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Title: Ventilatory restrictive impairment in thalassemic patients: Gender differences and correlation with hypogonadism and iron overload

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Body: BACKGROUND and AIM Ventilatory restrictive (RES) impairment has been described in β-thalassemia, but no evidence exists on the causal mechanism. We investigated relationships among lung function, iron overload and clinical parameters in a homogeneous series of β-thalassemia major adult patients. METHODS We studied 79 patients (males M/ females F 44/35; age 34.5±6.8 years) with β-thalassemia major on regular transfusion and iron chelation. Iron overload was assessed by serum ferritin, liver iron concentration (LIC) by SQUID susceptometry, cardiac iron by MRI T2*. Lung volumes, diffusion capacity, chelator drugs, hypogonadism (H), hypothyroidism and osteoporosis were evaluated in stable hematologic conditions. RESULTS 30/79 pt (38%) [21/44 (47.7%) M and 9/35 (25.7%) F] showed RES, 6 bronchial obstruction with no gender differences (3M 3F). In F LIC was higher 2249±903 vs 1497±553 mgFe/gliver dw; $p<0.008$ in RES vs normals and correlated with total lung capacity ($r=-0.402$ $p<0.03$). No differences were present for hypothyroidism, osteoporosis or 3 iron chelators. Among RES patients 57%M and 88%F were H. H males showed higher cardiac iron MRI T2* 29.6±12.7 vs 39.6±9.2 ms; $p<0.03$) but similar LIC in respect to non H, without correlation with total lung capacity. In F cardiac and hepatic iron levels were not different between H and non H. CONCLUSIONS RES is present in 1/3 of well compensated adult thalassemic (M/F 1.88). Iron (LIC) was higher in RES F vs normals and H males have higher MRI T2*. Different gender impact of H on lung and chest growth, severity and efficacy of replacement therapy can explain data but the involved mechanisms is still unclear.