

Serum estradiol is associated with inhibin B in healthy 1-6 years old girls

NIELS H. BIRKEBAEK¹, HANNE FREDERIKSEN², MIA E SCHJØRRING¹, KONSTANTINOS KAMPERIS¹, KURT KRISTENSEN¹, SØREN RITTIG¹, ANDERS JUUL², AND ESSEN T. VESTERGAARD¹

1. Department of Pediatrics, Aarhus University Hospital, Aarhus, Denmark
2. Department of Growth and Reproduction, Rigshospitalet, Copenhagen, Denmark

BACKGROUND

The female gonadal axis is activated in mini-puberty and thereafter it is quiescent until puberty. We have shown that many girls with no clinical sign of puberty in the age group 1-6 years have a rather strong luteinizing hormone (LH) and follicle stimulating hormone (FSH) response to a gonadotropin releasing hormone (GnRH) test. However, stimulated LH and FSH values decreased in the age interval 1-6 years and no LH/FSH values rose above 0.43. Serum estradiol has until recently not been detectable in pre-pubertal girls after the mini-puberty, but with new highly sensitive techniques estradiol may be measurable in most 1-6 year old girls. As both estradiol and inhibin B are produced in the granulosa cells we have examined how they associate in the age interval 1-6 years.

OBJECTIVE AND HYPOTHESIS

The objectives of the study were to investigate the associations between serum estradiol, serum inhibin B, GnRH stimulated LH (LH₃₀) and sex hormone binding proteins (SHBG) in the age group 1-6 years.

METHODS

Forty eight healthy girls aged 3.5 years (range 0.8-5.9 years) were included in the study. All girls underwent a GnRH test. Estradiol concentrations were determined by on-line TurboFlow-liquid chromatography tandem mass spectrometry, inhibin B by two-sided enzyme-linked immunosorbent assay, and LH₃₀ and SHBG by sandwich immunometry (Cobas 8000).

RESULTS

Estradiol was measurable in samples from 40 girls. Medians and interquartile ranges of serum estradiol, serum inhibin B, LH₃₀, and serum SHBG are shown in table. Serum estradiol ($r=-0.42$, $p<0.01$), serum inhibin B ($r=-0.38$, $p<0.01$), LH₃₀ ($r=-0.59$, $p<0.01$) but not serum SHBG ($r=0.07$, $p=0.66$) decreased significantly by age (figure 1). Serum estradiol associated positively with serum inhibin B ($r=0.69$, $p<0.01$), while there were no associations between serum estradiol and LH₃₀ and serum SHBG (figure 2), respectively. Neither did serum inhibin B associate with LH₃₀ ($r=-0.10$, $p=0.51$).

Number	48
Age (year)	3.5 (0.8;5.9)
BMISDS	0.00 (-0.47;0.76)
Estradiol (N=40) (pmol /L)	6.66 (4.47;8.32)
Inhibin B (pg/ml)	13.00 (8.00;21.50)
LH ₃₀ (IU/L)	3.43 (2.39;5.19)
SHBG (nmol/L)	154 (114;177)

Table
Age and BMISDS (median and range) Estradiol, inhibin B, LH₃₀ and SHBG (median and interquartile range)

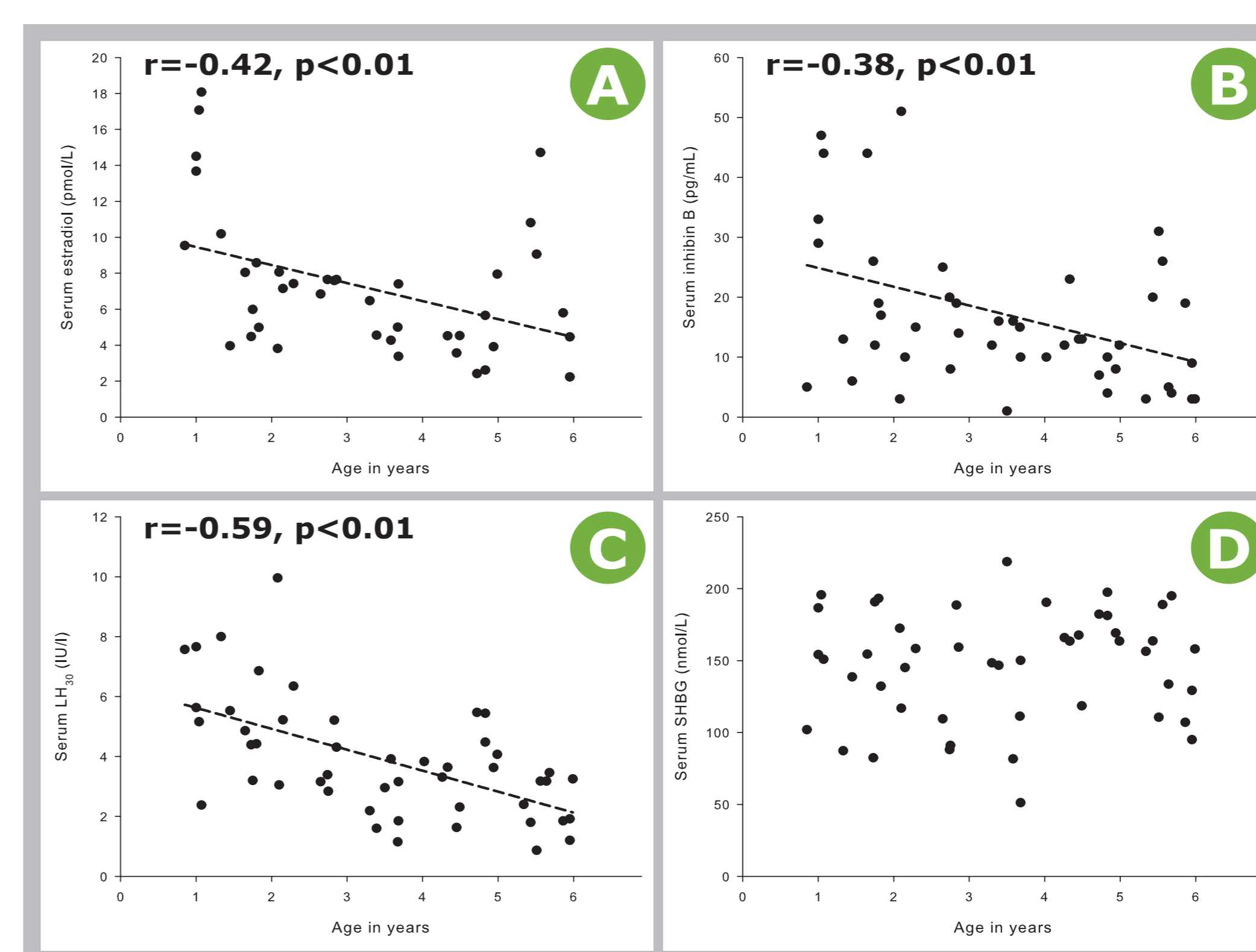


Figure 1A-D
Estradiol, Inhibin B, LH₃₀, and SHBG versus age

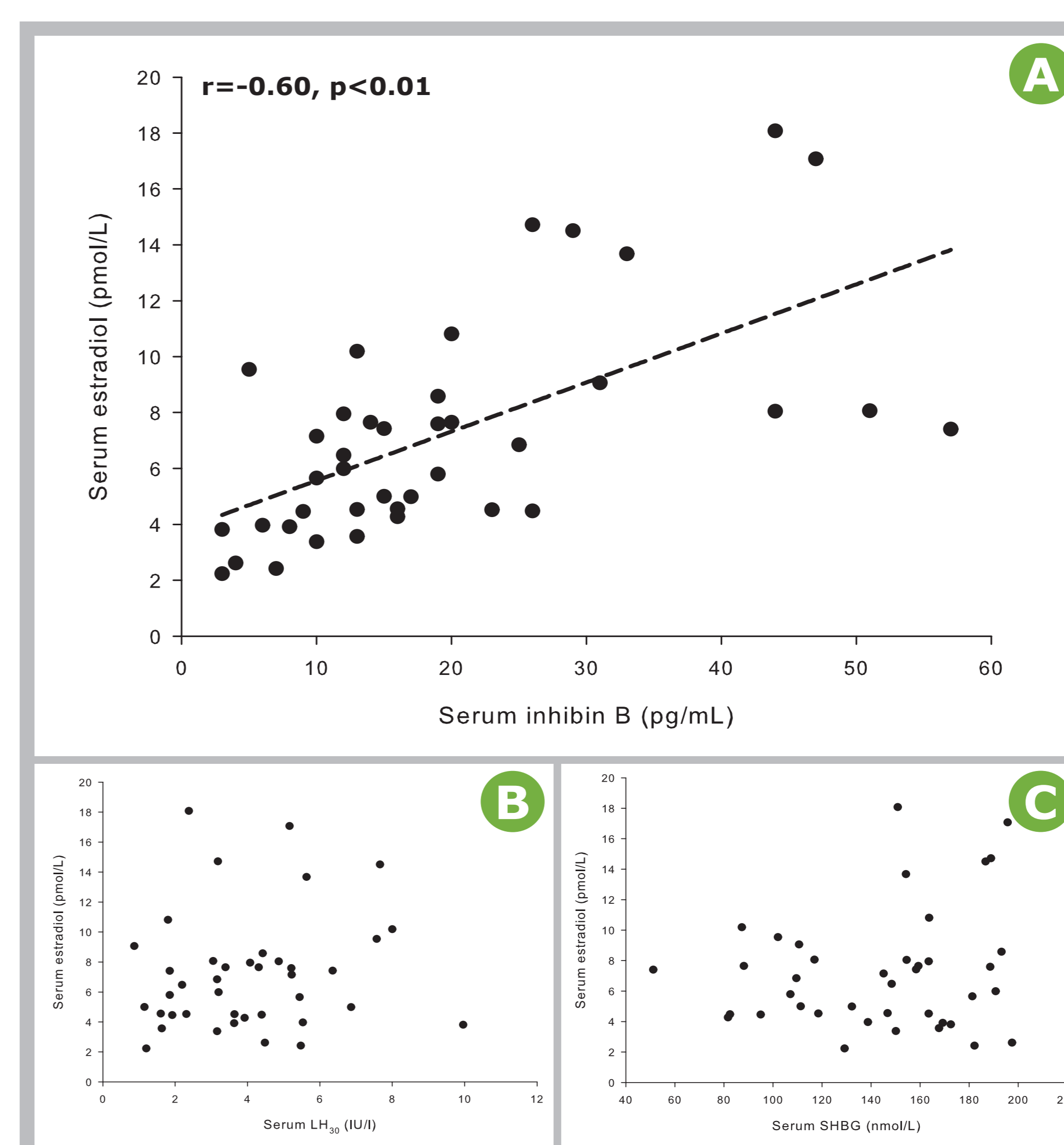


Figure 2A-C
Estradiol versus Inhibin B, LH₃₀ and SHBG, respectively

CONCLUSION

By ultrasensitive technique circulating estradiol was measurable in most pre-pubertal girls in the age group 1-6 years. Serum estradiol, serum inhibin B and LH₃₀ decreased in the age interval 1-6 years. We observed a positive association between serum estradiol and serum inhibin B. This association did not seem to be LH driven.