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# FEMALE SEX HORMONES ARE NEGATIVELY ASSOCIATED WITH MASLD IN CHILDREN WITH OVERWEIGHT AND OBESITY


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## INTRODUCTION & AIM

Metabolic dysfunction-associated steatotic liver disease (MASLD) affects **47%** of children and adolescents with obesity.[1]

It is significantly **more prevalent in boys** compared to **girls**.[2] Prevalence of MASLD decreases in girls during puberty, while it increases in boys.[3]

This suggests that sex-hormones play a role in het development of MASLD.

**AIM**: To evaluate the associations between sex-hormones and MASLD in children with overweight and obesity.

## METHODS

Cross-sectional study in **290 children** with overweight, obesity or severe obesity, aged 4-18 years from the **Centre for Overweight Adolescents and Children's Healthcare** (COACH) at Maastricht UMC+.

Study measurements:

- **Steatosis** on ultrasound (US)
- **Steatohepatitis,** via serum ALT concentration
- **Serum sex hormone measurements**:
  - Anti-mullerian hormone (AMH)
  - Androstenedione (A4)
  - Dehydroepiandrosterone sulfate (DHEAS)
  - Estrone (E1) and Estradiol (E2)
  - Follicle stimulating hormone (FSH) and Luteinizing hormone (LH)
  - Sex-hormone binding globulin (SHBG)
  - Total, free and bioavailable testosterone (TT, FT, BT)

## HIGHER PREVALENCE OF MASLD IN BOYS

290 children (51% girls) with a median age of 11.5 years [IQR 9.1-14.0y] were included. Based on International Obesity Task Force (IOTF) criteria, 29.7% of children had overweight, 38.3% had obesity and 32.1% had severe obesity.

The prevalence of **steatosis** (based on US) and **steatohepatitis** (based on ALT) was **higher in boys** compared to girls in each puberty stage (Tanner stage; G/M 1=pre-pubertal, G/M 2-3=intra-pubertal, G/M 4-5= post-pubertal).

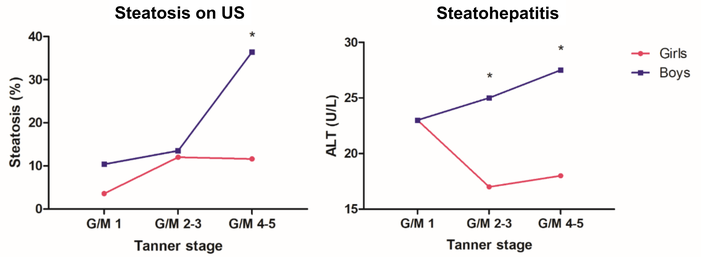


**Figure 1. Presence of steatosis on ultrasound and ALT serum concentration, stratified by sex and Tanner stage.**
Data presented as median or percentage. *P≤.05.

## SEX HORMONES IN GIRLS AND BOYS

**Table 1. Sex hormones, stratified by sex**

| | Total (n=290) | Girls (n=148) | Boys (n=142) | p-value* |
|---|---|---|---|---|
| **LH (U/L)** | 0.6 [0.1 - 2.5] | 1.0 [0.2 - 3.5] | 0.4 [0.1 - 1.9] | **.004*** |
| **FSH (U/L)** | 2.0 [1.0 - 4.1] | 2.6 [1.4 - 5.1] | 1.7 [0.7 - 2.5] | **<.001*** |
| **E1 (pmol/L)** | 40 [19 - 96] | 66 [24 - 143] | 30 [17 - 58] | **<.001*** |
| **E2 (pmol/L)** | 20 [10 - 86] | 59 [10 - 140] | 10 [10 - 45] | **<.001*** |
| **TT (nmol/L)** | 0.4 [0.3 -1.3] | 0.4 [0.3 - 0.9] | 0.5 [0.3 - 5.6] | **.008*** |
| **FT (pmol/L)** | 6.7 [4.1 - 23.3] | 6.5 [4.3 - 16.5] | 7.2 [3.7 - 140.1] | **.048*** |
| **BioT (pmol/L)** | 156 [95 - 555] | 152 [100 - 387] | 167 [87 - 3283] | **.048*** |
| **A4 (nmol/L)** | 4.1 [2.1 - 7.2] | 4.6 [2.4 – 8.1] | 3.7 [1.8 - 6.2] | **.004*** |
| **DHEAS (µmol/L)** | 2.2 [1.2 - 4.0] | 2.0 [1.1 - 3.7] | 2.7 [1.3 - 4.5] | .117 |
| **AMH (ng/mL)** | 4.8 [2.3 - 31.0] | 2.4 [1.3 - 3.8] | 31.5 [7.8 - 62.3] | **<.001*** |
| **SHBG (nmol/L)** | 34 [21 - 50] | 33 [22 - 50] | 35 [18 - 52] | .948 |

Data presented as median [interquartile range, Q1-Q3]. Mann-Whitney U test *P≤.05.

In **girls**, LH, FSH, E1, E2 and A4 are significantly higher.

In **boys**, TT, FT, BioT and AMH concentrations are significantly higher.

## ASSOCIATIONS BETWEEN SEX HORMONES AND MASLD

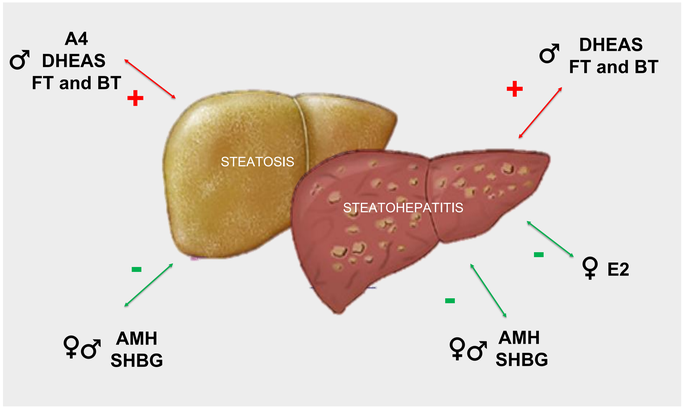


**Figure 2. Significant associations between sex-hormones and MASLD***
Logistic and linear regression analyses, adjusted for BMI z-score and sex (♀ girls, ♂ boys) . *P≤.05.

The predominantly female sex hormone **estradiol**, and hormones **AMH** and **SHBG** are associated with **less steatosis** and **less inflammation** in children with overweight and (severe) obesity.

The predominantly male sex hormones, including **free** and **bioavailable testosterone**, **androstenedione** and **DHEAS** are associated with **more steatosis and more inflammation** in children with overweight and (severe) obesity.

## REFERENCES


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