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(RESEARCH ARTICLE)

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Study of iron deficiency in a population of blood donors in Tlemcen - Algeria

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Abstract

Blood transfusion is an essential substitutive therapy for multiple diseases. To minimize a potential risk of transfusion-transmitted infections, the WHO recommends using regular blood donors. However, regular donors constitute a population at risk of anaemia due to subclinical iron deficiency which is not covered by most hemovigilance donor systems. Thus, the aim of the present study is to determine the prevalence of the deficiency among donors from Tlemcen, Algeria. These donors were selected to perform a blood count and a dosage of ferritinemia. Statistical analyses using SPSS software, and Excel was performed. The prevalence of iron deficiency was calculated at 35.2% and anaemia at 22%. Ferritinemia was strongly related to the different characteristics of the donation, mainly in women population. Hemovigilance systems should integrate blood donor safety focus their efforts on protection against iron deficiency. Unlike Haemoglobin, serum ferritin remains the most sensitive and early marker for donor protection against this deficiency.

Keywords: Iron deficiency; Blood donor; Serum ferritin; Anaemia; Haemoglobin.

1. Introduction

Even today, transfusion is a medical act that saves lives and supports cutting-edge medicine based on the use of labile blood products (LBP). Medically adapted to the correction of one or more deficiencies, the prescription of LBPs provides one or more therapeutic elements including the Iron/Haemoglobin couple, an oxygen carrier (1).

A marked increase in LBP needs has been observed. At the same time, blood samples as well as the number of blood donors (BD) tend to evolve further, thanks to the mission of blood banks, which consists of regulating the practice of blood donation. In an approach aimed at increasing the loyalty rate which would ensure self-sufficiency in LBP, it is essential to pursue the policy of improving product quality and safety, including that of BD.

Each year, government must raise vast sums to finance the safety of blood recipients, however the importance of BD's health is not enough considered by hemovigilance systems. Iron balance in BD is an influential safety issue. A full blood donation (400-500 ml) eliminates almost 250 mg of iron. This corresponds to the depletion of 4 to 10% of iron reserves. In fact, food provides about 10 to 15 mg of iron per day, however, only a small fraction of this contribution is absorbed, namely about 1 to 2 mg /Day for an adult (2). With continued depletion of iron stores, the body either adapts to low iron by increasing its absorption or develops an iron deficiency anaemia (3).

There are three major compartments of iron in the body: the labile iron, the functional iron, and the storage iron. Ferritin (FRT) stores iron. In the case of iron overload, FRT is degraded in the lysosomes. On the other hand, when the content of the labile iron pool decreases, the FRT releases its iron. The movement of iron in the body have few exchanges with

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the external environment. Biochemical assessment of stored iron relies on serum FRT. In healthy subjects, plasma, or erythrocyte FRT concentration is correlated with tissue FRT and therefore with iron reserve. The increase of 1µg/L of the FRT concentration corresponds to the storage of 8 mg of iron (no longer valid beyond of 1000µg/L). The decrease in plasma and/or erythrocyte FRT concentration is pathognomonic for iron deficiency (4).

A low FRT proves that the iron in reserve is insufficient but not that the erythropoiesis is concerned. Therefore, it does not make it possible to say whether anaemia is attributable to an iron deficiency or not. Increases in FRT concentration, independent of iron stores, are common and may mask iron deficiency (4).

Thus, it is well known that iron deficiency anaemia is the ultimate stage of iron deficiency. This last, in the absence of anaemia, can also have negative consequences, in particular a reduction in physical capacities and intellectual performance, a lower resistance to infections and disturbances during pregnancy. This leads to push action from anaemia prevention to iron deficiency prevention(4).

Today, studies continue to demonstrate that the Hb count alone is inadequate for detecting a subclinical iron deficiency in BDs. The results may exceed the limiting pathological values for iron deficiency anaemia even if iron stores are depleted. Not being correlated with the state of iron status, the Hb level shows poor sensitivity in real-time detection of the impact of blood donations on iron stores. Serum FRT level appears to be more sensitive.

The patient suffering from secondary hemochromatosis benefits from bleeding or drug chelation, while the iron-deficient BD does not even benefit from screening! In return for his approach of solidarity, could the BD benefit from effective and early prevention against iron deficiency anaemia by only respecting the current hemovigilance rules?

Being partly attributable to the well-founded fear of preteritizing the supply of LBP(2), this lack of initiative could be unfounded by considering the BD as a source of LBP whose use should be rational and whose misuse could turn out to be catastrophic.

2. Materials and methods

The main objective of our study was to assess the prevalence of iron deficiency in a BD population. The influence of the donation characteristics on the iron stores was also evaluated. This is a cross-sectional study, with an analytical aim, of a population of whole BD that took place at the Hemobiology ward and the Blood Bank of the Tlemcen University Hospital Center and was spread over a period of 6 months, from December 2016 to May 2017. The subjects concerned are those who came to voluntarily donate their blood and who gave their informed consent to participate in this study. These subjects meet the eligibility criteria for donors of whole blood or blood components. Subjects who received iron therapy within the previous six months were excluded.

Sampling was exhaustive, the subjects were selected after interrogation and a pre-donation clinical examination. No pre-donation biological test has been used for the BDs selection. As a result, 101 BDs were recruited in this study and benefited from haematological and martial assessments, namely Hemogram, reticulocyte level and serum FRT level.

Subsequently, 91 donors were subjected to statistical analysis and 10 donors were excluded. The reasons for this exclusion were either the presence of microcytic pseudo-polycythaemia at the hemogram or microcytosis with hypochromia, without anaemia and with normal iron stocks.

The biological data and those related to the characteristics of the donation were entered on the Excel 2007 software. The bivariate statistical analysis was carried out using the IBM SPSS statistics 20 software according to the khi^2 test ($\chi 2$) at a 5% level of significance, to study the relationship between the rate of Hb, serum FRT and the different factors of interest in their qualitative aspect. In addition, the Pearson coefficient was applied to study the possible correlations between the different quantitative variables. The NFS was carried out on the ADVIA automaton®2120i. Serum FRT was performed on Automate ARCHITECT i1000 SR.

3. Results

The population studied included 91 BD including 62 male subjects and 29 female subjects. 68.1% and 31.9% respectively (M/F ratio = 2.13). For the slices of age between 25 and 31 years old, and 53 to 60 years old, it is the women who prevail. For the other slices of age, it's always the man who predominates. Note that for a total number of more than 8 donations, it is the man who predominates.

The frequency of donation varies from 0 to 4 times/year for men and from 0 to 3 times/year for women, which enabled us to distinguish 5 categories, the male gender predominates for donations of 3 times/ year or more. In addition, the distribution is almost equal between the two sexes for a frequency of twice a year. We note that female donors are encountered more for donation intervals of 5 to 6 months and over 6 months, whereas the distribution is almost equal for an interval of 4 months.

The prevalence of iron deficiency was 35.2% (32/91), that of anaemia was 22% (20/91) and that of iron deficiency anaemia was 17.4% (16/91) in the BD population studied.

In men, the prevalence of iron deficiency was 27.4% (17/62), that of anaemia was 16.1% (10/62) and that of iron deficiency anaemia was 11.29%. (7/62). In women, the prevalences were respectively: 51.7% (15/29), 34.5% (10/29) and 31.03% (9/29).

Women were significantly more exposed to iron deficiency (P = 0.008) and to anaemia (P=0.049) compared to men (Figures: 01-02).

We studied the relationship between FRT/Hb levels and: age, total number of donations, interval between the last two donations, donation frequency (number of donations during the 12 months preceding inclusion).

For women, the average serum FRT concentration was 14.58 ng/mL (**DS** = 10.29). The average age was 34.07 years (**DS** =11.6). The average total number of donations was 8.4 donations (**DS** = 6.96).

The correlation study between serum FRT concentration and the various factors of interest showed that serum ferritin was:

- Significantly and inversely related with the total number of donations (r = -0.49; p = 0.006); as well as the frequency of donation (r = -0.57; p = 0.001).
- Not significantly related to age (r = 0.21; p = 0.28).

The transformation of the variables (age, total number of donations, frequency of donations) into classes and the study of their relationships made it possible to observe the following results:

- the prevalence of iron deficiency increases significantly with the frequency of donation (P =0.025) and with the number of total donations (P =0.033) (Figures: 03-04).
- the prevalence of iron deficiency is significantly higher (P = 0.002) with the shortening of the donation interval (Figure 05).
- The prevalence of iron deficiency was higher for the age groups < 45 years (Figure 06).
- The average rate of Hb was 12.17 g/dL (DS=1.23).

The study of correlation has shown that the rate of Hb was:

- Significantly and directly linked with age (r= +0.415; p=0.025).
- Not significantly related to other donation characteristics.

The transformation of the specific variables of donation and the study of their relationship on the level of Hb allowed:

- To observe that menstruating adult women were more likely to develop anaemia compared to post-menopausal women (Figure 07).
- The prevalence of anaemia increases with the importance of: (Figures: 08-09)
    - Frequency of donations.
    - Total number of donations.

For men, the average serum FRT concentration was 29.55ng/mL (**DS**=26.75). The average age was 34.52 years (**DS** =10.08). The average total number was 18.5 donations (**DS** = 16.17).

The correlation study between serum FRT concentration in men and different donation characteristics showed that serum ferritin was:

- Significantly and inversely related with the frequency of donation (r = -0.354; p = 0.005).
- Not correlated neither with age nor with the total number of donations, respectively (r = 0.19; p = 0.125); (r=-0.10; p=0.4).
- The transformation of variables into classes and the study of their combinations have shown in frequent donors:
- An increase in the prevalence of iron deficiency for a frequency of 3 to 4 times/year (Figure 10).
- Men with a total donation of more than 12 times were more exposed to depletion of iron stores 36.7% (11/30) (Figure 11).
- Iron deficiency was more common in the 18-24 age group (Figure 12).

For a donation interval of 3 or 4 months, blood donors were more exposed to iron deficiency compared to those who had an interval of 5 to 6 months or more (Figure 13).

The average rate of Hb was 14.17 g/dL (**DS**=1.15).

The study of correlation has shown that the rate of Hb was:

- Significantly and inversely related with the total number of donations (r = -0.25; p =0.05).
- Not significantly related with age and the donation frequency respectively (r= 0.05; p =0.67); (r= - 0.18; p =0.5).

The transformation of the different variables into classes and the study of their relationship with the level of' Hb permitted to observe that:

- Anaemia was more frequent for the slice of age 18 to 24 compared to other age groups.
- Blood donors who gave their blood with a frequency of 3 or 4 times during the 12 months preceding the inclusion were more exposed to anaemia than the others (Figure 14).
- For a donation interval of 3 or 4 months, BDs were more exposed to anaemia, respectively 16% and 21.1% (Figure 15).

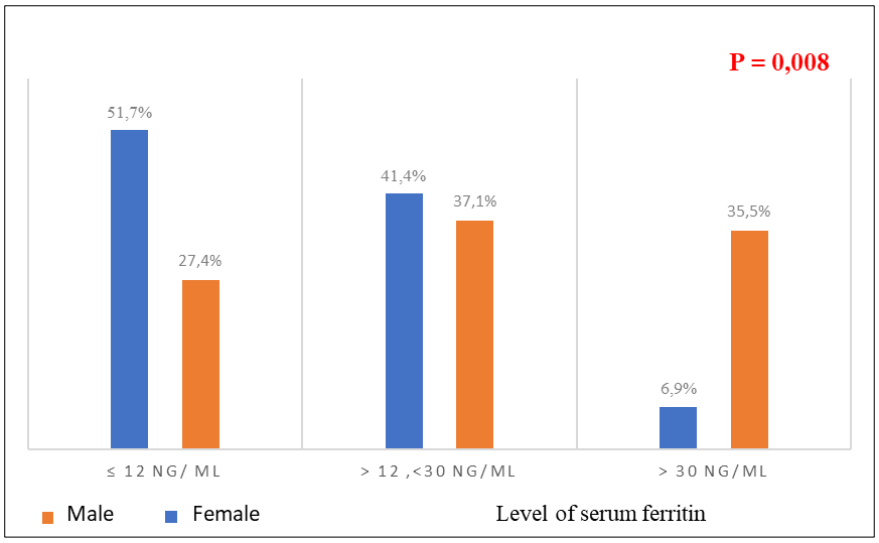

Figure 1 Distribution of male and female donors according to serum ferritin level

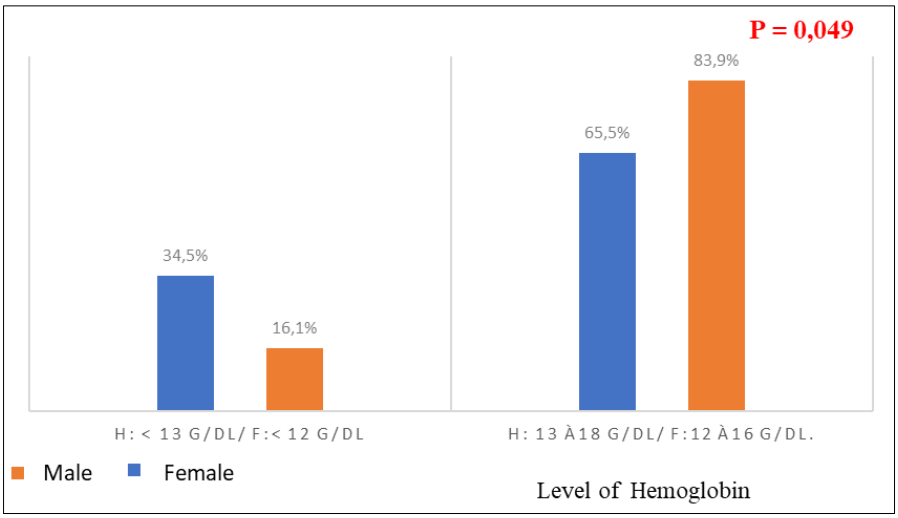

Figure 2 Distribution of male and female donors according to haemoglobin level

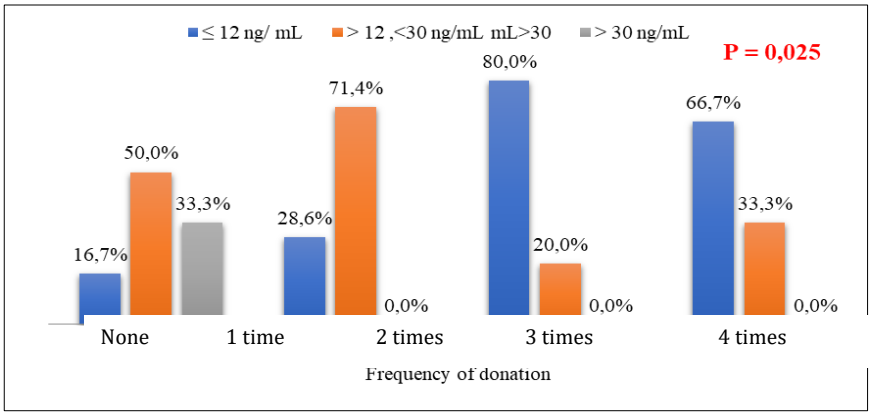

Figure 3 Distribution of serum ferritin levels in women according to the frequency of donation.

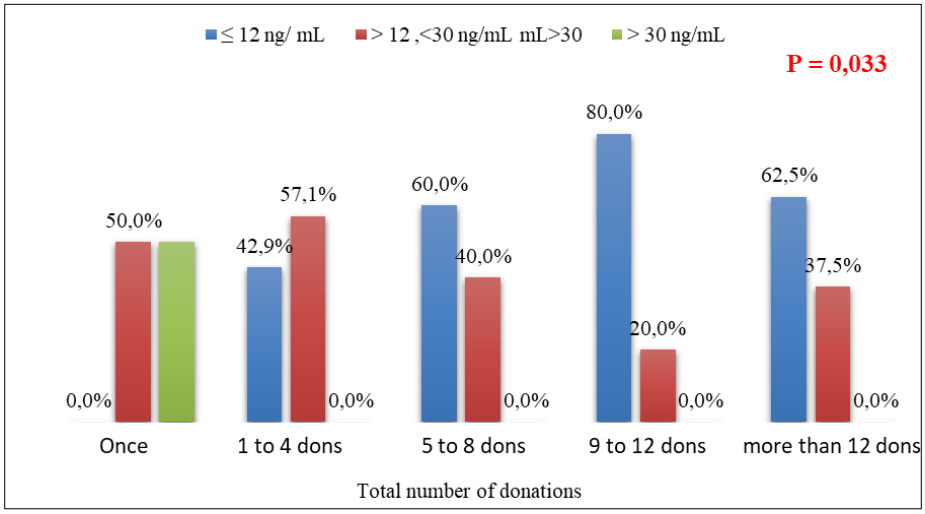

Figure 4 Distribution of serum ferritin levels among women according to the total number of donations

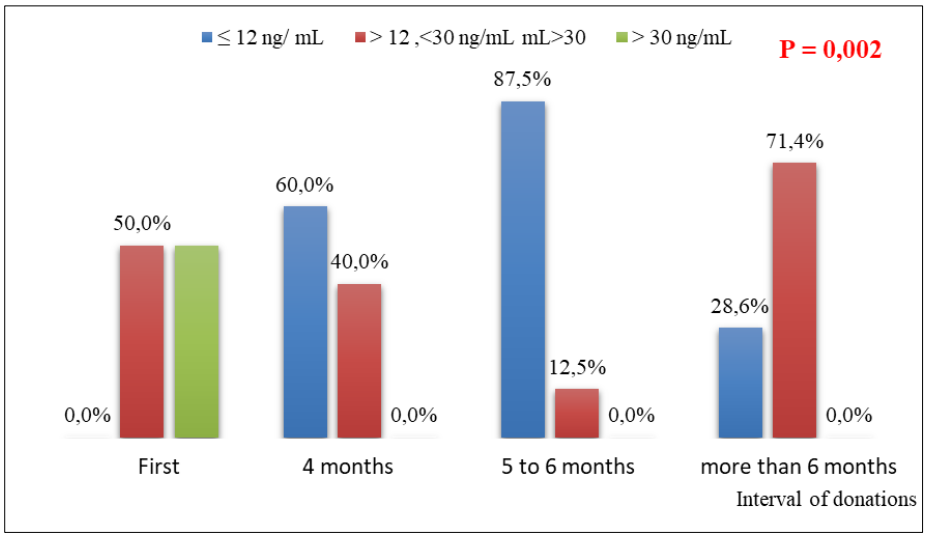

Figure 5 Distribution of serum ferritin levels in women according to donation interval

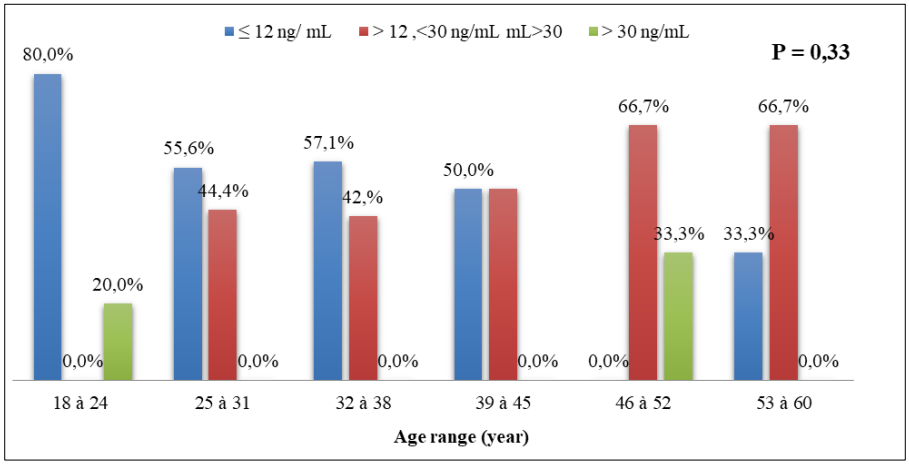

Figure 6 Distribution of serum ferritin levels in women according to age groups

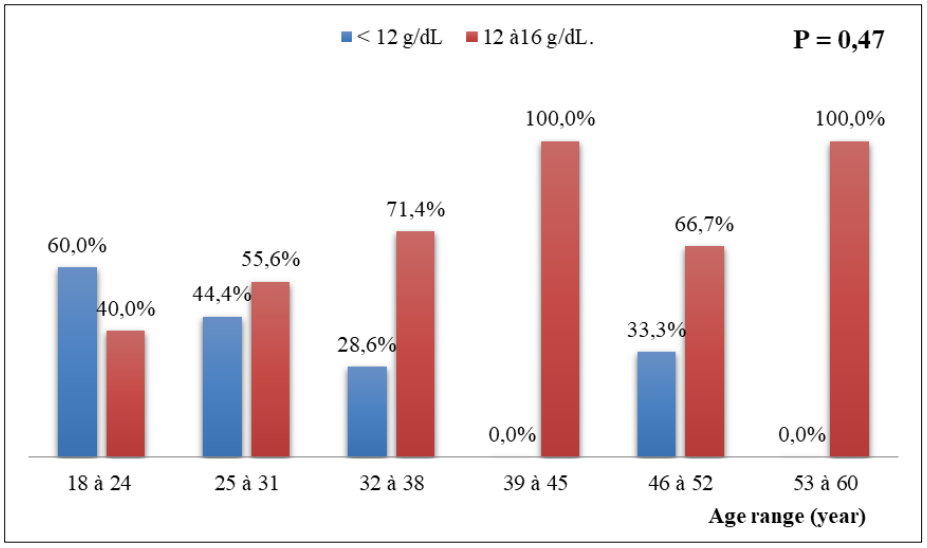

Figure 7 Distribution of hemoglobin levels in women according to age groups.

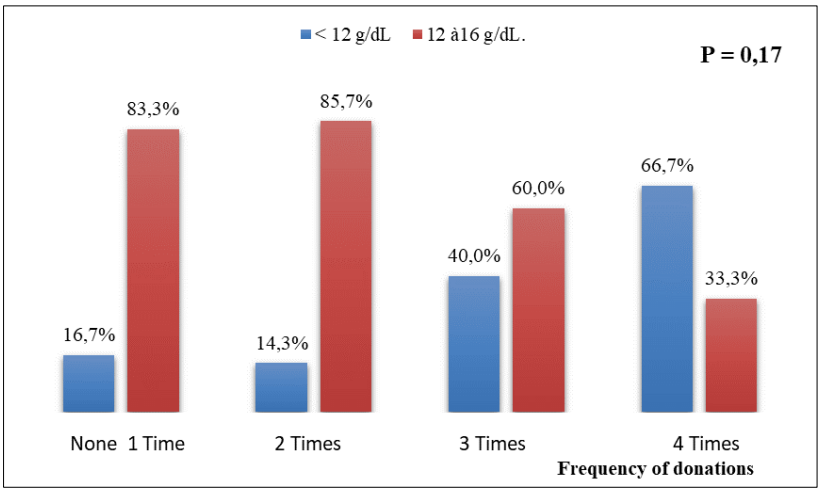

Figure 8 Distribution of hemoglobin levels in women according to the frequency of donation

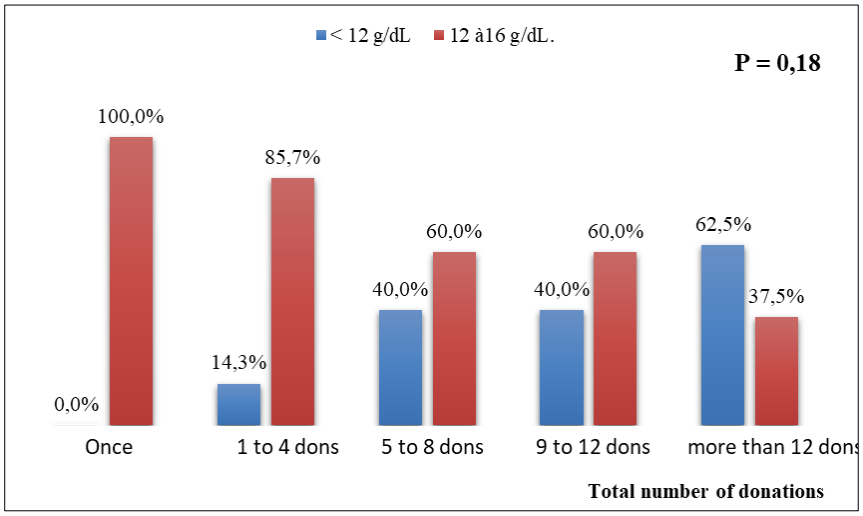

Figure 9 Distribution of hemoglobin levels among women according to the total number of donations.

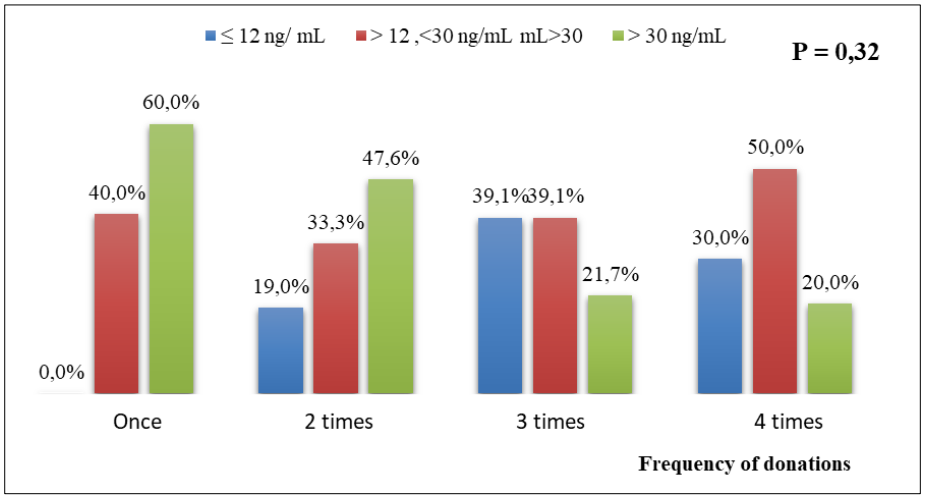

Figure 10 Distribution of serum ferritin levels in men according to the frequency of donation

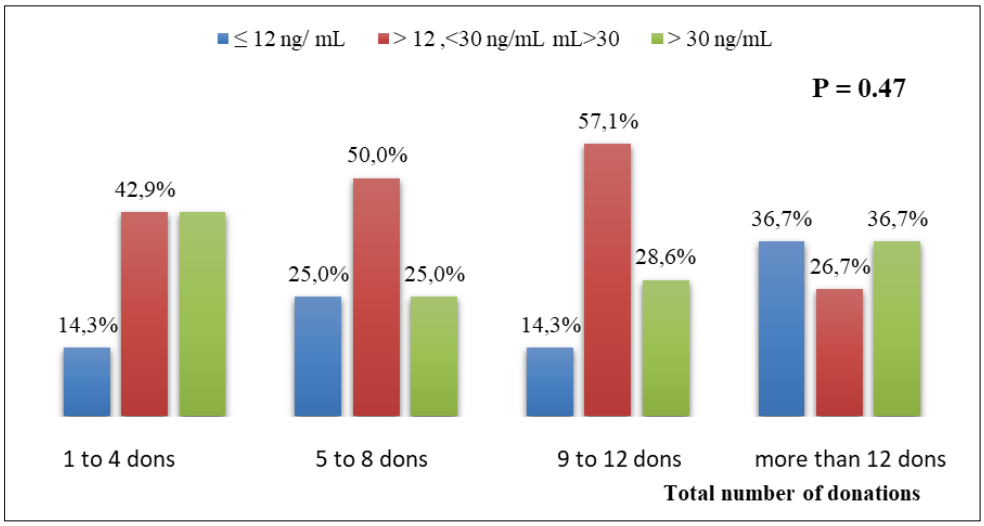

Figure 11 Distribution of serum ferritin levels in men according to total number of donations.

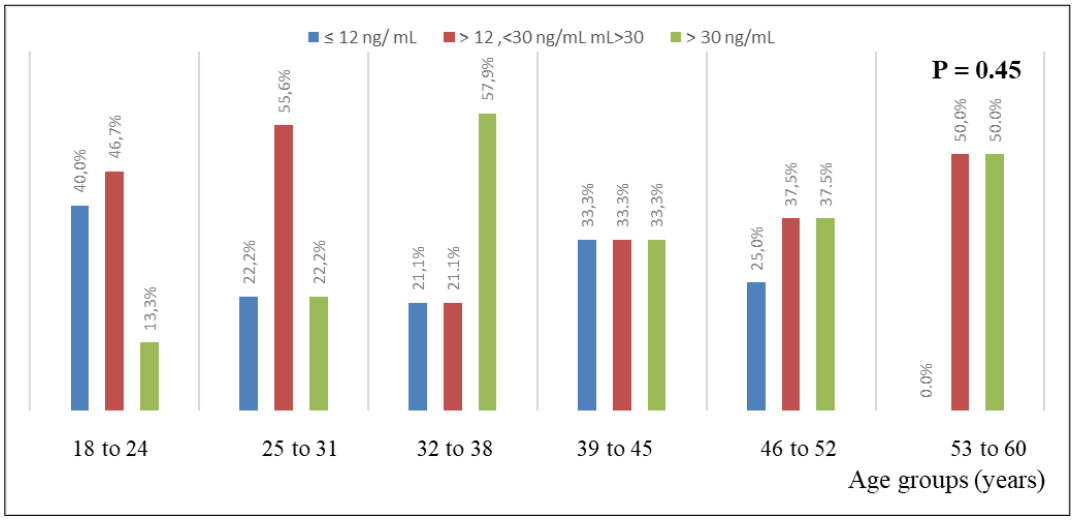

Figure 12 Distribution of men serum ferritin according to age groups

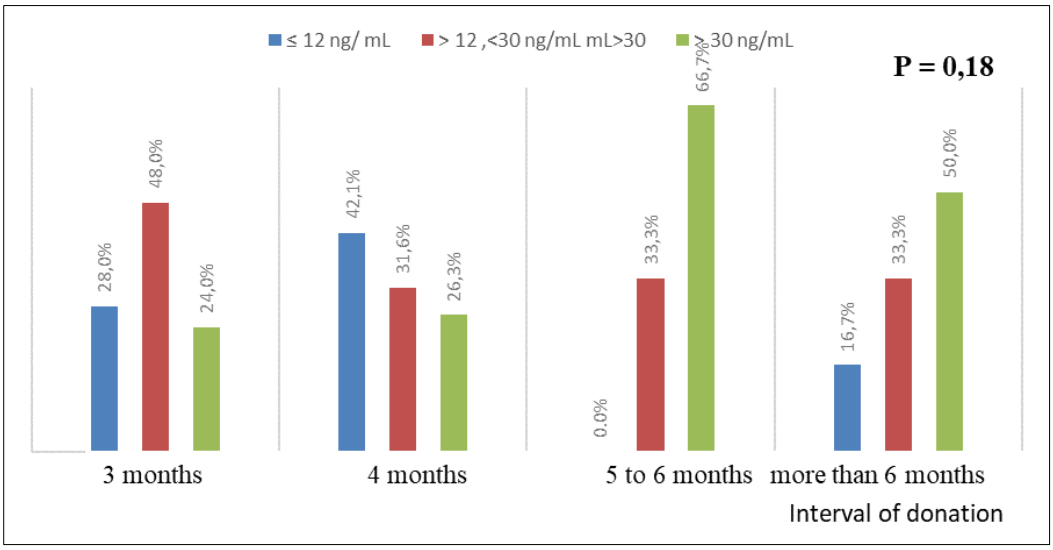

Figure 13 Distribution of serum ferritin levels men according to the donation interval.

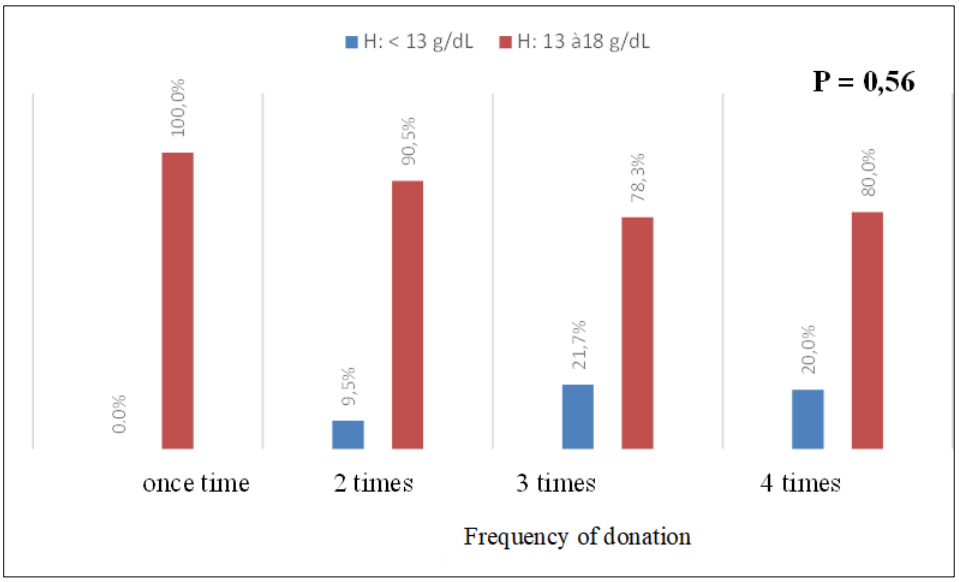

Figure 14 Distribution of hemoglobin levels in men according to frequency of donation.

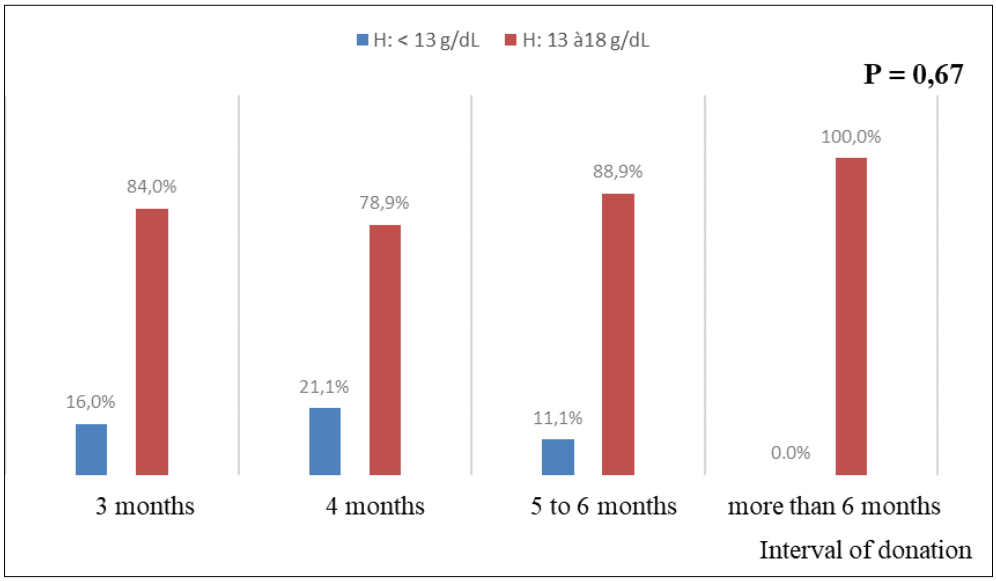

Figure 15 Distribution of hemoglobin levels in men according to donation interval

4. Discussion

Our study represents an overview of a deficiency problem posed by blood donation in our country among BD. These results could be used by transfusion canters to improve strategies for BD recruitment.

Our population shows a clear predominance of men over the BD population with an M/F ratio = 2.13. However, certain countries, especially France, has managed to establish a balance between the two gender (7). The predominance of men is since they show more mobility and a stronger motivation to donate. Also, there are restrictions to women giving blood, due to many circumstances as: breastfeeding, pregnancy, menstruation. Moreover, the average age of donation is 34.4 years in a population of BDs mainly aged under 38, unlike senior donors who show up less and less.

The frequency of the donation of the last year, coupled with the interval between the last two donations confirms that a good part of the population of the BD present a certain regularity of the donation, without exceeding the recommendations specified in the rules of Algerian Good Practices of Transfusion.

In our study, 22% of the subjects had anaemia whose origin was mainly iron deficiency, which is comparable to the Mondial prevalence of anaemia (8). In addition, it appears that the prevalence of iron deficiency (35.2%) is about twice as high as that of iron deficiency anaemia (17.4%). This situation is due to the delayed decrease in Hb related to the depletion of iron stores. These results extrapolate to the study population those of Boyeldieu and al (France), who limited themselves to proving this in the female gender only (9). With losses greater than the fractions absorbed, iron deficiency sets in gradually, beginning with the gradual reduction of stored iron, followed by the development of iron-deficient erythropoiesis, and culminating in iron deficiency anaemia. For this reason, the Hb level is a poor indicator of the decrease in iron stores and iron-deficient erythropoiesis because anaemia appears as the last step in this sequence. The prevalences differ from one study to another, they are sometimes higher than ours and sometimes lower: - The prevalences reported in our study are higher than that of the study by Jerimeah and al (Nigeria) (10). The prevalences of iron deficiency, anaemia and iron deficiency anaemia are respectively 20.6%, 13.7% and 12%. - The prevalence reported in our study is lower than that of the study by Nzengu-Lukusa and al (DRC) (11). The latter revealed an iron deficiency in 63.2% of BD, 36.5% of anaemia and 25.9% in whom the anaemia was iron deficient. The divergence of the results is explained by methodological differences including the type and inclusion criteria of the BD considered, the size of the samples which was larger than that of ours as well as the threshold values adopted for the rate of 'Hb and that of serum FRT. The comparison between the two genders shows that the prevalence of iron deficiency is significantly higher in women than in men (about twice as much), as is the case for anaemia. This is in line with the results of the RISE study (USA) which show that 2/3 of women and half of men suffered from an iron deficiency (5). Similarly, Lee and al (Hong Kong) found in regular donors deferred due to low Hb levels, a prevalence of iron deficiency of 35.1% for men versus 65.3% in women (12). It is quite logical that this is due to the physiological difference, firstly because the iron needs in women are higher (1.5 mg against 1 mg in men) due to excessive blood loss and increased needs (menstruation, pregnancy, etc.) (5). Also, as total body iron content in males average is around 50 mg/kg (~3500 mg) while in females who have lower Hb levels and less blood volume in proportion to weight, the average is about 35 mg / kg (~ 2100 mg) knowing that 70% to 80% of body iron exists in the RBCs in the form of Hb(13). Cook and al (Jamaica) (14), estimated mean tissue iron stores of only 776 ± 313 mg in men and 309 ± 346 mg in women. So, it is not surprising that the loss of approximately 250 mg of iron with each whole blood donation with limited absorption capacity leads to a high incidence of iron deficiency especially in regular donors (13). In women, a significant and inverse correlation exists between the frequency of donation, the total number of donations on one hand and serum FRT on the other hand. This is manifested by an increase in iron deficiency with the increase in these two donation characteristics. On the other hand, a significant relationship was found between iron deficiency and the donation interval since the restoration of losses takes much longer when the intervals are shortened. Depending on age, premenopausal women (<45 years) are more exposed to iron deficiency, which is supported by a significant and direct correlation between Hb and age. Multiple studies agree with ours: - Lee and al found a significant and inverse relationship between the level of FRT and the frequency in both sexes. The proportion of iron-deficient donors which increases with the frequency of donation, rising from 5.8% in women who have made at most one donation in the previous 12 months to 29.5% in donors who have made two blood donations total or more during the same period (12). - Boulahriss (Morocco) also found that the serum FRT concentration was significantly lower in blood donors at the rate of 3 to 4 times a year with at least ten cumulative donations, compared to the same parameters in first-time blood donors (15). The frequencies were 62% and 14% respectively. Added to this is the study by H. Javadzadehb (Iran) study which shows that 77.8% of women in the group of regular donors are iron deficient, whereas only 12.5% are in the group of recent donors (16); the regularity here is defined as the average of 2 to 3 donations per year, which is in perfect agreement with our results. In addition, this study shows a significant decrease in serum FRT concentration of 38.1 ng/mL in women during their first donation against 13.4 ng/mL in women with a total number of donations between 5 and 10. - In Australia, Hannah and al (Australia) confirmed the presence of iron deficiency in new donors in the order of 12% among women. This deficiency was 26.4% among women with a history of at least one donation during the previous 24 months. In this population of female BDs, deficiency increased with increasing frequency of donation and decreased with age (17). - Partially like our study, Rosvik (Norway) (18) found a significant interaction in women between the number of donations and the time elapsed since the previous donation on serum FRT and on Hb. Age was positively related to serum FRT, but not to Hb. The decrease in serum FRT and Hb with the number of annual donations was less significant for longer intervals. - Likewise, Milman (Denmark), in a study of 1359 women (19), found that blood donation had a profound influence on iron status, particularly in pre-menopausal donor women. In the latter, iron deficiency was 31.7% against 15.2% of non-donors and in 7% of post-menopausal donors against 2.9% of non-donors. Our study is in agreement with that of H.javadzadeh (Iran) 2003 where iron deficiency was present in 5% of post-menopausal women donors, which was significantly lower than in women donors of childbearing age where iron deficiency was 43% (16). Even if the Hb level was independent of the other characteristics of the donation in women, it is important to note that the prevalence of anaemia increases

with the increase in the number of cumulative donations and the annual frequency. - The results of the Goldman study (Canada) show an increase in the prevalence of anaemia between new donors and those with more than two donations. In women it goes from 3.8% to 10.2% (20). - Similarly, Boulahriss showed a significant and inverse relationship between Hb concentrations and the number of donations (15). In male BD, serum FRT concentrations are inversely related to the frequency of donation, as well as prevalences of iron deficiency that are more expressed beyond the 12 cumulative donations. Simultaneously, a significant and negative correlation exists between the level of Hb and the total number of cumulative donations. Many studies have been carried out to assess the impact of the frequency of blood donation during the year preceding inclusion on serum FRT and Hb levels, the results found diverge from one study to another: - The surveys by AM Moghadamet Coll (3) and Yousefi Nejad et al (Iran) (21), carried out on male subjects in Iran are in partial agreement with our results. Serum FRT and Hb levels were significantly and inversely correlated with annual donation frequency. - The results of the studies by SM Abdullah (Saudi Arabia) (23) and Milman N (Denmark) (24) carried out on male BD, came to support ours by effectively showing that serum ferritin decreased significantly following repeated blood donations. - In parallel with our results, the studies of CT Terada and al (Brazil) (25), Milman and al (Denmark) (20), Rosvik (18), observed no correlation between the levels of Hb and the frequency of donation in male BDs. The frequency of donations per year was more predictive for the decrease in iron stores. The partial difference between the present study and other research can be explained by differences in baseline Hb values, sensitivity and specificity of laboratory measurements, minimum donation interval, age ranges, dietary habits, and ethnic types of survey participants as well as recruitment criteria. Iron deficiency was related to the frequency of donations. Ferritinemia is linked to iron requirements, which in humans represent 2. 8 mg per day for 3 donations per year and 3.5 mg for 4 donations per year. These needs cannot be satisfied by the average daily iron absorption. However, the prevalence of anaemia was significantly related to the total number of donations. The latter, not being time-bound, can allow the body to restore iron reserves simultaneously with compensation processes that will maintain Hb levels above normal. It is interesting to note that donors belonging to the age group of 18 to 24 years in our study were more exposed to iron deficiency and anaemia compared to those belonging to other age groups. Similarly, in the survey by Mittal et al (India) (27), among individuals who had donated blood once in the previous year, younger male donors (under 30) had lower serum FRT concentrations than those over 50.

This is because serum FRT in males is relatively stable from late childhood until adolescence. When the push of growth in adolescence ceases, a gradual increase in serum FRT is observed starting the age of about 16 until 35, when FRT levels stabilize. The serum FRT level in healthy men remains relatively constant in old age (24).

5. Conclusion

Iron deficiency has a high prevalence in BDs. In this study, half of female donors and a third of male donors present iron deficiency. The close link with the characteristics of the donation means that the deficit increases when donations are cumulative and close.

Several working groups have shown that iron deficiency apart from anaemia is a real problem of public health. Iron deficiency without anaemia and the anaemia secondary to donation escape the current practice of collecting whole blood. Their potential effect on the well-being and physical or cognitive performance is not clearly announced at the time of donation in the face of a permanent challenge of blood supplying, it is not simple to tackle the problem and achieve consensus.

In several countries, the ability to donate is determined by the isolated dosage of the Hb before the donation. From the cumulative evidence, it is obvious that this parameter is insufficient to detect BD presenting an iron deficiency, it ensures that the individuals at risk can only be tracked by the estimation of serum FRT rates, which imposes on hemovigilance donors' systems to orient from the protection against iron deficiency anaemia towards protection against iron deficiency, which is precocious, radical, and effective. Such guidance will certainly contribute to a remarkable reduction in the number of postponements of donation because of anaemia.

In Algeria in the context of whole blood donation, the selection of BDs is based on a simple clinical examination, without recurring to an evaluation of Hb and iron reserves (predonation biological test). In the absence of a hemovigilance donors' system, the current practice of blood collection does not protect the engaged BDs against iron deficiency anaemia and iron deficiency which could affect the satisfaction of blood needs on the long run.

Faced with the national challenge aimed at retaining BDs, and following the results of our study, it is recommended to set up a system of biological monitoring of BDs by a predonation assessment including:

- First, the systemic execution of a dosage of Hb as a detection test for blood donation eligibility, to protect the BDs against anaemia.
- The dosage of serum FRT to evaluate iron reserves to precociously protect the BDs against iron deficiency. It is preferable to carry out the assessment of this parameter first in high-risk groups, in particular:
  - For all women of childbearing age wishing to donate blood for the first time.
  - In regular donors: females at least one test per year, males due to a frequency of 3 to 4 donations per year, at least one test per year.

The regular BDs with exhausted iron stocks (<12 ng/dL) or decreased (< 30 ng/dL) can either:

- Benefit from an oral iron supplementation (substitute or preventive). In this context, the role of iron treatment in this population deserves further study.
- Modify their donation rate (prolongation of donation intervals) while adopting a diet rich of iron.

The BD comes to the collection canters manifesting a generous act and an altruistic spirit and believing it has no sneaky effect on his health. Thus, the offer of a clinical and biological monitoring could only be perceived as an appreciation of his act and an expression of gratitude.

Compliance with ethical standards

Disclosure of conflict of interest

The authors and all co-authors declare that they have no conflicts of interest in relation to this document.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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