Library & Archive Services

Part of Knowledge & Analytical Services

Llywodraeth Cymru
Welsh Government

Literature Search Report
Subject: Under Diagnosis of Genetic Haemochromatosis
Requested by: <<Redacted – S40(2) Applied>>
Date requested: 17/09/2018 Date required: 12/10/2018

Contents

For further information or feedback please contact:
<<Redacted – S40(2) Applied >>

Sources and search terms

Search Terms

"hereditary hemochromatosis" AND "under diagnosis" OR "mis-diagnosis" OR "missed diagnosis"

"Genetic haemochromatosis" AND "under diagnosis" OR "mis-diagnosis" OR "missed diagnosis"

"hereditary hemochromatosis" AND "under diagnosis" OR "mis-diagnosis" OR "missed diagnosis" AND "Education, Medical"

"Genetic haemochromatosis" AND "under diagnosis" OR "mis-diagnosis" OR "missed diagnosis" AND "Education, Medical"

Databases

PubMed, Cochrane Library, COPAC, British Library's Index to thesis collection https://ethos.bl.uk/

Websites

NICE

Journal Articles and reviews

Links to full text are included where available,
otherwise articles may be obtained by inter-library loan.

title: Longitudinal changes in LIC and other parameters in patients receiving different chelation regimens: Data from LICNET

Source: Eur J Haematol. 2018;100:124–130

Abstract:
Objectives: The liver remains the primary site of iron storage, with liver iron concentration (LIC) being a strong surrogate of total body iron. MRI-R2 can accurately measure LIC. The LICNET (Liver Iron Cutino Network) was established to diagnostics of liver iron overload by MRI-R2 subjects with hemochromatosis in hematological disorders.
The aims of the study were to look at variation in LIC measurements during time across different chelation regimens.
Methods: This was a cross-sectional study of 130 patients attending 9 Italian centers participating in the LICNET. LIC comparisons over time (T0 and T1) were made using t test and/or Wilcoxon test.
Results: LIC significantly decreased from MRI1 to MRI2 although at high variance (median change −0.8 mg Fe/g dw, range: −29.0 to 33.0; P = .011) and 7.7% of patients shifted from LIC values of high risk (>15 mg Fe/g dw) to an intermediate-risk category (7-15 mg Fe/g dw). Median change in LIC and correlation with serum ferritin levels (SF), during different chelation regimens, is reported.
Conclusions: These findings suggest as longitudinal variation in the LIC is possible, across all chelation regimens. It confirms as SF levels not always can be used for estimating changes in LIC.

Full Text: https://doi.org/10.1111/ejh.12989

title: A Case Study of Hemochromatosis and Conflicting Point Shear Wave Measurements in the Assessment of Liver Fibrosis

Source: Ultrasound Q. 2017 Mar;33(1):49-50

Abstract: There are multiple factors that affect the shear wave speed in the assessment of liver stiffness. In this case report, we present a case of hemochromatosis that has elevated liver stiffness suggestive of significant fibrosis or cirrhosis; however on liver biopsy, no fibrosis was identified. This article will discuss the possibility that liver iron deposition may affect SWE measurements of the liver, leading to inaccurate assessment of liver fibrosis. In these cases, a liver biopsy may be required for accurate liver assessment.

title: Hereditary haemochromatosis

Source: BMJ. 2016 Jun 30;353:i3128

Abstract: The symptoms of iron overload are mostly non-specific at the time of diagnosis. In a cohort study of 251 patients with haemochromatosis, about 75% of patients had lethargy and weakness. Other symptoms were somnolence, memory disturbances, generalised arthralgia, and reduced libido or impotence in men.11 These symptoms can also be caused by other medical conditions or attributed to stress and ageing. Data on the predictive value of these symptoms to identify haemochromatosis in the general population are lacking. An observational study found a similar prevalence of these non-specific symptoms in people with and without iron overload, which delays diagnosis.

title: Diagnosis and Management of Hereditary Hemochromatosis

Source: Clinics in Liver Disease, 2015-02-01, Volume 19, Issue 1, Pages 187-198

Abstract: This article highlights the current information and data regarding the diagnosis and management of hemochromatosis.

(See also references)

title: Improved detection of hereditary haemochromatosis
Source: J Clin Pathol. 2015 Mar;68(3):218-21
Abstract: AIMS:

There is high prevalence of hereditary haemochromatosis (HH) in North European populations, yet the diagnosis is often delayed or missed in primary care. Primary care physicians frequently request serum ferritin (SF) estimation but appear uncertain as how to investigate patients with raised SF values. Our aim was to develop a laboratory algorithm with high predictive value for the diagnosis of HH in patients from primary care with raised SF values.

METHODS:

Transferrin saturation (Tsat) was measured on SF samples sent from primary care; 1657 male and 2077 female patients age ≥ 30 years with SF ≥ 200 µg/L. HFE genotyping was performed on all 878 male and 867 female patients with Tsat >30%.

RESULTS:

This study identified 402 (206 men; 196 women) C282Y carriers and 132 (58 men; 74 women) C282Y homozygotes. Optimal limits for combined SF and Tsat values for HH recognition were established. The detection rate for homozygous C282Y HH for male patients with both SF ≥ 300 µg/L and Tsat >50% was 18.8% (52/272) and 16.3% (68/415) for female patients with both SF ≥ 200 µg/L and Tsat >40%.

CONCLUSIONS:

The large number of SF requests received from primary care should be used as a resource to improve the diagnosis of HH in areas of high prevalence.
Full Text: https://jcp.bmj.com/content/jclinpath/68/3/218.full.pdf

title: Recent advances in hemochromatosis: a 2015 update : a summary of proceedings of the 2014 conference held under the auspices of Hemochromatosis Australia
Source: Hepatol Int. 2015 Apr;9(2):174-82
Abstract: This review focuses on iron metabolism, the genetics of hemochromatosis, current treatment protocols and various screening methods. Even though the most common form of hereditary hemochromatosis, C282Y gene mutations in the HFE gene, has been extensively studied, novel mutations in both HFE and non-HFE genes have been implicated in this disease. These have important implications for the Asia-Pacific region. In overload, deposition of iron in various body tissues leads to toxic damage. Patients commonly present with non-specific symptoms of malaise and lethargy. Biochemical, imaging and genetic testing can be carried out to confirm diagnosis. Venesection forms the mainstay of treatment and at present cascade screening of affected families is recommended over population-level screening.

(See also references)

title: HFE-related haemochromatosis: an update for the rheumatologist
Source: Current Rheumatology Reports, 2014;16:393–9
Abstract: Diagnosis of HFE-related hemochromatosis is usually based on fasting serumferritin levels and transferrin saturation levels.

title: Diagnosis and management of hereditary haemochromatosis
Source: Br J Gen Pract 2013; 63 (611): 331-332
Abstract: Although C282Y homozygosity is relatively common, many individuals remain asymptomatic throughout their lifetime, which is likely to contribute to underdiagnosis of the condition.
Full Text: https://bjgp.org/content/63/611/331/tab-pdf

(See also references)

title: Hereditary hemochromatosis: missed diagnosis or misdiagnosis?
Source: Am J Med. 2013 Nov;126(11):1010-5
Abstract: Abnormal iron study results in patients with nonhereditary hemochromatosis genotypes commonly lead to a misdiagnosis of hereditary hemochromatosis and inappropriate treatment with phlebotomy. This error often is seen in the setting of elevated iron study results secondary to chronic liver diseases. Furthermore, hereditary hemochromatosis is commonly diagnosed and treated without HFE genotyping. We suggest that phlebotomy centers require a documented HFE genotype before initiating phlebotomy.

title: Evaluation of educational interventions for three lesser-known illnesses
Source: Delaware medical journal, 2013, 85(6), 179-185
Abstract: OBJECTIVES: The objective of this research was to evaluate the effectiveness of educational campaigns designed to inform physicians about the symptoms of LKIs and the basis to test patients for the diseases.

METHODS: A multi-level educational intervention was designed and conducted. The prevalence rate of testing, diagnosis, and the ratio of diagnoses to testing (D/T ratio) for hemochromatosis, celiac disease, and Lyme disease were determined for pre-intervention, intervention, and post-intervention time periods. Using the prevalence rates, ANOVA regression analysis was used to estimate the effect of the educational intervention on clients in Medicare Professional System, Medicare Institutional System, and Christiana Care outpatient data.

BACKGROUND: Lesser known illnesses (LKI) such as hemochromatosis, celiac disease, and Lyme disease are likely to be under-diagnosed due to the often varied and sometimes vague symptoms and lack of familiarity with testing. Insufficient testing and diagnoses of these LKI could result in poor outcomes for patients and unnecessary costs.

title: Therapeutic erythrocytapheresis in the initial treatment of hereditary hemochromatosis
Source: Acta Medica (Hradec Kralove). 2012;55(4):180-5
Abstract: BACKGROUND:

The current treatment of hereditary hemochromatosis (HH) consists of performing periodic whole blood phlebotomies. Erythrocytapheresis (EA) can remove up to three times more red blood cells per single procedure and could thus have a clinical benefit. A prospective study of 30 consecutive cases of HH were included in a periodic EA program.

(See also references)

title: Effect of the A736V TMPRSS6 polymorphism on the penetrance and clinical expression of hereditary hemochromatosis
Source: Journal of Hepatology, December 2012 Volume 57, Issue 6, Pages 1319–1325
Abstract: Not only the p.736V variant was negatively associated with HH penetrance in Italian subjects, but in a highly homogeneous group of C282Y +/+ male patients without acquired cofactors, it was an independent predictor of the presence of cirrhosis at diagnosis.
Full Text: https://www.clinicalkey.com/service/content/pdf/watermarked/1-s2.0-S0168827812006174.pdf?locale=en_US

(See also references)

title: Diagnosis and management of hemochromatosis: 2011 Practice Guideline by the American Association for the Study of Liver Diseases
Source: Hepatology, Volume 54, Issue1, July 2011, Pages 328-343
Abstract: Intended for use by physicians, these recommendations suggest preferred approaches to the diagnostic, therapeutic, and preventive aspects of care. They are intended to be flexible in contrast to standards of care, which are inflexible policies to be followed in every case.
https://aasldpubs.onlinelibrary.wiley.com/doi/epdf/10.1002/hep.24330

(See also references)

title: Hereditary Hemochromatosis: Pathogenesis, Diagnosis, and Treatment
Source: Gastroenterology, 2010-08-01, Volume 139, Issue 2, Pages 393-408.e2
Abstract: Hepcidin deficiencies are the central pathogenic factor in hemochromatosis. (A) In healthy subjects, hepcidin secreted by the liver regulates iron release from macrophages and duodenal enterocytes by interacting with the FPN expressed on their surfaces. HFE, TfR2, and HJV are all required to adjust hepcidin expression to current iron needs. Loss of any one of these hepcidin regulators leads to unrestricted flow of iron into the plasma iron pool.

title: EASL clinical practice guidelines for HFE hemochromatosis
Source: J Hepatol. 2010 Jul;53(1):3-22
Abstract: This Clinical Practice Guideline (CPG) has been developed to assist physicians and other healthcare providers as well as patients and interested individuals in the clinical decision making process for HFE-HC. The goal is to describe a number of generally accepted approaches for the diagnosis, prevention, and treatment of HFE-HC.
Full Text: https://www.clinicalkey.com/service/content/pdf/watermarked/1-s2.0-S0168827810001972.pdf?locale=en_US

title: 428 DIAGNOSIS OF HEREDITARY HEMOCHROMATOSIS AND INVOLVEMENT OF PATIENTS IN TREATMENT DECISION MAKING: AN INTERNATIONAL QUANTITATIVE SURVEY OF 210 PATIENTS
Source: Journal of Hepatology, April 2009 Volume 50, Supplement 1, Page S161
Abstract: Treatment of Hereditary Hemochromatosis (HH)
requires both accurate diagnosis and patient compliance in attending
phlebotomy appointments. The study quantified the routes to diagnosis,
patient perceived involvement in treatment decisions and the sources of
information considered most useful in learning about their condition.
Full Text: https://www.journal-of-hepatology.eu/article/S0168-8278(09)60430-X/pdf

title: Hereditary haemochromatosis
Source: Best Pract Res Clin Gastroenterol. 2009;23(2):171-83
Abstract: Haemochromatosis should currently refer to hereditary iron overload disorders presenting with a definite and common phenotype characterised by normal erythropoiesis, increased transferrin saturation and ferritin and primarily parenchymal iron deposition related to innate low (but normally regulated) production of the hepatic peptide hormone hepcidin. Since the discovery of the haemochromatosis gene (HFE) in 1996, several novel gene defects have been detected, explaining the mechanism and diversity of iron overload diseases. Overall, at least four main types of hereditary haemochromatosis (HH) have been identified. This review describes the systematic diagnostic and therapeutic strategy and pitfalls for patients suspected for HH and their relatives.
Full Text: https://www.clinicalkey.com/service/content/pdf/watermarked/1-s2.0-S1521691809000274.pdf?locale=en_US

title: The biochemical and clinical penetrance of individuals diagnosed with genetic haemochromatosis by predictive genetic testing

Source: European Journal of Gastroenterology & Hepatology [01 May 2008, 20(5):379-383]

Abstract: HFE-related genetic haemochromatosis (GH) is the commonest inherited genetic disorder in Caucasian populations with approximately one in 180 of individuals in the west of Scotland homozygous for the common C282Y mutation. The clinical diagnosis of GH, however, remains relatively uncommon - suggesting either under diagnosis or low clinical penetrance.We aimed to assess the biochemical and clinical penetrance of GH in first-degree relatives of patients with known GH, who subsequently themselves screened positive for the common GH mutations.Individuals were identified from two large teaching hospitals in North Glasgow from July 1997 to July 2005 diagnosed with GH after predictive genetic testing after a relative was found to have GH. Details of patient history, biochemistry and known comorbidity at diagnosis and results of related further investigations were collected.Sixty-three individuals were identified, 31 (49%) of whom were males. Fifty-five individuals (87%) were C282Y homozygous and the remaining eight were compound heterozygotes for C282Y and H63D. All 31 male patients were found to have evidence of iron overload as opposed to 63% of females. Elevated liver enzyme levels were encountered in 15 patients (24%). All except one had evidence of iron overload. Four individuals underwent a liver biopsy, two of whom had hepatic fibrosis. Four patients were found to be diabetic. A full clinical history was obtained from 54 of 63 individuals, 38 (70%) of whom were entirely asymptomatic. Thirteen individuals complained of joint pains and a further nine complained of fatigue.This study suggests that although biochemical penetrance of GH is high, the clinical penetrance is low.

title: The biochemical and clinical penetrance of individuals diagnosed with genetic haemochromatosis by predictive genetic testing

Source: Eur J Gastroenterol Hepatol. 2008 May;20(5):379-83

Abstract: BACKGROUND:

HFE-related genetic haemochromatosis (GH) is the commonest inherited genetic disorder in Caucasian populations with approximately one in 180 of individuals in the west of Scotland homozygous for the common C282Y mutation. The clinical diagnosis of GH, however, remains relatively uncommon - suggesting either under diagnosis or low clinical penetrance.

AIM:

We aimed to assess the biochemical and clinical penetrance of GH in first-degree relatives of patients with known GH, who subsequently themselves screened positive for the common GH mutations.

METHODS:

Individuals were identified from two large teaching hospitals in North Glasgow from July 1997 to July 2005 diagnosed with GH after predictive genetic testing after a relative was found to have GH. Details of patient history, biochemistry and known comorbidity at diagnosis and results of related further investigations were collected.

RESULTS:

Sixty-three individuals were identified, 31 (49%) of whom were males. Fifty-five individuals (87%) were C282Y homozygous and the remaining eight were compound heterozygotes for C282Y and H63D. All 31 male patients were found to have evidence of iron overload as opposed to 63% of females. Elevated liver enzyme levels were encountered in 15 patients (24%). All except one had evidence of iron overload. Four individuals underwent a liver biopsy, two of whom had hepatic fibrosis. Four patients were found to be diabetic. A full clinical history was obtained from 54 of 63 individuals, 38 (70%) of whom were entirely asymptomatic. Thirteen individuals complained of joint pains and a further nine complained of fatigue.

CONCLUSION:

This study suggests that although biochemical penetrance of GH is high, the clinical penetrance is low.

title: Screening for hemochromatosis by measuring ferritin levels: a more effective approach

Source: Blood. 2008 Apr 1;111(7):3373-6

Abstract: Because the penetrance of HFE hemochromatosis is low, traditional population screening measuring the transferrin saturation is unlikely to be cost-effective because the majority of subjects detected neither have clinical disease nor are likely to develop it. Three independent studies show that only patients with serum ferritin concentrations more than 1000 microg/L are at risk for cirrhosis, one of the main morbidities of hemochromatosis. Among 29,699 white subjects participating in the Scripps/Kaiser hemochromatosis study, only 59 had serum ferritin levels more than 1000 microg/L; 24 had homozygous mutant or compound heterozygous mutant HFE genotypes. In all but 5 of the other subjects, the causes of elevated ferritin were excessive alcohol intake, cancer, or liver disease. Screening for hemochromatosis with serum ferritin levels will detect the majority of patients who will be clinically affected and may detect other clinically significant disease in patients who do not have hemochromatosis genotypes. Because the ferritin level of the majority of adult homozygotes for HFE mutations does not rise over long periods of time, excluding subjects with serum ferritin levels less than or equal to 1000 microg/L should not result in missed opportunities for early treatment of patients who could benefit.

Full Text: http://www.bloodjournal.org/content/bloodjournal/111/7/3373.full.pdf

title: Genotyping the HFE gene by melting point analysis with the LightCycler system: Pros and cons

Source: Blood Cells Mol Dis. 2006 Mar-Apr;36(2):288-91

Abstract: The assay that combines rapid-cycle PCR with allele-specific fluorescent probe melting profiles performed on the Roche Diagnostics LightCycler is commonly employed for genotyping the HFE gene. We report three illustrative cases of the pros and cons of this method. In two cases, atypical melting curves allows the identification of new DNA substitutions in the HFE gene, whereas, in the third case, a typical melting curve of c.845G>A mutation (C282Y) homozygosity overlooks a nucleotide change and promotes misdiagnosis of HH.

title: Hereditary hemochromatosis: genetic complexity and new diagnostic approaches

Source: Clinical Chemistry 2006 Jun;52(6):950–68

Abstract: This review describes new insights in mechanisms of iron overload, which are needed to understand new developments in diagnostic medicine.

Full Text:
https://www.researchgate.net/profile/Joannes_Marx/publication/7152172_Hereditary_hemochromatosis_Genetic_complexity_and_new_diagnostic_approaches/links/02e7e517bf6156ba16000000.pdf

title: Haemochromatosis.

Source: Gut 2003;52:ii23-ii30

Abstract: However, itmust be emphasised that while the presence of mutations in the HFE gene indicates the existence of the genetic form of HC, the clinical diagnosis of HC is made when iron overload is present (see later).

Full Text: https://gut.bmj.com/content/gutjnl/52/suppl_2/ii23.full.pdf

title: Underdiagnosis of hereditary haemochromatosis: lack of presentation or penetration?

Source: Gut 2002;51:108-12

Abstract: Consequently, the purpose of this study was to determine whether underdiagnosis or incomplete penetrance could explain the discrepancy between genetic prevalence (genotype) and clinical expression (phenotype). In particular, non-specific symptoms (fatigue, arthropathy, and impotence) and their association with iron indices (transferrin saturation and serum ferritin) were analysed. Seventy nine C282Y homozygous relatives identified from family screening were selected without reference to their health status and can be considered to be clinically unselected. This approach overcomes ascertainment bias that results in an overestimate of disease expression when patients are detected based on symptomatology. Furthermore, this approach can be considered to be a substitute or surrogate method for population screening as the identification of 79 C282Y homozygous individuals from population screening would have necessitated screening at least 7000 individuals based on a homozygote frequency of 1 in 83 for this mutation in Ireland.

Full Text: https://gut.bmj.com/content/gutjnl/51/1/108.full.pdf

RESULTS:

We found that 78% of men (mean age 42 years) and 36% of women (mean age 39 years) who were identified as C282Y homozygotes following family screening had iron overload, as defined by a transferrin saturation >or=52% combined with a serum ferritin >or=300 microg/l for men and >or=200 microg/l for women. The frequency of reports of non-specific symptoms in those individuals with iron overload was not significantly different from those who did not have iron overload.

(See also references)

title: Diagnosis and management of genetic haemochromatosis

Source: Best Pract Res Clin Haematol. 2002 Jun;15(2):277-93

Abstract: Haemochromatosis may be inherited or acquired. The commonest inherited form is HFE-related genetic haemochromatosis (GH). This is associated with homozygosity for the C282Y mutation in the HFE gene. Individuals with GH present in several ways depending upon the severity of iron overload. However, only a small proportion of genetically susceptible individuals develop disease. Diagnosis of GH is based on measurement of transferrin saturation, serum ferritin levels and mutation analysis of HFE. Liver biopsy is not necessary for diagnosis. It is used to establish the severity of liver disease in selected patients. Other complications of iron overload are identified by specific tests. Initial management of GH is by weekly venesection until borderline iron deficiency is achieved. The serum ferritin is then maintained at 50 microg/l by 3-6 monthly venesection. Specific organ damage is managed appropriately. Early diagnosis and treatment before irreversible damage has occurred gives a normal life expectancy. Non-HFE related inherited iron overload may be due to mutations in other iron related genes. Management is along the same lines as for GH, although if venesection is not tolerated, other approaches may be necessary.

title: A common intron 3 mutation (IVS3 -48c-->g) leads to misdiagnosis of the c.845G-->A (C282Y) HFE gene mutation

Source: Blood Cells Mol Dis. 2000 Jun;26(3):229-33

Abstract: Amplification of the region of the HFE gene that contains the c.845G-->A (C282Y) mutation is usually performed using one amplimer that binds to a sequence in intron 3 and another that binds to a sequence in intron 4. Previously, a mutation that interferes with efficient binding to the intron 4 site has been described. We now find that another common mutation in intron 3, IVS3 -48c-->g, prevents binding of the amplimer to that site. This polymorphism occurs at a gene frequency of 0.128 in the African-American population and at a frequency of only 0.006 in the European population. DNA samples heterozygous for the IVS3 -48c-->g polymorphism and C282Y were undistinguishable from samples homozygous for the C282Y mutation when they were examined by allele-specific oligonucleotide hybridization (ASOH) and showed only a weak normal band when examined by electrophoresis following restriction endonuclease digestion. Although the polymorphism occurs in a DNA sequence almost identical to the intron 3 splice donor site, we found no evidence of alternative splice forms. Moreover, serum iron, transferrin saturation, and serum ferritin levels were normal in subjects heterozygous for the polymorphism. It appears, therefore, that the main importance of this polymorphism is that it may lead to misdiagnosis of heterozygotes for the C282Y mutation as

homozygotes. We therefore recommend exonic amplimers that avoid sites that contain polymorphisms and that can be multiplexed for detection of the c.187C-->G (H63D) and c.845G-->A (C282Y) mutations.

title: Hereditary hemochromatosis: should clinicians screen for this common disease?
Source: J Am Acad Nurse Pract. 2000 Jul;12(7):273-9
Abstract: Hereditary hemochromatosis is a serious condition of abnormal iron metabolism that is often missed until complications involving multiple organ systems occurs. It is an autosomal recessive condition primarily affecting Caucasians of Western European origin. This article discusses the pathophysiology, diagnosis, and management of this condition. Questions related to population screening are examined and recommendations made for a cost-effective screening program.

title: Incorrect diagnosis of hereditary hemochromatosis
Source: Am J Hematol. 2000 Feb;63(2):104-5

title: Diagnosis of hemochromatosis
Source: Ann Intern Med. 1998 Dec 1;129(11):925-31
Abstract: If untreated, hemochromatosis can cause serious illness and early death, but the disease is still substantially under-diagnosed. The cornerstone of screening and case detection is the measurement of serum transferrin saturation and the serum ferritin level. Once the diagnosis is suspected, physicians must use serum ferritin levels and hepatic iron stores on liver biopsy specimens to assess patients for the presence of iron overload. Liver biopsy is also used to establish the presence or absence of cirrhosis, which can affect prognosis and management. A DNA-based test for the HFE gene is commercially available, but its place in the diagnosis of hemochromatosis is still being evaluated. Currently, the most useful role for this test is in the detection of hemochromatosis in the family members of patients with a proven case of the disease. It is crucial to diagnose hemochromatosis before hepatic cirrhosis develops because phlebotomy therapy can avert serious chronic disease and can even lead to normal life expectancy.

title: Review article: the screening, diagnosis and optimal management of haemochromatosis
Source: Aliment Pharmacol Ther. 1997 Aug;11(4):631-9
Abstract: Haemochromatosis was first recognized as a disease entity over a century ago and its hereditary nature recognized over 60 years ago. However it was only in late 1996 that the haemochromatosis gene was cloned and a single C282Y mutation confirmed as being the cause of all HLA-linked iron overload in Caucasian populations. Haemochromatosis is common, occurring in approximately 1 in 300 people in Caucasian populations, and untreated can cause serious morbidity and early death. However, the disease remains much underdiagnosed for reasons such as lack of awareness of the disease, the presence of normal liver function tests and the lack or non-specific nature of symptoms. A commercially available DNA-based test for the haemochromatosis gene is likely to be available in the near future but its place in the diagnosis and management of the disorder is not yet clear. Assessment of body iron stores by measurement of serum ferritin and transferrin saturation, hepatic iron stores and hepatic architecture by liver biopsy will remain important in the future. The haemochromatosis mutation itself has as yet no known influence on morbidity other than via iron loading and organ failure, in particular, hepatic cirrhosis. Thus, diagnosing patients before the development of hepatic cirrhosis is crucial because iron depletion by venesection treatment before the development of cirrhosis results in a normal life expectancy.

title: Diagnosis of hemochromatosis probands in a community hospital
Source: Am J Med. 1997 Dec;103(6):498-503
Abstract: Abstract

PURPOSE:

To evaluate factors that lead to the diagnosis of hemochromatosis probands in a community hospital, including education of physicians about hemochromatosis and iron overload, specialty of physicians, diagnostic indicators of hemochromatosis, and clinical manifestations of hemochromatosis probands.

PATIENTS AND METHODS:

We conducted a hemochromatosis education program for health care personnel associated with a community hospital and the public during 1990 to 1994. Data on physicians who diagnosed probands, diagnostic indicators of hemochromatosis, and manifestations of hemochromatosis and associated illnesses were tabulated. Iron grades of all hospital liver biopsy specimens obtained from Caucasian subjects during 1990 to 1994 were also analyzed.

RESULTS:

We identified 162 hemochromatosis probands; 66.7% were diagnosed by physicians who participated in our education program. Primary care and internal medicine subspecialty physicians diagnosed 66.7% and 29.6% of probands, respectively, based on elevated serum iron parameters and hepatic enzyme concentrations (51.9% and 36.4% of probands, respectively). Iron overload occurred in 90.7%, and was associated with clinical manifestations in most. Of 844 hospital liver biopsy specimens from Caucasians, 8.5% had increased iron grades; 4.6% represented hemochromatosis.

CONCLUSIONS:

Physicians with current education readily diagnose hemochromatosis probands during routine health care delivery, but most probands identified in this manner have iron overload. Our results suggest that community physicians and hospitals could contribute substantially to hemochromatosis screening programs, permitting detection of more homozygotes before the development of iron overload.

title: Hemochromatosis. The missed diagnosis

Source: Arch Intern Med. 1986 Jun;146(6):1209-10
Abstract: Hemochromatosis is a hereditary disorder of the control of iron metabolism wherein the absorptive intestine accepts from the diet more iron than the body requires; because no excretory mechanism exists, the excess must be deposited in storage organs, ultimately to their detriment.

Research and reports

title: Hereditary Haemochromatosis: diagnosis & management from a GP perspective: Quick Reference Guide

Source: Irish College of General Practitioners , Quality in Practice Committee;Irish Haemochromatosis Association, 2013
Abstract: This document has been produced for General Practitioners with a view to enhancing the diagnosis, treatment and management of patients with Haemochromatosis in the Primary Care Setting.
Full Text:
https://www.icgp.ie/speck/properties/asset/asset.cfm?type=LibraryAsset&id=FFCFC171%2D9C57%2D88DC%2D969B489C1502715A&property=asset&revision=tip&disposition=attachment&app=icgp&filename=Hereditary%5FHaemochromatosis%2Epdf

(See also references)

title: ANALYSIS OF HEREDITARY HAEMOCHROMATOSIS AND CLINICAL CORRELATIONS IN THE ELDERLY
Author: CSH BOUWENS

Source:

Thesis presented in partial fulfilment of the requirements for the degree of Master of Science in Medical Sciences
University of Stellenbosch, December 2000
Abstract: Underdiagnosis of HH can partly be ascribed to the non-specific nature of the presenting features and the wide variety of disorders associated with this disease.

British Society Haematology guidelines 2017

Serum ferritin values are raised in about 80% of male and 50% of female homozygotes (Adams & Barton, 2007). Although measurement of SF might then be considered an effective approach for screening for GH, the vast majority of patients with raised SF do not have GH. Males with SF >300 lg/l and Tsat >50% and females with SF >200 lg/l and Tsat >40% will have a 19% and 16% likelihood of being C282Y homozygotes. Symptoms are, however, often vague and longstanding. Nonetheless, suspicion should be raised for male subjects of north European ancestry presenting with unexplained weakness or fatigue, abnormal liver function tests, arthralgia/ arthritis, impotence, diabetes of late onset, cirrhosis or bronze pigmentation.