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Lab test findings in the elderly

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LETTER TO THE EDITOR

A specific issue of the eJIFCC, with several papers [i.e. 1-6], focuses on the harmonization of laboratory information provided by different services with different clinical settings. Hopefully, these publications will also consider the fact that the reference interval of several analytes is different in elderly patients compared to the younger age groups.

A common accompanying phenomenon in the elderly (above 75 years of age) is the increased risk of chronic morbidities. This is associated with an increased requirement for health care activities that include the patients' assessment and monitoring. Blood sampling and laboratory testing are an inherent part of this process.

When a clinician considers the results of laboratory tests (as 'good' or 'bad'), the reference range used by the laboratory is the cornerstone and the basis of further evaluations. In the majority of laboratories healthy reference range is declared according to test descriptions and literature; just a minority perform a systematic analysis among individuals of a population considered as healthy. However, this is where the problem lies: in general, blood donors or other adults aged 20-40 years are enrolled to assess

healthy reference range. And very rarely elder (and completely healthy) subjects are asked to participate. This is not an issue until the analyte to be tested is not affected by the age itself. This factor, however, has a direct or indirect effect on a number of laboratory tests, as it is highlighted in a recent review [7]. In addition to age and comorbidities (e.g. diabetes mellitus, rheumatism, osteoporosis, etc.) elder patients also have various disadvantages such as obesity, low socioeconomic status, disabilities and poor (unhealthy) diet. These all may have an impact on laboratory results. (see Table 1)

Therefore, it is a common scenario that the laboratory reports of elderly patients may present a number of flags indicating a deviation from 'normal reference range' [8, 9]. That is often alarming for the patient (and his or her physician). A resultant consequence (provided that the doctor is not fully aware, whether a slight abnormality is acceptable for the patient) is the prescription of novel laboratory tests that generate novel questions.

The direction of anticipated abnormalities (compared to the reference range obtained in younger subjects) is summarized in Table 2.

SOME ANALYTES WITH PARTICULAR IMPORTANCE

Decreased hemoglobin/hematocrit

In the elderly, the impairment of the intestinal absorbance of iron and vitamin B12 may lead to a decrease in hemoglobin and erythrocyte synthesis. Occult blood loss is also common. There is an increased tendency for hemolysis. Therefore, it is recommended to decrease the lower level of reference range of hemoglobin (e.g. 115 g/l and 110 g/l for males and females, respectively). However, it is challenging to differentiate real anemia from the effect of aging. In the majority of patients the cause of anemia

Table 1 Factors having an effect on the result of lab tests in the elderly

Physiological changes gonadal hormones' levels are decreasing, bone loss is increasing; renal function is impaired; blood fat levels are increased.
Life style modification inactivity and associated alteration of body compartments; muscular mass is decreased; less supply of vitamin D due to less exposure to sun.
Dietary factors problems with digestion and absorption, dental problems lead to insufficient intake of nutrient rich food – vitamin and mineral trace deficiency. Further risks are alcoholosim and obesity. In US patients (according to CDC) aged 50 – 74 years up to 40 per cent of cancers are linked to obesity. Increased body weight is a risk factor for at least 13 cancers (i.e. esophageal, thyroid, breast, gall-bladder, gastric, liver, pancreas, renal, ovarian, uterine and colorectal cancers). [10]
Medicinal therapy (due to co-morbidities) may also cause abnormality in some lab test results.
Advertisement e.g. dietary supplements.

Table 2 Some analytes with altered results in the elderly

Increasing
alkaline phosphatase, antinuclear antibody, fibrinogen, FSH, LH, SHBG, gamma glutamil transferase, gastrin, uric acid, interleukin-6, insulin, cholesterol, parathormone (PTH), prostate specific antigen (PSA), rheuma factor, copper, triglycerol, ESR
Decreasing
aldosterone, vitamin B12, dihydroepiandrosterone (DHEA), vitamin D, ferritin, phosphate, HDL-cholesterol, IGF-1, interleukin-1, calcium (total), creatinine clearence, creatine kinase, magnesium, growth hormone, estradiol, free testosterone, T3, iron

is a chronic disease e.g. occult blood loss or renal failure. Anemia is of particular importance as elderly patients with anemia are at higher risk for circulatory and oxygenation problems hallmarked by fatigue, dyspnea, paresthesia (that are often attributed to elder age and, therefore, is not treated.)

The area of gas exchanging alveolar surface is also decreased, leading to a decrease in arterial oxygen tension by 4 mmHg per decade; this process results in latent hypoxia. Hypoxia is often associated with cognitive problems (that are further aggravated by the side effects of medicines used commonly).

Increase in blood glucose levels

Serum glucose levels increase proportionally to age, while glucose tolerance is decreasing. The reference range of fasting glucose is wider in the elderly (3.9 – 6.7 mmol/l). However, blood glucose levels are often low due to decreased body weight and dietary problems. Simultaneously, serum insulin levels also increase indicating insulin resistance; this is responsible for impaired glucose tolerance observed in up to 25% of patients above 75 years. Therefore, postprandial blood glucose levels are often higher when performing an oral glucose tolerance test (upper limit = 5.5 mmol/l + [age in years /18].

Increased erythrocyte sedimentation rate (ESR)

The ESR is increasing proportionally with age (in general by 0.22 mm/h per year above 20 years of age), but its exact cause is not known. Therefore, the upper limit of reference range in the eldery is 40 mm/h and 45 mm/h in males and females, respectively. (The contribution of the common occurrence of systemic inflammation in the elderly to high ESR is not fully clear. One should remember not to use ESR as a basis of diagnosis of inflammation in the elderly.)

Decrease of iron levels and stores

Serum iron levels decrease in the elderly, probably due to impaired production of gastric juice. Simultaneously, iron stores decrease also. The other common cause of low iron levels and systemic iron deficiency is chronic blood loss; therefore, malignancy should be searched for.

Increase of total cholesterol and triglyceride levels

Total cholesterol levels increase by up to 1 mmol/L in 60 years of age. No further elevation is anticipated thereafter; rather, in very old subjects the level of this analyte decreases. Triglyceride levels increase by 30 and 50 per cent in males and females, respectively, between 30 and 80 years of age. HDL-levels increase somewhat in aged men, while decrease in aged women.

Decreased renal function

In general, aged people take several medicines simultaneously. The metabolites are partly excreted via the kidney. Therefore, it would be of utmost importance to assess renal function to establish optimal dosage. In the elderly the number of functioning nephrons decreases by 30 – 45%; this is accompanied by the decrease of glomerular filtration rate. However, creatinine levels change rarely, as the lean body mass decreases. Therefore, net BUN and creatinine levels are not appropriate to estimate renal function; instead, eGFR calculation is required that incorporates patient's age.

Low albumin levels

Simultaneously with aging the level of some specific proteins, particularly that of albumin decrease (leading to a decrease of total protein levels). This is partly due to impairment of liver functions and an inappropriate diet. As albumin is the major carrier protein in blood, you should not be surprised, if a patient with low albumin levels presents with low calcium or hormone levels.

Thyroid function impairment is common

Hypothyreosis is not an inevitable consequence of ageing; however, it is a quite common phenomenon in aged patients (of note, its signs and symptoms include weakness, slowness and tiredness that are falsely attributed to old age). Therefore, it is recommended to screen patients' TSH levels. Roughly, TSH reference range is comparable to that in younger age. One should remember that medicines used commonly in old patients may influence thyroid hormone levels (eg. glucocorticoid hormones suppress TSH, while lithium inhibits thyroxin secretion).

WHAT SHOULD BE DONE?

Analytes changing with age are challenging as the doctor should decide whether a laboratory test result deviates from the 'healthy' (younger) reference range due to physiology or due to a disease. Unfortunately, there is no clear-cut answer, just our common advice: one should never establish a diagnosis exclusively on laboratory test results. Instead, laboratory test results can be used as an aid and prior results along with clinical history should be always considered.

The determination of old age-specific reference range would be an enormous support for the evaluation. This is, however, not an easy task. Subjects encounter the doctor (mostly) if they have complaints; healthy subjects normally avoid the doctor. The major question with the subject presenting at the clinic is not that (s)he has any problem (the answer: yes, (s)he has, otherwise (s)he would not have come); instead: what is the cause of the problem. Indeed, the goal of laboratory investigation is the exclusion or reinforcement of a diagnosis in an otherwise diseased person.

Therefore, it is not a healthy reference range that is required for this population; instead, a 'non-affected' reference range that is characteristic for said population (that is representative for the given subject). (e.g. the 'non-affected' reference range of troponin is different from the healthy reference range in an old patient with moderate renal failure.) The routine establishment of such reference ranges even for routine

laboratory tests, however, is not performed in domestic and foreign laboratories. Furthermore, the age-adjusted reference range for any analyte is also affected by the analytical environment; therefore, one cannot provide general exact numbers.

Therefore, it is recommended for physicians caring for older patients to request as few laboratory tests as they can. The major risk with large number of laboratory tests: if more laboratory tests are performed, the risk of false-positivity (and associated diagnostic doubts) is increased. The premise of fewer laboratory test is that the doctor should be clear with the anticipated information hoped from the test result, i.e. how the laboratory test result will improve his/her clinical decision making.

If you still decide to ask a laboratory test, it is recommended to strictly adhere to standardized sampling conditions.

Unfortunately, the laboratory and age specific reference ranges (that would improve the patient's assessment) are not commonly available. The use of individual reference tables available in literature is also controversial as reference ranges depend on local laboratory settings including instrument and reagents.

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