



Figure 1S. Relation between age and (A) serum iron ($r = 0.021$, $p = \text{ns}$), (B) TSAT ($r = 0.058$, $p = 0.003$) and (C) serum ferritin ($r = 0.327$, $p < 0.0001$) in patients with reported ferroportin variants.

Table 1S. Phenotypical features by gender.

	Female (n=123)	Male (n=195)	<i>p</i>
Age (years)	n=112	n=184	
median (range)	36 (2-80)	44 (6-87)	ns
Hb (g/dl)	n=52	n=79	
median (range)	13.1 (7.5-15.6)	15.0 (9.5-18.4)	0.01
MCV (fl)	n=30	n=22	
median (range)	91 (77-107)	91 (73-108)	ns
Serum iron (μmol/l)	n=28	n=44	
median (range)	20.9 (6.7-94.0)	29.4 (6.2-86.0)	ns
TSAT (%)	n=108	n=165	
median (range)	31 (2-100)	40 (7-104)	0.0003
Ferritin (μg/l)	n=114	n=186	
median (range)	1011 (4-8943)	1452 (12-18695)	0.004
Iron Removed (g)	n=11	n=36	
median (range)	6.0 (3.2-24.4)	10.5 (1.6-80.0)	ns
Tolerance to Phlebotomy			
Good	17	41	
Poor	7	10	ns
ALT (IU/L)	n=26	n=27	
median (range)	22 (11-539)	52 (11-219)	ns
HIC (μg/g dry weight)	n=23	n=49	
median (range)	9542 (1083-36270)	10881 (307-58590)	ns
Fibrosis (n)	8	42	
No fibrosis (n)	11	24	ns
Alcohol consumption			
Yes (n)	7	21	
No (n)	17	38	ns

HIC: Hepatic Iron Content

Table 2S. Characteristics and iron parameters of probands versus probands' relatives.

	Probands (n=66)	Relatives of probands (n=186)	<i>p</i>
Age (years)	n=64	n=168	
median (range)	45 (9-71)	34 (2-87)	0.01
Gender (n)			
female	25	76	
male	40	109	0.007
Hb (g/dl)	n=34	n=60	
median (range)	14.3 (7.5-16.6)	14.1 (11.1-18.4)	ns
Serum iron (μmol/l)	n=19	n=41	
median (range)	27.0 (8-94)	26.5 (8.2-74)	ns
TSAT (%)	n=59	n=156	
median (range)	36 (5-100)	35 (2-104)	ns
Ferritin (μg/l)	n=63	n=173	
median (range)	1896 (65.1-12000)	932 (4-10510)	0.00002

HIC: Hepatic Iron Content

Table 3S. Phenotypical features by the reported presence of hereditary HFE and non-HFE iron overload conditions.

	Abnormalities (n=53)	No abnormalities (n=113)	<i>p</i>
Age (years)	n=45	n=110	
median (range)	32 (10-87)	41 (2-82)	ns
Gender			
Female	21	38	
Male	24	74	ns
Hb (g/dl)	n=20	n=52	
median (range)	14 (10.1-16.1)	14.8 (7.5-16.7)	ns
Serum iron (μmol/l)	n=26	n=43	
median (range)	27.4 (6.7-94)	32 (6.2-86)	ns
TSAT (%)	n=47	n=103	
median (range)	40 (2-99)	43 (5.6-104)	ns
Ferritin (μg/l)	n=53	n=100	
median (range)	1150 (4-14829)	1597 (12-12000)	ns
HIC (μg/g dry weight)	n=19	n=31	
median (range)	10044 (1083-45477)	13950 (999-58590)	ns

HIC: Hepatic Iron Content

Table 4S. Phenotypical features by the reported current use of alcohol.

	Yes (n=28)	No (n=56)	<i>p</i>
Age (years)	n=28	n=55	
median (range)	40.5 (19-72)	43 (6-79)	ns
Gender			
Female	7	17	
Male	21	38	ns
Hb (g/dl)	n=24	n=42	
median (range)	14.9 (11-16.6)	14.1 (7.5-18.4)	ns
Serum iron (µmol/l)	n=3	n=15	
median (range)	48.9 (19,2-53)	33.5 (10.7-86)	ns
TSAT (%)	n=28	n=48	
median (range)	35 (10-100)	40.5 (14-100)	ns
Ferritin (µg/l)	n=28	n=56	
median (range)	2101 (71-10510)	1586 (142-12178)	ns
HIC (µg/g dry weight)	n=6	n=32	
median (range)	14816 (8750-21929)	10331 (3350-58590)	ns

HIC: Hepatic Iron Content

Table 5S. Phenotypical features of patients with functional GOF ferroportin variants by hepcidin sensitivity.

	GOF hepcidin resistant (n=32)	GOF hepcidin sensitive (n=10)	p
Age (years)	n=30	n=9	
median (range)	39.3 (2-77)	57 (37-72)	0.007
Gender (n)			
Female	14	2	
Male	18	8	ns
Serum Iron ($\mu\text{mol/l}$)	n=20	n=2	
median (range)	44.0 (8.8-74)	38.5 (28.1-49)	ns
TSAT (%)	n=31	n=9	
median (range)	92 (9-104)	42 (30-100)	0.0004
Ferritin ($\mu\text{g/l}$)	n=24	n=10	
median (range)	540 (12-3751)	980 (585-2960)	ns
Response to phlebotomy (n)			
Good	10	1	
Poor	0	1	ns

Table 6S. Phenotypical features of patients with functional LOF ferroportin variant by hepcidin sensitivity.

	LOF hepcidin resistant (n=68)	LOF hepcidin sensitive (n=57)	<i>p</i>
Age (years)	n=67	n=53	
median (range)	32 (6-74)	38 (6-87)	ns
Gender (n)			
Female	31	19	
Male	35	34	ns
Serum Iron (µmol/l)	n=21	n=14	
median (range)	14.0 (8.2-46)	28.7 (6.2-94)	0.01
TSAT (%)	n=57	n=38	
median (range)	28 (10-81)	35 (7-99)	0.0005
Ferritin (µg/l)	n=68	n=53	
median (range)	1853 (24-18695)	1066 (24-21665)	ns
Response to phlebotomy (n)			
Good	17	2	
Poor	8	4	ns

Table 7S. Phenotypical features by hepcidin sensitive GOF and LOF ferroportin variants.

	GOF hepcidin sensitive (n=10)	LOF hepcidin sensitive (n=57)	<i>p</i>
Age (years)	n=9	n=53	
median (range)	57 (37-72)	38 (6-87)	0.02
Gender (n)			
Female	2	19	
Male	8	34	ns
Serum Iron (µmol/l)	n=2	n=14	
median (range)	38.5 (28.1-49.0)	28.7 (6.2-94)	ns
TSAT (%)	n=9	n=38	
median (range)	42 (30-100)	35 (7-99)	ns
Ferritin (µg/l)	n=10	n=53	
median (range)	980 (585-2960)	1066 (24-21665)	ns
Response to phlebotomy (n)			
Good	1	2	
Poor	1	4	ns

Table 8S. Phenotypical features by hepcidin resistant GOF and LOF ferroportin variants.

	GOF hepcidin resistant (n=32)	LOF hepcidin resistant (n=68)	<i>p</i>
Age (years)	n=30	n=67	
median (range)	39.5 (2-77)	32 (6-74)	ns
Gender (n)			
Female	14	31	
Male	18	35	ns
Serum Iron (µmol/l)	n=20	n=21	
median (range)	44.0 (8.8-74.0)	14 (8.2-46.0)	0.00002
TSAT (%)	n=31	n=57	
median (range)	92 (9-104)	28 (10-81)	<0.00001
Ferritin (µg/l)	n=24	n=68	
median (range)	540 (12-3751)	1853 (24-18695)	0.003
Iron distribution			
Macrophage	0	9	
Hepatocyte	5	0	0.0005
Response to phlebotomy (n)			
Good	10	17	
Poor	0	5	ns