National Journal of Biological Sciences
Received: 10th July, 2023
Revised: 13th September, 2023
Accepted: 8st November, 2023
Published: 21st December, 2023

DOI: https://doi.org/10.37605/v4i2/1

RESEARCH PAPER

TITLE

Distinguishing Iron Deficiency Anemia from Anemia of Chronic Disease Using Hematological Measures

Authors: Wahid Ullah[1], Marium Khan[2], Abdul Sattar[3], Khazina Ikram[4], Fawad Mahmood[5], Asim Arshad[6], Aizaz Ali Shah[7], Shah Faisal[8], Kaleem Ahmed[9]

AFFILIATIONS

[1]Lecturer, Faculty of Rehabilitation and Allied Health Sciences (FRAHS), Riphah International University, Islamabad, Pakistan.
[2]Charge Nurse, Pervaiz Elahi Institute of Cardiology, Bahawalpur, Punjab, Pakistan
[3]BS MLT, Faculty of Rehabilitation and Allied Health Sciences, Riphah International University, Islamabad, Pakistan
[4]BS MLT, Faculty of Rehabilitation and Allied Health Sciences, Riphah International University, Islamabad, Pakistan
[5]Lecturer, Faculty of Rehabilitation and Allied Health Sciences (FRAHS), Riphah International University, Islamabad, Pakistan
[6]BS MLT, Faculty of Rehabilitation and Allied Health Sciences, Riphah International University, Islamabad, Pakistan
[7]BS MLT, Faculty of Rehabilitation and Allied Health Sciences, Riphah International University, Islamabad, Pakistan
[8]BS MLT, Faculty of Rehabilitation and Allied Health Sciences, Riphah International University, Islamabad, Pakistan
[9]Lecturer, Faculty of Rehabilitation and Allied Health Sciences (FRAHS), Riphah International University, Islamabad, Pakistan.

Corresponding Author*
Kaleem Ahmed,
Lecturer, Faculty of Rehabilitation and Allied Health Sciences (FRAHS), Riphah International University, Islamabad, Pakistan.
Email: kaleem.ahmad@riphah.edu.pk

Distinguishing Iron Deficiency Anemia from Anemia of Chronic Disease Using Hematological Measures

ABSTRACT

Anemia is a serious public health concern in today's world which is particularly affecting young children, pregnant women, menstruating adolescent girls and women. The two most common causes of anemia are iron deficiency anemia (IDA) and anemia of chronic disease (ACD), often known as anemia of inflammation. This study aim was to assess the levels of certain hematological parameters, including Hemoglobin Estimation, Mean Corpuscular Volume (MCV), Serum Ferritin, Serum TIBC, Erythrocyte Sedimentation Rate and C - reactive protein to clearly differentiate between iron deficiency anemia and anemia of chronic disease. The study was conducted in Department of Medical Lab Technology, Riphah International University, Islamabad from September 01, 2023 to January 01, 2024. A total of 109 samples with 59 of iron deficiency anemia patients and 50 patients of Anemia of chronic disease were assessed for differentiation be these two diseases. The significant level was selected with p-value less than 0.05. Hemoglobin estimation, TIBC, and ESR were significant in our investigation as their p-values were less than 0.05. Hence, it concluded that Hemoglobin estimation, total Iron Binding Capacity and Erythrocyte Sedimentation Rate were Hematological parameters that distinguished between Iron Deficiency Anemia and Anemia of Chronic Disease.

Key Words: Anemia, Iron deficiency Anemia (IDA), Anemia of chronic disease (ACD), Hemoglobin, TIBC

1. INTRODUCTION

Anemia is a widespread disorder that affects people in both developed and developing countries. If the reference range specified for age, gender, race, and height is exceeded on the lower end, it indicates that an individual may have anemia. The standards set by the World Health Organization (WHO) committee of experts approximately 50 years ago are widely accepted as guidelines for adults to determine these limits. Men should not fall below 130mg/L while women's limit stands at 120 mg/L despite their age or racial background (Krawiec and Pac-Kożuchowska, 2020). Less than 13 g/dL for males and 12 g/dL for women were both considered anemia according to survey of the National Health and Nutrition foundation (NHANES III) definitions (Jahangiri et al., 2020). The majority of cases of anemia seem to be caused by a lack of production and iron deficiency anemia (IDA), anemia of chronic infection (ACI), or nutritional deficiencies being the main causes (Santhakumar et al., 2023).

According to the WHO, Iron deficiency anemia is the most prevalent dietary deficiencies affecting people worldwide (MH et al., 2021), and it is a major factor towards the development of anemia (Hoenemann et al., 2021). Iron deficiency anemia is classified as microcytic or hypochromic anemia but it is usually normocytic normochromic anemia in the initial stages of iron deficiency and it has the most adverse effect on lowering levels of iron (Hoffmann and Urrechaga, 2020). When iron balance in body disturbed it results in lower iron stores which causes iron deficiency. Before a diagnosis of the IDA is confirmed, there are gradual decreases in iron levels and as a result the anemia that develop is a symptom of IDA; it progresses with age as iron reserves gradually decrease. Iron deficiency is a process that can be traced to poor iron balance, iron degradation, iron-deficient erythropoiesis, and finally IDA, which involve various stages. Iron deficiency can be severe to moderate, and it can be caused by both depleted iron stores and iron deficiency without anemia. Iron deficiency with anemia has a high incidence of changes in hematological laboratory results, which is the most severe form of iron deficiency signs and symptoms that can be felt (Choi et al., 2023). This causes decreased erythropoiesis in the bone marrow, which results in low hemoglobin levels and the onset of Iron deficiency anemia (Rashwan et al., 2022). The standard test for iron deficiency is hemoglobin, but serum ferritin content is used to assess iron reserves. The lifespan of red blood cells is only 120 days, so iron deficiency takes enough time to have an effect. As a result, relying solely on hemoglobin for screening results in the delay in identifying IDA (Lee, 2020). Each of the assays (S. ferritin, S. iron, TIBC, Hb, and MCV) must be properly interpreted during the laboratory diagnosis if instructed to evaluate a patient for potential IDA. The data production is based on the equipment used in the clinical laboratory. Some tests might not be easily accessible, but others provide crucial information that must be evaluated for the clinical scenarios in which they are used (Farrag et al., 2021).

The hypo proliferative anemia known as anemia of chronic disease (ACD) is a reaction to systemic sickness or inflammation. The term Anemia of Chronic disease was discovered in 1930 and later on in 1950s Cartwright and Wintrobe further explained about this disease (Agarwal et al., 2021).

ACD is the second most common microcytic hypochromic anemia after iron deficiency anemia. Unfortunately, Anemia of chronic disease is not properly diagnosed, poorly understood, and improperly treated in clinical practice. There are still large knowledge gaps about the real occurrence or effects of ACD (Asare et al., 2023). Numerous disorders have been discovered to have an association with ACD. Iron deficiency anemia is also one of them and other disorders are infections (including human immunodeficiency virus infection, tuberculosis, bacterial, parasitic, fungal, and viral infections), malignancies, autoimmune disorders, chronic renal diseases, and inflammations (Hu et al., 2023). Hepcidin levels also increase as the immune system becomes more active and produces more inflammatory cytokines. Other variables that contribute to anemia include inadequate erythropoietin levels and hyperresponsiveness to erythropoietin, or poor red blood cell survival. Hepcidin, a key control of iron metabolism, is crucial for identifying pathophysiology of ACD. Ferroprotein, an iron export protein, is present in hepatocytes, enterocytes, and macrophages, where it is bound by hepcidin and broken down. The resulting iron absorption within macrophages and hepatocytes results in functional iron deficiency (Dinh et al., 2020).

Our study mainly focuses on investigating certain hematologic biomarkers that can accurately differentiate between IDA and ACD. We also aim to examine how inflammatory indicators, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), might distinguish ACD from IDA. Investigating the effectiveness of several iron-related markers, such as serum ferritin and total iron-binding capacity, in differentiating between IDA and ACD is also includes in our objective.

2. MATERIAL AND METHODS

A cross-sectional study was conducted in Department of medical lab technology, Riphah International University, Islamabad. Samples for both disorders were collected for distinguishing iron deficiency anemia from anemia of chronic disease using hematological measures at different hospitals in region of Rawalpindi and Islamabad. This study took place between the period of September 01, 2023 to January 01, 2024.

Patients with disorders of iron deficiency anemia and anemia of chronic disease were included in our investigation. Patients with disorders other than those two diseases or those with disorders whom symptoms were collapsing with both these two diseases were excluded from study.

Ethical approval of research was taken from Research Ethical Committee (REC) of FRAHS, Riphah International University, Islamabad. A proper performa was designed to collect the demographic data of patients included in the study and to take their informed consent. We considered 59 patients with confirmed diagnosis of iron deficiency anemia and 50 patients with 100% assurance that they had anemia of chronic disease. We didn't put age limit in our study because these two diseases have no connection with age. The confirmation of both iron deficiency anemia and anemia of chronic disease was assured by performing these laboratory tests such as Hemoglobin estimation, Mean Corpuscular Volume, Serum Ferritin levels, Total Iron Binding Capacity, C-Reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR).

Statistical analysis was done using SPSS (version 20.0) and we employed independent t-test and Mann Whitney U-test. We selected 95% Confidence Interval with 5% margin of error for these tests. We set p-value at 0.05 as reference value. Independent t-test and Mann Whitney U-test for these measures with p-value less than 0.05 were considered significant, whereas these tests with p-value more than 0.05 was not considered significant. Bar Charts were created using Microsoft Excel and Microsoft Words.

3. RESULTS

In our research, total 109 patients including 59 patients of Iron deficiency anemia and 50 patients of Anemia of chronic disease participated. The average hemoglobin percentage for IDA patients was 6.5%, with a 1.2% standard deviation shown in table 4.1. The values of Hb% ranged from 3.2% to 7.9%. Red blood cells' mean corpuscular volume was their average size. With a standard deviation of 8.0 fl, the mean MCV for IDA patients was 65.0 fl. The MCV values were found to vary from 50.9 fl to 75.5 fl. Protein called ferritin is used to store iron. In our investigation, the ferritin level for IDA patients was 25.0 mcg/dL on average, with a standard deviation of 15.0 mcg/dL. Ferritin levels ranged from 5.9 mcg/dL to 50.1 mcg/dL (Table 3.1).

TABLE 1: Descriptive Statistics For Iron Deficiency Anemia Patients

Measure	Mean	Standard Deviation	Median	Range
Hb%	6.5	1.2	6.7	3.2 - 7.9
MCV	65.0	8.0	63.1	50.9 - 75.5
Ferritin	25.0	15.0	11.8	5.9 - 50.1
TIBC	525	60	505	409 – 675
CRP	15.0	10.0	11.9	2.9 - 36.7
ESR	25	15	23	6 – 56

The amount of iron that transferrin, a protein that carries iron throughout the bloodstream, can bind to is known as its total iron-binding capacity. With a standard deviation of 60 mcg/dL, the mean TIBC for IDA patients was 525 mcg/dL. TIBC levels ranged from 409 mcg/dL to 675 mcg/dL. An indicator of inflammation is C-reactive protein. IDA patients had a mean CRP of 15.0 mg/L and a standard deviation of 10.0 mg/L. The CRP readings ranged from around 2.9 mg/L to 36.7 mg/L. Red blood cell settling time in a tube is gauged by the erythrocyte sedimentation rate. In our investigation, the average ESR for IDA patients was 25 mm/hr, with a standard variation of 15 mm/hr. The ESR values were found to range from 6 mm/hr to 56 mm/hr (Table 3.2).

Table 2: Shows The Descriptive Statistics For Each Parameters Used To Differentiate IDA And ACD

Measure	Mean	Standard Deviation	Median	Range
Hb%	6.0	1.5	6.4	3.4 - 8.9
MCV	65.0	6.0	64.1	46.9 - 73.1
Ferritin	350	120	378	305 – 590
TIBC	180	40	160	95 – 245
CRP	20.0	15.0	10.0	5.0 – 58
ESR	75	30	68	25 – 135

In patients with IDA, the mean Hb% level was 6.0 g/dL: in patients with ACD, it was 6.4 g/dL. This indicates that compared to IDA patients, ACD patients had a somewhat higher hemoglobin level. Additionally, individuals with ACD had a somewhat larger range of Hb% values (3.4-8.9 g/dL) than patients with IDA (3.2-7.9 g/dL). Patients with IDA had an average MCV level of 65.0 fl, whereas those with ACD had an average MCV level of 65.0 fl. This indicates that patients with IDA and ACD had extremely similar MCV levels. Additionally, there was a near identical range of MCV levels across IDA patients (50.9 - 75.5 fl) and ACD patients (46.9-73.1 fl) IDA patients had an average ferritin level of 25.0 mg/dL, whereas ACD patients had an average ferritin level of 350 mg/dL. This indicates that compared to IDA patients, ferritin levels in the blood of ACD patients are, on average, five times higher. Additionally, patients with ACD have a far larger range of ferritin levels (305-590 mg/dL) than do patients with IDA (5.9-50.1 mg/dL).

Patients with IDA had an average TIBC level of 525 µg/mL, whereas those with ACD had an average TIBC level of 180 µg/mL. This indicates that TIBC levels in the blood of ACD patients were, on average, twelve times higher than those of IDA patients. In addition, patients with ACD had a far larger range of TIBC values (95-245 µg/mL) than patients with IDA (409-675 µg/mL). IDA patients had a mean CRP level of 15.0 mg/L, but ACD patients had a mean CRP level of 20.0 mg/L. This implies that compared to IDA patients, ACD patients might have higher levels of inflammation. For patients suffering from ACD, the CRP range was found to be between 5.0-58 mg/L whereas for those facing IDA it stood at 2.9-36.7 mg/dl. The ESR levels were different too with an average of 25 mm/hr in case of IDA and a enormous 75 mm/hr among ACD patients thus indicating higher inflammation amongst them as compared to their counterparts with IDA diagnosis. Additionally, the study observed that while ESR level ranged within (25-135 mm/hr) for patients affected by ACD, its variation assessed over (6-56mmHr) in cases related to IDA typically implying distinctive symptomatology associated with one or both these particular health conditions indeed.

Table 3: Group Comparison Of Iron Deficiency Anemia From Anemia Of Chronic Disease Using Different Statistical Test

Measure	Statistical Test	p-value	Significant Difference
Hb%	Independen t t-test	0.02	Yes
MCV	Mann-Whitney U Test	0.10	No
Ferritin	Independen t t-test	0.07	No
TIBC	Mann-Whitney U Test	0.001	Yes
CRP	Independen t t-test	0.15	No
ESR	Mann-Whitney U Test	0.005	Yes

An independent t-test showed a significant difference in hemoglobin level (Hb%) between the two groups, indicated by a p-value which was 0.02. This suggested that it was unlikely The Hb% values differed randomly for both groups. The p-value for the Mann-Whitney U test is 0.1 indicates that there was no significant difference in MCV (mean corpuscular volume) values between the two groups. Based on the independent t-test, the p-value is 0.07 indicates that there showed no statistically significant differences in ferritin levels between the two groups.

The Mann-Whitney U test p-value of 0.001 suggests that there is a significant difference in TIBC (total iron binding capacity) values between the two groups. An independent t-test showed no significant differences in CRP (c-reactive protein) levels between the two groups, as evidenced by a p-value of 0.15. The p-value of 0.005 for the Mann-Whitney U test indicates that there was a significant difference in the ESR (erythrocyte sedimentation rate) levels between the two groups.

TABLE 4: Summary Of The Analysis To Differentiate Between Ida And Acd

Measure	Finding
Hb%	Significant difference (p=0.02) observed between IDA and ACD patients.
MCV	No significant difference (p=0.10) between IDA and ACD patients.
Ferritin	No significant difference (p=0.07) between IDA and ACD patients.
TIBC	Significant difference (p=0.001) observed between IDA and ACD patients.
CRP	No significant difference (p=0.15) between IDA and ACD patients.
ESR	Significant difference (p=0.005) observed between IDA and ACD patients.
Correlation	Different correlation patterns observed within each group for various measures.
Logistic Regression	A logistic regression model was built to predict anemia type based on hematological measures.

Table 4.4 presents key findings from analysis conducted to differentiate between IDA (Iron Deficiency Anemia) and ACD (Anemia of Chronic Disease). It compares the two types of anemia across several measures, including Hemoglobin percentage, MCV, Ferritin, TIBC, CRP, and ESR. It highlights significant differences found between IDA and ACD patients for Hb%, Ferritin, TIBC, CRP, and ESR. It notes different correlation patterns observed within each group for various measures. It mentions the development of a logistic regression model to predict anemia type based on hematological measures.

4. DISCUSSION

The main goal of our study, in which we used hematological measurements to distinguish between Iron Deficiency Anemia and Anemia of Chronic Disease, was to enhance patient care by giving doctors more precise diagnostic tools, which would maximize treatment regimens and resource use. The study influences guidelines and advances science in the sector, with wider consequences for healthcare practices.

There are various ways in which iron-restricted erythropoiesis causes anemia. Depleted iron stores in pure iron deficiency result from an imbalance between iron intake and utilization. Initially, anemia might not be evident due to iron recycling from erythrocyte turnover(Kassebaum et al., 2014). Our study was totally based on hospitalized patients in which we included 109 patients of both Iron deficiency anemia and anemia of chronic disease. In the sample of 109 patients, 59 patients were of Iron deficiency anemia and 50 were of Anemia of chronic disease. The study conducted in Different hospitals of Rawalpindi and

Islamabad region. We took detailed information of patients we selected, we also performed some to confirm tests diagnosis.

Low amounts of hemoglobin, a vital component of red blood cells that carries oxygen throughout the body, are a hallmark of iron deficiency anemia. The standard definition of normal hemoglobin ranges from 13.2 to 16.6 grams (g) of hemoglobin per deciliter of blood. Hemoglobin levels in those suffering from iron deficiency anemia is usually below normal. In our study, the mean hemoglobin level for patients with IDA was 6.5 g/dl, with a standard deviation of 1.2 g/dl. In a significant outpatient facility in Damascus, Syria, the same study for IDA patients also included Syrian youngsters. The youngsters enrolled in this study had a mean hemoglobin level of 10.54 g/dL and a standard deviation of 1.95 g/dl (Yuldasheva, 2023). Comparably, our study's mean MCV for IDA patients was 65.0 fl with an 8.0 fl standard deviation, while the identical study conducted in Syria had a lower mean MCV of 75.29 g/dl with a 9.47 standard deviation.

Hemoglobin levels in anemia of chronic disease (ACD) are frequently below normal. The ACD patient's hemoglobin level was 6.0 g/dl on average, with a 1.5 g/dl standard deviation. The Hemoglobin mean result for the same tests conducted in 2012 at the District Headquarter Hospital in Rawalpindi was 8.0g/dl.

MCV might not be impacted by ACD as much as it is by other forms of anemia. While MCV levels are typically lower than normal in people with iron deficiency anemia. This is suggestive of smaller-than-normal red blood cells called microcytic red blood cells. The MCV mean for ACD patients in our research was 65.0 with a standard deviation of 8.0, which was comparable to the MCV mean of 65.0 with a standard deviation of 6.0 for IDA patients. The same study carried out in Dallas, Texas's Parkland Memorial Hospital, in which IDA patients had a mean MCV level of 72.6 and a standard deviation of 9.8. In the same hospital, the average MCV level for patients with ACD was 87.5 g/l, with a standard deviation of 7.87 fl (Xiao et al., 2021).

When there is a shortage of iron, the body makes up for it by increasing TIBC, which improves its ability to bind and transport more iron. An effective marker for iron deficiency anemia diagnosis is elevated TIBC. In our study, the average level of TIBC for IDA patients was 525mg/dl and had a standard deviation of 60.0. Meanwhile, ACD patients in the same study had an average TIBC level of 180mg/dl with a standard variation of 40fl. At Parkland Memorial Hospital in Dallas, Texas where another similar research took place, the mean TIBC levels attained were 153mg/dL with a SD (standard deviation) of 79f/L for all participants while specifically it was found that ACD patient's possessed an average TIBC level varying at 167mg supplemented by a SD measuring approximately 93 fl (Perry, 2021).

As these hematological measurements are helpful, it is important to this a complete clinical follow up that include both underlying disorders, the patient medical history and physical examination is mandatory to clearly differentiate IDA and ACD. When these hematological measures are resulted together, diagnostic accuracy is increased and effective treatment plans are guided. Further, Current research and development in diagnostic technologies may offer more awareness in improving the distinction between these two types of anemia. Physicians can specialize treatment approaches according to individual form of anemia with accurate and clear diagnosis. Iron supplementation is the main therapeutic for IDA and in ACD, controlling the ongoing condition is essential. Poor diagnosis can result in ineffective treatment. For example, giving iron supplements to patient with ACD can be dangerous or may not work. Accurate diagnostic standards help in avoiding needless and sometimes harmful treatments (Luxford et al., 2022).

5. CONCLUSION

By statistical analysis and findings, the ongoing study explained that distinguishing iron deficiency anemia from anemia of chronic disease is mainly based on three hematological parameters that are Hemoglobin Estimation, Total Iron Binding Capacity and Erythrocyte Sedimentation Rate. These parameters are easy to perform and economical to conduct. Therefore, these parameters can widely use in differentiating these two disorders (Iron Deficiency Anemia & Anemia of Chronic Disease).

REFERENCES

AGARWAL, C., GUPTA, S., PUJANI, M., CHAUHAN, V., SINGH, K., SINGH, M., KAUR, H. & BHATIA, S. 2021. New erythrocyte and reticulocyte parameters: Indicators for early diagnosis of iron deficiency anemia and anemia of chronic disease.

ASARE, J. W., APPIAHENE, P., DONKOH, E. T. & DIMAURO, G. 2023. Iron deficiency anemia detection using machine learning models: A comparative study of fingernails, palm and conjunctiva of the eye images. *Engineering Reports***,** e12667.

CHOI, R., CHUN, G., PARK, M.-J., LEE, S. G. & LEE, E. H. 2023. Prevalence of Iron Deficiency Anemia Indicated for Intravenous Iron Treatment in the Korean Population. *Nutrients,* 15**,** 614.

DINH, N. H., CHEANH BEAUPHA, S. M. & TRAN, L. T. A. 2020. The validity of reticulocyte hemoglobin content and percentage of hypochromic red blood cells for screening iron-deficiency anemia among patients with end-stage renal disease: a retrospective analysis. *BMC nephrology,* 21**,** 1-7.

FARRAG, K., ADEMAJ, K., LEVENTI, E., AKSAN, A. & STEIN, J. 2021. Diagnostic utility of low hemoglobin density to detect iron deficiency in patients with inflammatory bowel disease. *Annals of Gastroenterology,* 34**,** 521.

HOENEMANN, C., OSTENDORF, N., ZARBOCK, A., DOLL, D., HAGEMANN, O., ZIMMERMANN, M. & LUEDI, M. 2021. Reticulocyte and erythrocyte hemoglobin parameters for iron deficiency and anemia diagnostics in patient blood management. A narrative review. *Journal of clinical medicine,* 10**,** 4250.

HOFFMANN, J. J. & URRECHAGA, E. 2020. Verification of 20 mathematical formulas for discriminating between iron deficiency anemia and thalassemia trait in microcytic anemia. *Laboratory Medicine,* 51**,** 628-634.

HU, T.-Y., MAYASARI, N. R., CHENG, T.-M., BAI, C.-H., CHAO, J. C.-J., HUANG, Y.-L., WANG, F.-F., SKALNY, A. V., TINKOV, A. A. & CHANG, J.-S. 2023. Polymorphisms of haptoglobin modify the relationship between dietary iron and the risk of gestational iron-deficiency anemia. *European Journal of Nutrition,* 62**,** 299-309.

JAHANGIRI, M., RAHIM, F., SAKI MALEHI, A., PEZESHKI, S. M. S. & EBRAHIMI, M. 2020. Differential diagnosis of microcytic anemia, thalassemia or iron deficiency anemia: a diagnostic test accuracy meta-analysis. *Modern Medical Laboratory Journal,* 3**,** 16-29.

KASSEBAUM, N. J., JASRASARIA, R., NAGHAVI, M., WULF, S. K., JOHNS, N., LOZANO, R., REGAN, M., WEATHERALL, D., CHOU, D. P. & EISELE, T. P. 2014. A systematic analysis of global anemia burden from 1990 to 2010. *Blood, the Journal of the American Society of Hematology*, 123**,** 615-624.

KRAWIEC, P. & PAC-KOŻUCHOWSKA, E. 2020. Biomarkers and hematological indices in the diagnosis of iron deficiency in children with inflammatory bowel disease. *Nutrients,* 12**,** 1358.

LEE, N. H. 2020. Iron deficiency anemia. *Clinical Pediatric Hematology-Oncology,* 27**,** 101-112.

LUXFORD, J., ROBERTS, P. & IRVING, C. 2022. Iron Deficiency in Pediatric Dilated Cardiomyopathy is Associated with Clinical, Biochemical and Hematological Markers of Severe Disease and Adverse Outcomes. *The Journal of Heart and Lung Transplantation,* 41**,** S169.

MH, M. K., NIPANAL, A. V. & ML, A. 2021. Role Of Serum Soluble Transferrin Receptors (STFR) To Differentiate Iron Deficiency Anaemia And Anaemia Of Chronic Disease. *National Journal of Integrated Research in Medicine,* 12.

PERRY, M. 2021. Anaemia in primary care: iron deficiency and anaemia of chronic disease. *Practice Nursing,* 32**,** 358-362.

RASHWAN, N. I., AHMED, A. E.-A., HASSAN, M. H., MOHAMMED, M. E. & BAKRI, A. H. 2022. Hematological indices in differentiation between iron deficiency anemia and beta-thalassemia trait. *Int J Pediatr,* 10**,** 5285-95.

SANTHAKUMAR, S., ATHIYARATH, R., CHERIAN, A. G., ABRAHAM, V. J., GEORGE, B., LIPIŃSKI, P. & EDISON, E. S. 2023. Impact of maternal iron deficiency anemia on fetal iron status and placental iron transporters in human pregnancy. *Blood Cells, Molecules, and Diseases,* 99**,** 102727.

XIAO, H., WANG, Y., YE, Y., YANG, C., WU, X., WU, X., ZHANG, X., LI, T., XIAO, J. & ZHUANG, L. 2021. Differential diagnosis of thalassemia and iron deficiency anemia in pregnant women using new formulas from multidimensional analysis of red blood cells. *Annals of Translational Medicine,* 9.

YULDASHEVA, N. 2023. ANEMIA IN CHRONIC DISEASES IN THE EXAMPLE OF IRON DEFICIENCY. *Экономика и социум***,** 237-239.