

TESTOSTERONE LEVEL IN A LARGE MALE COHORT – IMPLICATIONS FOR DEFINING NORMAL RANGE

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Introduction

- Testosterone is an essential hormonal parameter, still:
 - *few data available on its level in general population,*
 - *data on its seasonal and diurnal dynamics are scarce.*
- Age differences in children have been recognized (1), but adults are regarded as a homogenous cohort (2, cutoff > 3 ng/mL)
 - *complicated differentiation of physiologic age decrease from late hypogonadism (3, 4).*
- Different adult norms are in use
 - 3.00 to 8.49 ng/mL – Layton et al (5),
 - 2.64 to 9.16 ng/mL – Labcorp (6),
 - 2.50 to 9.50 ng/mL – Pathology Handbook (7).
- Excessive rate of abnormal results when applying the existing norms. Applying manufacturer's reference range (2.3-10.2 ng/mL) to the SIA «Centrālā laboratorija» cohort, 28% of adult tests were abnormal:
 - 6% low and 9% high at age 18-40,
 - 11% low and 6% high at age 41-55,
 - 41% low and 2% high at age >55.

Are the existing reference ranges really applicable?

Conclusions

The studied population was not exactly normal, still, the cohort is sufficient for preliminary inferences.

- The obtained 5th-95th pediatric percentiles at age 0-17 match previously published series (2, 8) and could be tentatively used as reference.
- The study demonstrated that testosterone level significantly decreases with age.
 - *To assure proper result interpretation, at least 3 adult age groups should be separated: 18-40 (peak level), 41-55 (decrease of upper norm) and >55 (decrease of lower norm as well).*
 - *This approach allows to reduce the unreasonable 41% of abnormally low results in elders and reclassifies half of the elevated results at 18-40.*
- *Further studies and clinical validation would be necessary to confirm the findings.*
- The found diurnal and seasonal variations may be significant for optimal testing regimen and for result interpretation.

References

1. Rey et al, American Journal of Men's Health. 2020
2. Mulhall et al, AUA Guideline, Journal of Urology. 2018
3. Rivas et al, Proc (Bayl Univ Med Cent). 2014
4. Swerdloff, Wang, Andrology. 2020
5. Layton et al, J Clin Endocrinol Metab. 2014
6. Labcorp (labcorp.com)
7. Pathology Handbook (www.pathology.med.umich.edu/handbook)
8. Holmes et al, J Mass Spectrom Adv Clin Lab. 2021

Objectives and methods

The aim of the study was to retrospectively analyze total testosterone levels in a large cohort of male outpatients for

- *age-related,*
- *seasonal*
- *and diurnal variability.*

Study design

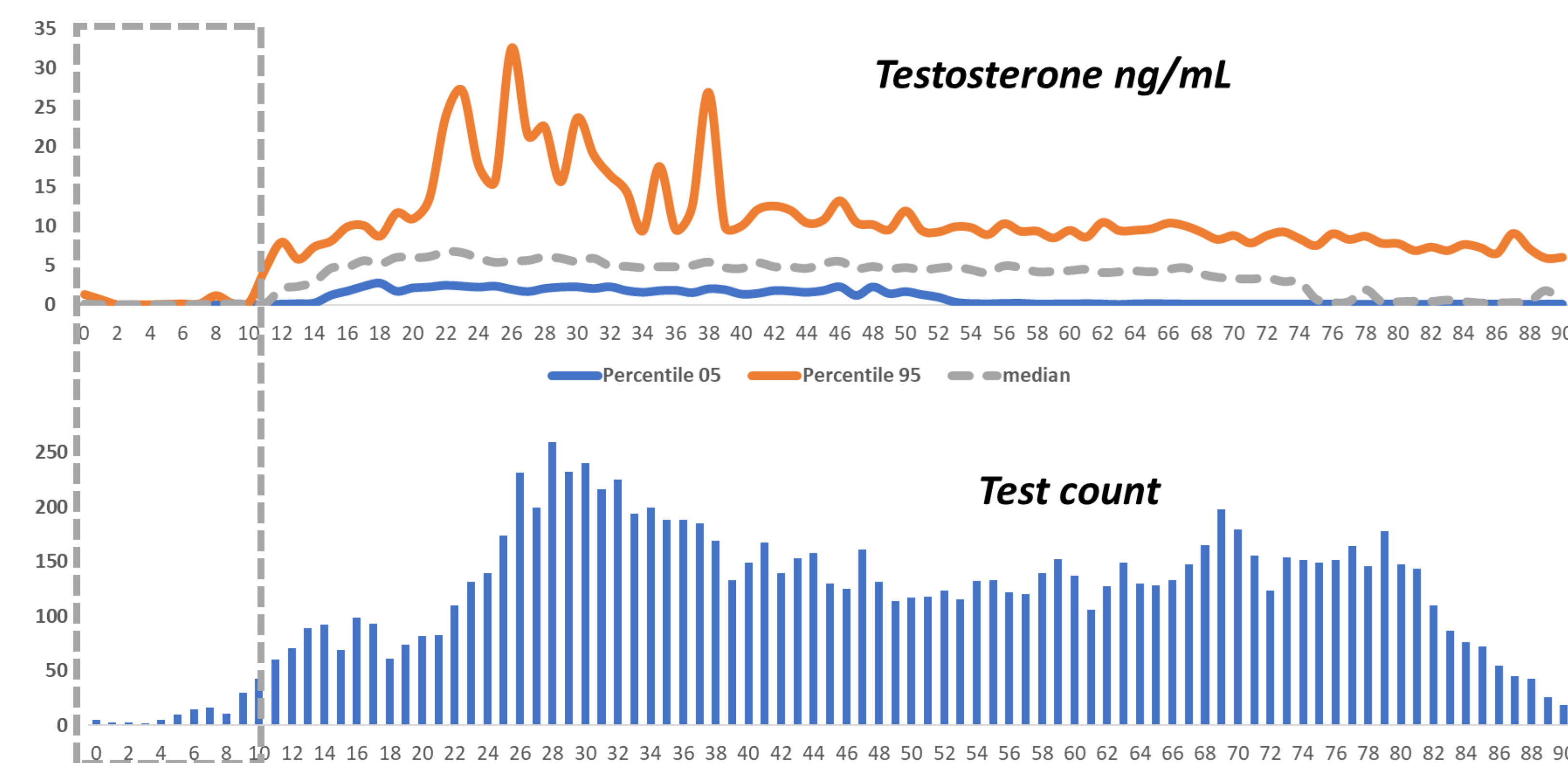
Continuous single institution cohort.

10.945 anonymized outpatient male total testosterone tests were retrieved from SIA “Centrālā laboratorija” database

- performed in 2015-2021,
- platform - ARCHITECT i4000SR immunoassay (Abbott),
- statistics - IBM SPSS v.25.

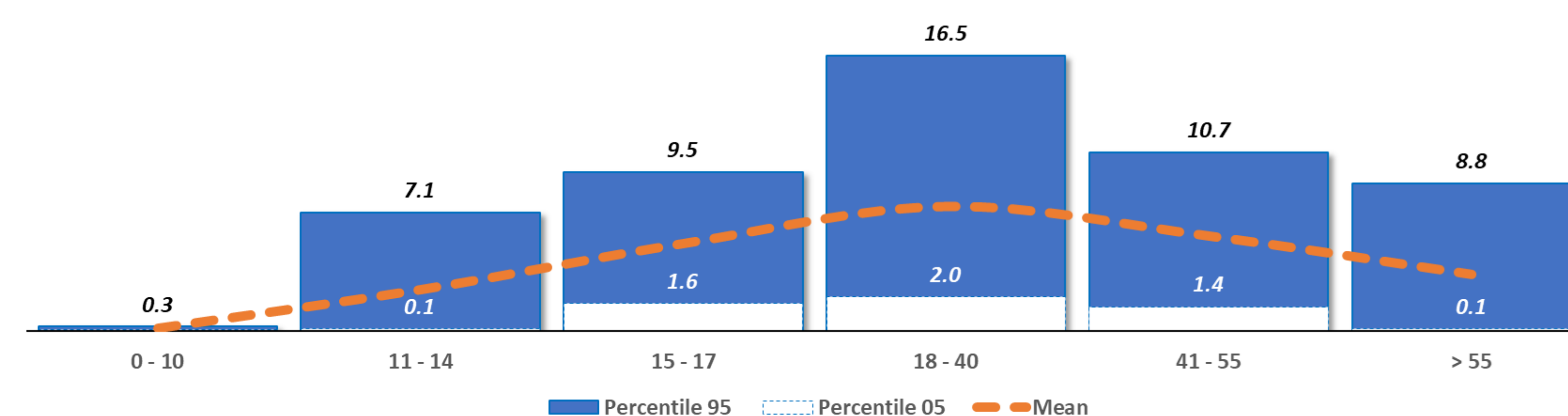
RESULTS

Figure 1. Testosterone level and number of tests by age, children 0-10 marked.



In the studied cohort, testosterone level and number of tests substantially varied by age (figure 1).

Figure 2. Testosterone in age groups



In age groups (figure 2):

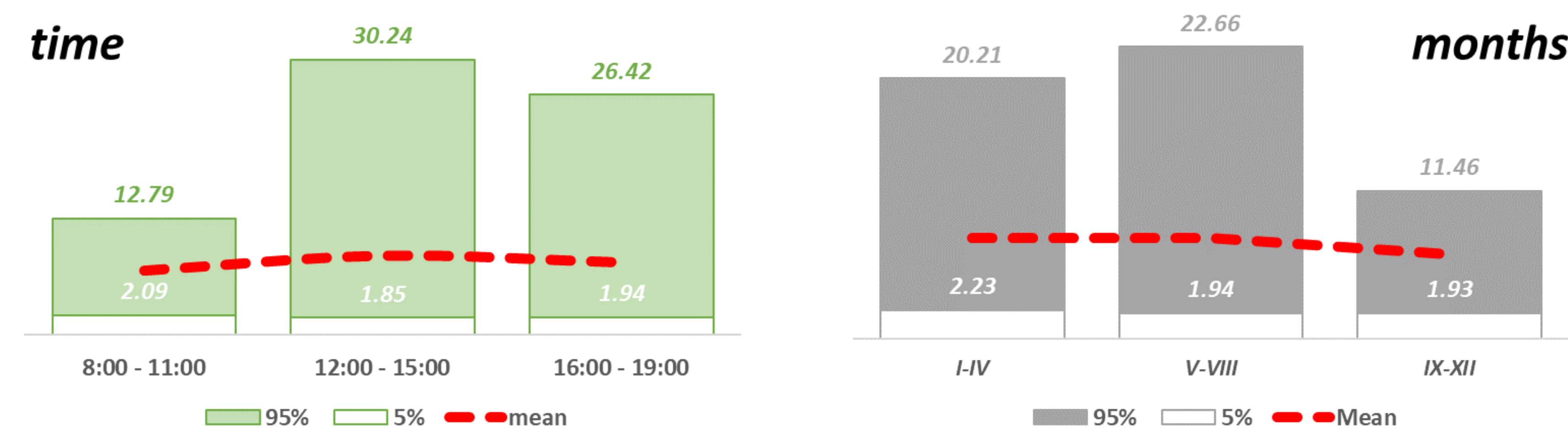
- Mean testosterone level was near zero at age 0-10 (mean 0.15 ng/mL, 5th – 95th percentile 0.02-0.25 ng/mL).
- Transition period was at age 11-14 (2.48, 0.12-7.11 ng/mL),
- Overt increase was observed at 15-17 (5.23, 1.63-9.54),
- Peak at 18-40 (7.45, 2.04-16.50),
- Decrease was noted at 41-55 (5.69, 1.44-10.70)
- And plateau was formed after 55 (3.39, 0.13-8.82 with lower norm near zero).

Differences were highly significant (Kruskal-Wallis $p < 0.01$)

When applying manufacturer reference range of 2.3-10.2 ng/mL, 27.70% adult tests were abnormal:

- 6% low and 9% high at age 18-40,
- 11% low and 6% high at age 41-55,
- **41% low** and 2% high at age >55.

Figure 3. Testosterone daily and yearly dynamics in age group 18-40



At age 18-40, 95th percentile was lower in the morning (Kruskal-Wallis $p < 0.01$) and dropped in September-December ($p < 0.01$), figure 3.

Variations in overall level and in other age groups were insignificant