was 48.17% (95% CI 36.84–59.69) and the prevalence of anemia was 12.08%(95% CI 8.16–17.53). Diabetics (61.03%) were more likely to have ID compared to nondiabetics (35.38%), p 0.022. The prevalence of ID was similar in persons with anemia (47.45%) and persons without anemia (48.27%), p-value 0.983. The prevalence of ID has been constant for at least the past 20 years, making ID in HF an underdiagnose and/or undertreated condition among patients with HF and should be addressed.

Conclusions: One in every two persons with HF has ID. Also, prevalence of ID was similar in patients with anemia and without anemia. Anemia should not be considered a prerequisite for screening for ID in patients with HF.

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1. Background

Heart failure (HF) affects about 6.5million persons in the USA, constituting a major public health problem [1,2]. Patients with HF suffer reduced functional capacity, poorer quality of life and decreased survival. Despite advances in management, patients with HF remain significantly debilitated. Research efforts have sought to identify contributing amendable factors and helpful interventions aimed at improving health status, functional capacity, quality of life and mortality. Iron deficiency (ID), among other factors, is associated with worse disease experience and outcomes in patients with HF. Of note, correction of iron deficiency is associated with improved outcomes [3,4] that has prompted leading cardiology organizations to issue a class IIb recommendation screening and correction of ID in patients with HF [5,6].

The prevalence of iron deficiency in patients with chronic HF has been reported to be as high as 50% [7,8]. HF patients with ID experience decreased aerobic performance, increased exercise intolerance, reduced functional status and increased hospitalization and readmission rates as well as increased mortality [7,9,10]. Iron deficiency is also an independent predictor of mortality [11] with some studies reporting that ID has a greater predictive power than anemia for mortality and adverse disease outcome among patients with HF [7]. Traditionally, the presence of ID was only considered clinically relevant in the presence of anemia. However, with iron deficiency being the most common cause of anemia in the population, anemia probably reflects an overt extreme of severe iron deficiency with an impact on hemoglobin and red cell production.

Though there continues to be updated on the prevalence of ID in patients with HF, there have been no national population estimates in the past two decades. Taking advantage of recently available

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ferritin and transferrin data from national health and nutritional survey (NHANES) 2017/2018 survey, we set out to update the nationwide prevalence of ID among patients with stable HF and its association with anemia in the USA. Also, the updated prevalence of ID in HF would inform us on the impact of care providers in optimizing HF management by integrating correction of extant ID.

2. Methodology

2.1. Survey design

The NHANES, conducted by the National Center for Health Statistics, collects nationally representative data on the health and nutritional status of the non-institutionalized US population. It utilizes a multistage probability sampling design and collects information from approximately 5,000 persons per year. Detail information on the survey is available from the survey documentation [12]. Included in our analysis were persons 20 years and older with a self-reported diagnosis of heart failure.

3. Data collection

Survey participants were interviewed in their homes to ascertain demographic characteristics age, gender, level of education, ethnicity, marital status, place of birth, health insurance, and smoking status using a Computer-Assisted Personal Interviewing system (i.e., interviewer-administered). Persons who reported current use of cigarettes were classified as smokers. Body mass index (BMI) was calculated from measured weight and height at subsequent follow-up visits in the mobile examination enter by trained health technicians using standardized protocols. The family poverty index was calculated by dividing the total family income by the poverty threshold, as defined by the US Census bureau, with adjustment for family size at the time of the interview [13]. Family poverty index ratio of <1 is considered 'below poverty line' and ≥1 is considered 'at or above poverty line'. Family PIR was grouped into three categories (PIR<1.00, PIR 1.00–2.99 and PIR≥3.00).

The diagnosis of CHF was self-reported. Hemoglobin, ferritin and transferrin levels were measured using standardized protocols as detailed in laboratory manual [14]. Iron deficiency was defined as serum ferritin levels <100 ng/mL or a ferritin level between 100 and 299 ng/mL with transferrin saturation <20%. Anemia was defined using recommended gender-specific cut offs of 13 g/dl and 12 g/dl [15] for men and women, respectively. All study questionnaires, exact question wording and response are available at no cost to the public [12].

4. Statistical analysis

Relevant questionnaire data files with variables of interest were combined with demographic information. Appropriate survey weights for dataset were applied to ensure estimates are representative of the entire non-institutionalized USA population in keeping with stipulated analytical guidelines [16]. Prevalence is expressed in percentages and results displayed according to ID status. Differences in prevalence of iron deficiency across different sociodemographic and comorbidities were assessed using Chi-squared test for categorical variables and equality of means for continuous. Analysis was done using STATA 15 and p values less than 0.05 considered statistically significant.

5. Results

A total of 187 persons ≥20 years had prevalent HF, corresponding to a 5.57million persons in the USA. The prevalence of ID was 48.17% (95% CI 36.84–-59.69) and the prevalence of anemia was 12.08% (95% CI 8.16–17.53). HF was more prevalent in men (60%) than women (40%). Most study participants were at least obese with a mean BMI of 33.1 (32.0–34.1). Most participants were married US born Non-Hispanic Whites and 45% had at least some form of college education. Ninety-eight percent of our study participants had health insurance and about 18% lived in poverty. The prevalence of smoking, diabetes, chronic kidney disease (CKD) and anemia was 15.79%, 49.85%, 55.69% and 12.08%, respectively. But for diabetes in which diabetics (61.03%) were more likely to have iron deficiency compared with nondiabetics (35.38%), p-value 0.022, there were no observed differences in the prevalence of ID across all other sociodemographic variables and comorbidities. Most notably, there were no statistically significant differences in the prevalence of ID between across categories of CKD and anemia. Table 1 shows the study characteristics of our participants as well as the prevalence of ID across various categories.

BMI: Body mass Index; GED: Graduate education diploma; USA.

6. Discussion

Using nationally representative data, the prevalence of ID in patients with HF in the USA is 48.17%. But for patients with comorbid diabetes who had higher rates of ID, there were generally no differences in the prevalence of ID across examined sociodemographic characteristics and comorbidities. Interestingly, prevalence of ID did not differ between patients with and without anemia.

Table 1. General characteristics of study participants and detailed prevalence of iron deficiency.

Variable	Categories	Total (%)	Iron deficiency (%)	No-iron deficiency (%)	p-value
Age (Years)	Mean (95% CI)	65.4(63.0–67.8)	66.6(63.2–70)	64.3(59.6–69)	0.463
BMI (Kg/m^2)	Mean (95% CI)	33.1(32.0–34.1)	34.1(32.8–35.1)	32.1(30.5–33.6)	0.06
Gender	Male	60.37	42.70	57.3	0.205
	Female	39.63	56.50	43.50	
Educational status	Less than high school	19.09	51.59	48.41	0.597
	High school or GED	36.93	48.58	51.42	
	Some college or Associate degree	34.79	40.95	59.05	
	College degree and above	9.20	66.75	33.25	
Ethnicity	Hispanic	7.84	34.22	65.78	0.310
	Non-Hispanic black	14.90	34.87	65.13	
	Non-Hispanic white	69.82	54.15	45.85	
	Others	7.44	33.38	66.62	
Marital status	Never married	09.14	20.74	79.26	0.194
	Married or living with partner	51.97	48.58	51.42	
	Divorced or separated	21.60	59.32	40.68	
	Widowed	17.29	47.53	52.47	
Place of Birth	USA	93.67	48.31	51.69	0.885
	Non USA	06.33	46.06	53.94	
Health Insurance	Yes	98.03	19.35	80.65	0.304
	No	1.97	48.75	51.52	
Poverty index ratio	Below 1	17.64	52.36	47.64	
	1 to 3	40.22	50.42	49.58	0.841
	3 and above	42.14	45.51	54.49	
					0.100
Smoking	Yes	15.79	63.23	36.77	
	No	84.21	45.35	54.65	
Diabetes	Yes	49.85	61.03	38.97	0.022
	No	50.15	35.38	62.52	
Chronic Kidney disease	Yes	55.69	50.99	49.01	0.611
	No	44.31	44.63	55.37	
Anemia	Yes	12.08	47.45	52.55	0.938
	No	87.92	48.27	51.73	
Hemoglobin		13.9(13.5–14.2)	13.6(13.2–14.0)	14.2(13.6–14.7)	0.107

Our prevalence is basically identical to that reported in several different cohorts and other studies around the globe [11,17,18]. Bearing in mind the consequences of iron deficiency among patients with HF, there is a need to get HF patients evaluated and managed in efforts to optimize care, thereby reducing the frequency of hospital admissions and readmissions with its associated cost to the society as well as mortality and also to afford those battling with HF the best possible quality of life [3,4,19–-4,19–22]. Though a disappointing observation, the stable prevalence of iron deficiency is not entirely unexpected as the concept of screening, diagnosing and treating iron deficiency in patients with HF remains relatively novel and yet to be fully embraced by providers despite the documented benefits [8]. Failure addressing ID among patients with HF certainly deprives them of rare opportunities to improve their disease experience and outcomes which are already greatly compromised. Correction of ID is safe, simple and may require not more than an office visit for IV replacement [3,10,23,24]. Hopefully, with the recent recommendations for screening and management of ID in HF from leading cardiology societies [5,6], we would see a change in attitude with consequent decrease in prevalence of ID. Though ID may have a quick and safe fix, every diagnosis of iron deficiency showed be followed by proper etiologic investigation. Given the high prevalence of iron deficiency with safe, quick and effective treatment, considering screening for ID at regular intervals among patients with heart failure might not be irrational.

The lack of association between ID and anemia serves as a wakeup call to physicians who often consider anemia as a prerequisite for iron studies. This further strengthens the need of universal screening for ID in patients with HF. The high prevalence and lack of predictive patterns across various sociodemographic and comorbidity categories make targeted screening unlikely. Though ID an indisputable independent predictor mortality in patient with HF [17,25], the exact mechanism through which ID adversely affect health or through which correction improves health outcomes remains an area for ongoing research. From a simplistic view, it would appear anemia secondary to iron deficiency is the most plausible mechanism. However, findings that ID with or without comorbid anemia has been shown as an independent prognostic marker have greatly dented this hypothesis [7,17,26,27].

7. Strengths and limitations

Though the most up-to-date nationwide study reporting prevalence of iron deficiency among patients with stable HF, our study is limited to noninstitutionalized persons ≥20 years and a significant proportion of HF in facilities have been excluded. Also, information on phenotype and severity of heart failure was absent to allow for detailed stratification. However, our findings are representative of the entire noninstitutionalized persons with HF in the USA.

8. Conclusions

One in every two persons with HF has iron deficiency, comparable to its prevalence some 20 years ago. Of note, the prevalence of ID did not differ among patients with anemia and those without anemia. Our findings suggest that more efforts need to be tailored towards screening and treating for iron deficiency in all patients with HF. Anemia should be considered a prerequisite for screening for iron deficiency. Finally, recommending regular interval screening for iron deficiency among patients with ID would not be irrational.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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References

[1] Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics—2020 update: a report from the american heart association. Circulation. 2020;141(9).
[2] Ditah CM, Rahman E, Agbor VN, et al. Disparities and drivers of early age at diagnosis of congestive heart failure in the USA. Int J Cardiol. 2019;293:143–147.
[3] Anker SD, Comin Colet J, Filippatos G, et al. Ferric carboxymaltose in patients with heart failure and iron deficiency. N Engl J Med. 2009;361:2436–2448.
[4] Ponikowski P, Veldhuisen DJV, Comin-Colet J, et al. Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency. Eur Heart J. 2015;36:657–668.
[5] Yancy CW, Jessup M, Bozkurt B, et al. ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure. J Am Coll Cardiol. 2017;70:776–803.
[6] Ponikowski P, Voors AA, Anker SD, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2016;37:2129–2200.
[7] Klip I, Comin-Colet J, Voors AA, et al. Iron deficiency in chronic heart failure: an international pooled analysis. Am Heart J. 2013;165:575–582.e3.
[8] Mistry R, Hosoya H, Kohut A, et al. Iron deficiency in heart failure, an underdiagnosed and undertreated condition during hospitalization. Ann Hematol. 2019;98:2293–2297.
[9] Ebner N, Jankowska EA, Ponikowski P, et al. The impact of iron deficiency and anaemia on exercise capacity and outcomes in patients with chronic heart failure. Results from the studies investigating co-morbidities aggravating heart failure. Int J Cardiol. 2016;205:6–12.
[10] Anand I, Gupta P. How I treat Anemia in Heart Failure. Blood. 2020;136(7):790–800.
[11] Cleland JGF, Zhang J, Pellicori P, et al. Prevalence and outcomes of anemia and hematinic deficiencies in patients with chronic heart failure. JAMA Cardiol. 2016;1:539.
[12] NHANES Questionnaires, Datasets, and Related Documentation; n.d. https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx?BeginYear=2017 (accessed March 7, 2020).
[13] Bureau UC How the census bureau measures poverty. Available at: https://www.census.gov/topics/income-poverty/poverty/guidance/poverty-measures.html [Accessed 2019 Jan 15
[14] NHANES 2017-2018 Laboratory methods. Available at: https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/labmethods.aspx?BeginYear=2017 [Accessed 2020 May 14
[15] World Health Organization. Nutritional anaemias: report of a WHO scientific group. Geneva, Switzerland: World Health Organization; 1968.
[16] NHANES survey methods and analytic guidelines. Available at: https://wwwn.cdc.gov/nchs/nhanes/analyticguidelines.aspx#analytic-guidelines [Accessed 2020 Mar 7
[17] Magrì D, De MF, Moscucci F, et al. Anemia and iron deficiency in heart failure: clinical and prognostic role. Heart Fail Clin. 2019;15:359–369.
[18] Haehling SV, Ebner N, Evertz R, et al. Iron deficiency in heart failure. JACC Hear Fail. 2019;7:36–46.
[19] Nanas JN, Matsouka C, Karageorgopoulos D, et al. Etiology of anemia in patients with advanced heart failure. J Am Coll Cardiol. 2006;48:2485–2489.
[20] McMurray JJV. What are the clinical consequences of anemia in patients with chronic heart failure? J Card Fail. 2004;10:12–14.
[21] Maggioni AP, Opasich C, Anand I, et al. Anemia in patients with heart failure: prevalence and prognostic role in a controlled trial and in clinical practice. J Card Fail. 2005;11:91–98.
[22] Katz SD, Mancini D, Androne AS, et al. Treatment of anemia in patients with chronic heart failure. Eur J Hear Fail Suppl. 2003;2:221–224.
[23] Anand IS, Gupta P. Anemia and iron deficiency in heart failure. Circulation. 2018;138:80–98.
[24] Beck-da-Silva L, Piardi D, Soder S, et al. IRON-HF study: a randomized trial to assess the effects of iron in heart failure patients with anemia. Int J Cardiol. 2013;168:3439–3442.
[25] Sahu KK, Mishra AK, Lal A, Siddiqui AD. Iron deficiency: an independent prognostic marker in heart failure, Ann. Hematol. 2020;99.
[26] Dec GW. Anemia and iron deficiency — new therapeutic targets in heart failure? N Engl J Med. 2009;361:2475–2477.
[27] Jankowska EA, Rozentryt P, Witkowska A, et al. Iron deficiency predicts impaired exercise capacity in patients with systolic chronic heart failure. J Card Fail. 2011;17:899–906.