Changes in full blood count parameters with age and sex: results of a survey of 900,000 patient samples from primary care


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Title
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Conflict of interest
- No conflicts of interest

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Changes in full blood count parameters with age and sex: results of a survey of 900,000 patient samples from primary care

To the Editor,

The full blood count (FBC) is a frequently requested blood test in both primary and secondary care. Given that the population in England is ageing, with 18.3% of the population aged 65 years and over in 2018,[1] it is important to ascertain how FBC parameters change in older patients. The aim of this study was to examine changes in FBC parameters with age and sex using a data set of over 900,000 patients gathered from primary care in England.

Methods
The reporting of routine blood tests in primary care for NHS England occurs electronically via the NHS spine data transfer service (DTS).[2] In July 2013, all blood test results were captured from the DTS over a 23-day period as part of an audit of data quality, sponsored by UK Department of Health and overseen by the Royal College of Pathologists. Anonymised FBC data were made available for analysis in accordance with NHS coding standards. The data were restricted to patients aged 1 to 100 years, and results where sex was not specified or values were absent were excluded. Where values were identified as missing for haemoglobin, red blood cell count (RBC) or mean corpuscular volume (MCV), the data for that patient was excluded. Parameters were analysed by year of life and sex. Haemoglobin was analysed for a subgroup of adult patients identified to have ferritin, B12, folate and creatinine results within their respective reference intervals. The means were graphed to identify trends in the selected parameters.

Results
Haemoglobin
For haemoglobin, 339322 results for males and 535716 results for females were included. In males, mean haemoglobin concentration increases from birth until approximately age 20 years. After this, it declines steadily until approximately age 70, when it starts to decline at increasing rate (Fig 1a). In females, mean
Haemoglobin concentration increases until approximately age 14, when it starts to decline slowly until age 30, then increases again until age 60, and thereafter declining with age. Haemoglobin concentration in males and females begins to converge after age 60 and equalises by approximately 90 years.

In order to exclude common causes of anaemia, namely haematinic deficiency and renal impairment, haemoglobin concentrations were further assessed in a subset of patients over 18 years where concomitant test results for ferritin, B12, folate and creatinine were within their respective reference intervals (Fig 1b-f). For males with ferritin>30μg/L, B12>200ng/L, folate>5μg/L or creatinine<100mmol/L, there were 6257, 6141, 4581 and 38186 haemoglobin results respectively, and 1151 haemoglobin results where all four parameters were within range for a single blood test (Fig 1f). For females with ferritin>30μg/L, B12>200ng/L, folate>5μg/L or creatinine<80mmol/L, there were 9960, 11583, 8829 and 53898 haemoglobin results respectively, and 2219 results where all four parameters were within range for a single blood test. The results of this sub-analysis showed similar changes with age as those seen with the full dataset, specifically progressive decline in haemoglobin concentration with increasing age over 60 years (Fig 1f).
Red cell distribution width, red cell count and mean corpuscular volume
For red cell distribution width (RDW), 127123 values for males and 200255 values for females were included. In both sexes, there is a decrease in mean RDW during childhood and adolescence. Thereafter, for males over 20 years, there is a linear increase in mean RDW with age (Fig 2a), while for females, mean RDW remains higher than males throughout the reproductive years and up until age 60, after which it follows the same linear increase with age. In both sexes, the percentage of patients with RDW >14.5%, the commonly used upper limit for the reference range, increases at approximately 1% per annum above age 60 years (Fig 2b).

For both red blood count (RBC) and mean corpuscular volume (MCV), 339322 results for males and 535716 results for females were included. For the RBC, the changes seen with age follow the same trends as described for haemoglobin level (Fig 2c). For the MCV, both sexes show a similar trend with a steep increase from birth until approximately age 20, followed by a slow steady rise throughout life (Fig 2d).
Discussion

Red cell indices

Anaemia is defined by the WHO as haemoglobin concentration of <120 g/L for females and <130 g/L for males.[3] From our dataset, the mean haemoglobin concentration for males aged 82 years and females aged 92 years meet these criteria meaning 50% of patients would be technically anaemic. This decline in haemoglobin remains evident even when those patients with common causes of anaemia, namely renal impairment (raised creatinine) or haematinic deficiency (low ferritin, folate or B12).[4] were excluded. Smaller samples of known healthy subjects have found similar results, for example Malhknec et al. found that 70% of males aged 80-89 years and 63% of females aged >90 years met the WHO criteria for anaemia.[5] Similarly, the study by Nilsson-Ehle et al, in which individuals with

![Figure 2 Graphs showing a) changes in red cell distribution width with age; b) increase in percentage of patients with a RDW >14.5% with age; c) changes in red blood cell count with age; d) changes in mean corpuscular volume with age.](image-url)
identifiable diseases were excluded from the analysis, found that haemoglobin fell with age even in healthy subjects and more prominently in males than females.[6]

Analysis of red cell indices reveals that, for both males and females over 60, there is a slow decline in erythrocyte production accompanied by progressive upward trends in anisocytosis and macrocytosis, as evidenced by falling RBC and rising RDW and MCV. For women in their reproductive years, we find a reduced RBC and raised RDW, possibly due to pregnancy-related changes in the FBC such by dilutional effects and iron deficiency. These trends are similar to those from a large study of Korean patients which interestingly did not find raised RDW in females, possibly due to exclusion of pregnant women.[7]

The key strength of our study is the very large number of samples evaluated from an unselected patient population in primary care. However, we have to interpret the results with caution, as there is no accessible clinical patient data accompanying the samples. Nonetheless, observations can clearly be drawn regarding the overall trends in red cell parameters throughout life irrespective of the underlying cause.

**Conclusion**

Analysis of this large primary care dataset highlights a number of trends in various FBC parameters throughout life with marked decline in haemoglobin level in the elderly. In particular, the analysis identifies a falling haemoglobin level and rising MCV and RDW with older age suggesting the need for geriatric reference ranges in order to avoid unnecessary investigation of anaemia in older patients. Whether these trends are due to age-related changes in bone marrow physiology resulting in declining haematopoietic function or the result of pathophysiological disease processes is unclear. Exclusion of patients with haematinic deficiency or renal impairment did not alter the trends seen suggesting they are primarily age-related. However, the lack of clinical data, and in particular the inability to exclude patients with anaemia of chronic disease, prevents definitive conclusion as to the explanation. In addition, recent evidence has shown that acquired clonal haematopoiesis of the bone marrow involving mutations in certain myelodysplasia-related genes, primarily the DNA methyltransferase DNMT3A, are common in
patients over 60 years and also associated with raised RDW.[8] However, whether this genetic mechanism is a significant contributor to the age-related trends evident in our large primary care dataset will require further studies.

References